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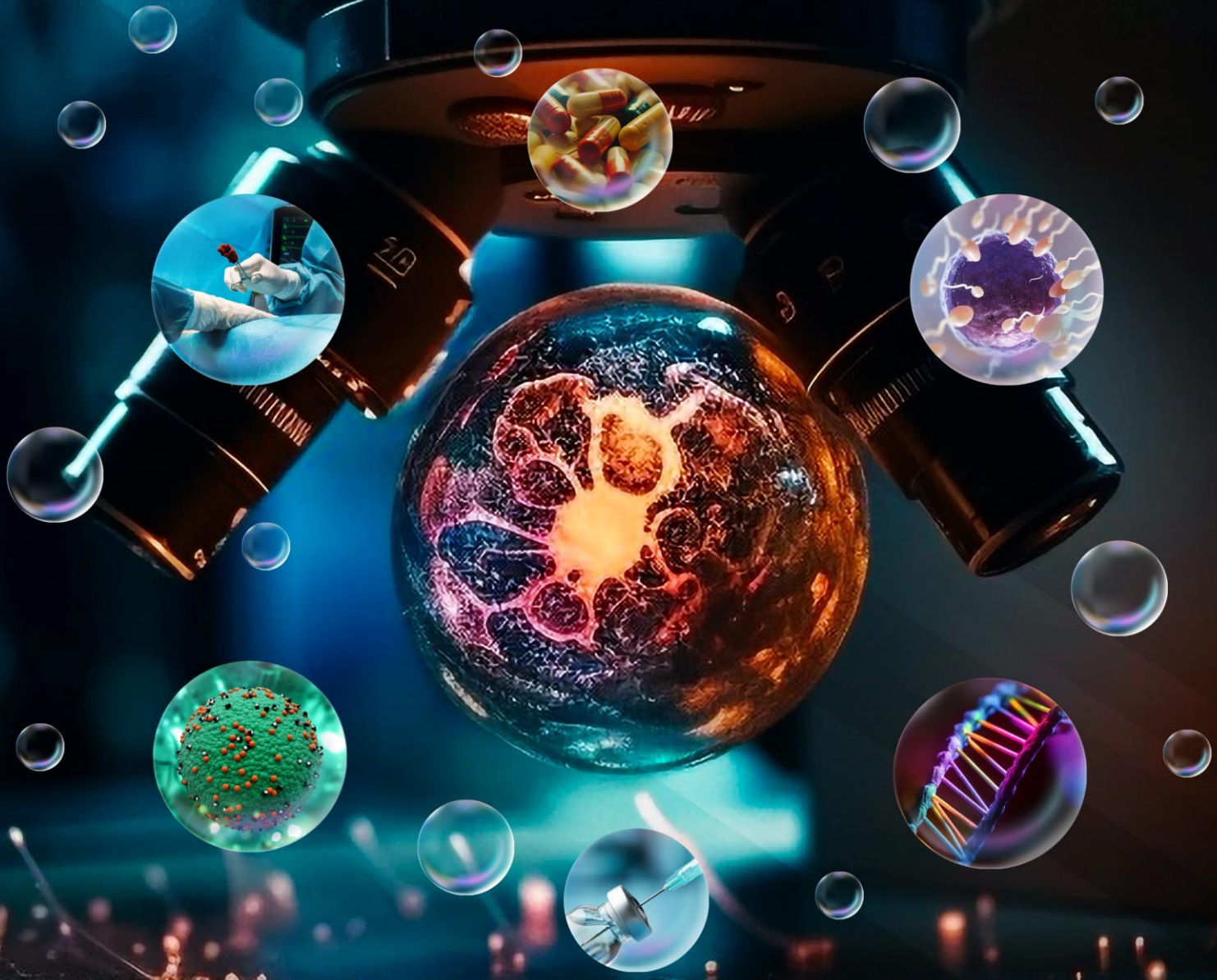

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NEWTECH STUDIO

۱. ۳D Bioprinting of Skin Tissue Engineering in Cosmetic and Reconstructive Surgery; Current Strategy, Challenges and Future perspective (Review)

bita dehghani,[۱] Mehdi Atari,[۲,*]

۱. Apadana Institute of Higher Education
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Introduction: Patients with diseases causing tissue and organ damage face physical and psychological challenges. Conventional surgical treatments often fall short in addressing these issues, especially in cases like deep burns that destroy hair follicles and impact appearance and mental health. Skincare products aim to enhance skin health, but there is a demand for natural ingredients and customization in the cosmetics industry. Reconstructive and plastic surgery treat a variety of disorders affecting different tissues, focusing on restoring physical integrity and functionality. Traditional biomaterials like silicones may not meet the precise needs of patients, and autologous tissue transplantation poses challenges like donor site damage. Tissue engineering and ۳D bioprinting are gaining attention for their ability to create customized implants and bionic skin substitutes that can address these limitations. With high resolution, flexibility, reproducibility, and efficiency, these technologies show promise in developing tissue-engineered skin to meet both industrial and clinical needs.

Methods: ۳D printing (۳DP) technologies have advanced to the point where highly detailed biomimetic scaffolds can be created, replicating the characteristics of native tissue more accurately than ever before. ۳D bioprinting allows for precise replication of native skin through computer-controlled placement of cells and scaffolds in controlled patterns, influencing macro, micro, and nanoarchitecture. This technique has applications in cosmetic and reconstructive surgery, offering authentic, scalable, and reproducible results compared to conventional methods. By strategically placing different cell types and structures, bioprinted skin reduces the complexity, risk, and recovery time associated with plastic surgery. Tissue engineering offers further possibilities for reconstruction, utilizing bioactive molecules and tissues to enhance beauty and reduce morbidity associated with implantable devices. Scaffold materials play a crucial role in tissue engineering, guiding cell differentiation and functionality. Synthetic and natural polymers have been utilized in bioengineered skin grafts, with potential for microneedles loaded with active ingredients. Various cell types, including fibroblast, keratinocytes, and stem cells, have been explored for creating artificial skin substitutes, with promising hydrogel systems offering new opportunities for tissue engineering and skin production.

Results: ۳D printing allows for customizing dressings to meet specific needs by providing spatial precision and flexibility to mimic natural tissues&#۳۹; characteristics. It offers advantages in customization, stability, design flexibility, and functional materials, with bio-ink options supporting skin regeneration. The scaffolds enable perfect cellular interactions and the development of new tissues through their large surface area and small pore sizes. Compared to traditional methods, ۳D bioprinting has advantages like timeliness and high repeatability when creating skin grafts matching

scar defects. A perfect skin scaffold should have mechanical, chemical, biological, and physical features like porosity, biodegradability, and elasticity. Artificial skin patches made through ٣D printing can help in scar management by dividing large scars into smaller segments. Researchers are exploring novel techniques, like reprogramming fibroblasts, to create pluripotent cells for tissue engineering. Combining these cells with ٣D printing may lead to functional tissue-engineered skin mimicking natural skin properties.

Conclusion: ٣D bioprinting technology offers a solution to surgical complications and adverse reactions associated with traditional procedures, providing customized products tailored to individual needs. It is used for tissue regeneration, scaffolds, and skin delivery platforms in tissue engineering applications. Benefits include reduced donor site morbidity and the creation of in vitro tumor models like malignant melanoma. Despite advancements, challenges remain in replicating complex skin structures. Seeded cells play a crucial role in skin repair and engineering, with the goal of restoring skin functions efficiently. However, obstacles such as resolution, vascularity, cell-scaffold combinations, and cost need to be addressed before clinical applications. This technology allows for the production of biomimetic skin substitutes, catering to both clinical and industrial needs. The ability to customize products based on individual requirements is a growing trend, with active ingredients or boosters added to mass-produced cosmetics for personalization. Users can select qualities based on their skin type, leading to tailored products. Small-scale ٣D skin tissue models are likely to be used initially for drug testing, cosmetics, and tumor modeling before clinical applications. Ultimately, ٣D bioprinting has the potential to revolutionize tissue engineering and cosmetic surgery, offering personalized treatment options and complex geometric distributions with biomaterials and growth factors.

Keywords: ٣D bioprinting, Skin Tissue Engineering, Cosmetic Surgery, Biomimetic, Biomaterials

٣D-Printed Composite Scaffolds of GelMA/Ions to improve Bone Tissue Regeneration

(Review)

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٣. Academic Center for Education, Culture and Research

Introduction: The effective treatment of severe bone defects remains a significant medical challenge, with synthetic bone substitutes being the primary approach for repair. Biomaterials that emulate the structural, mechanical, and biological characteristics of natural bone are widely used to address bone defects and promote in vivo bone regeneration. In tissue engineering applications, active scaffolds based on hydrogels have gained considerable interest due to their highly porous structure and flexibility, which mimic the extracellular matrix for cell growth. Consequently, ٣D bioprinting techniques are popular for creating scaffolds with diverse shapes and dimensions. Gelatin methacryloyl (GelMA), a modified form of gelatin using methacrylic anhydride, serves as a foundation for ٣D-printable hydrogel bioinks. GelMA can be covalently crosslinked under UV light in the presence of a photoinitiator, forming ٣D structures with customizable geometry and adjustable mechanical properties suitable for various scaffold requirements. These hydrogels demonstrate numerous beneficial biological features and are being explored for applications ranging from drug delivery to tissue engineering. GelMA's inherent Arg-Gly-Asp (RGD) sequences enhance biological interactions between cells and scaffolds. Significant advancements have shown that scaffold materials containing ions possess superior bone regeneration capabilities due to their ability to chemically bond with bone tissue in vivo. Notably, ions play a crucial role in regulating various cellular functions and enzymes, significantly impacting cellular homeostasis. Recent research has focused on incorporating bioactive ions into bone substitutes to stimulate vascularized bone repair. The objective of this review is to summarize the ways inorganic ions influence tissue regeneration and to provide an overview of studies on ٣D-printed scaffolds that incorporate bioactive ions

Methods: To create methacrylate gelatin, the initial phase involved dissolving gelatin in PBS (pH=٧,٤) at ٥٠ ◦C. Following complete gelatin solubilization in PBS (approximately ٤٥ minutes), methacrylic anhydride was introduced gradually. This substance interacted with the gelatin structure's functional groups for roughly ٢,٥ hours under constant magnetic stirring at ٥٠ ◦C. The final stage consisted of dialyzing the methacrylate gelatin to eliminate any remaining methacrylic anhydride. This dialysis process was conducted at ٤٠ ◦C for ٥ days, utilizing cellulose dialysis bags and distilled water. The resulting GelMA underwent lyophilization at ٠,٠٢٥ bars for ٢٤ hours to dry it. The composite materials were prepared using the following method: Initially, the optimal concentration of selected ions from the total GelMA amount was dispersed in PBS for ١ hour and then sonicated for ٥ minutes. Subsequently, GelMA was introduced and allowed to react for ٢٤ hours at ٤٠ ◦C. Once a uniform mixture was achieved, Irgacure was added at ١٪ w/v concentration relative to the total GelMA amount and dissolved through gentle stirring at ٤٠ ◦C. The resulting bio-ink was then loaded into the

۳D printing cartridge. All samples underwent biological characterization to determine the most cell-compatible ion concentration.

Results: Recent findings demonstrate that the newly created bio-inks, composed of ۲۵٪GelMA annorganic filler and ۳۰٪GelMA-annorganic filler, enabled the production of scaffolds with specific architectural designs. These structures could potentially serve as an appropriate environment for bone regeneration, as they promote cell attachment, expansion, and multiplication. The research indicates that ions like Zn^{2+} and Mg^{2+} have a beneficial impact on the process of osteogenic differentiation. The GelMA/ions scaffolds exhibited the ability to synergistically enhance in situ bone regeneration by increasing osteogenesis and stimulating endothelial cell functions. These results highlight the positive influence of ions on mechanical performance while preserving good cytocompatibility and the ability to support Bone marrow stromal cells (BMSCs) in their adhesion, proliferation, and osteogenic differentiation. The expression of osteopontin (OPN) and osterix (OSX) genes was verified at the protein level through immunofluorescence techniques combined with confocal microscopy.

Conclusion: The enhanced ۳D bioprinted framework, created by integrating inorganic ions into bioink, improves tissue regeneration and mimics natural biological formations. The main objective of this study was to examine ۳D printable hydrogels based on GelMA/ions with potential applications and to investigate the effect of GelMA/ions on bone regeneration.

Keywords: ۳D Printing- GelMA- Bone regeneration -Osteogenesis- Ions

A Brief Review of Dengue Fever (Review)

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Introduction: Dengue fever, also known as "breakbone fever," is a viral infection caused by an arbovirus and poses a significant public health concern globally. This RNA virus belongs to the Flaviviridae family and comprises four serotypes, designated "DENV1" to "DENV4," which are classified based on the interaction between the virus's surface antigens and the host's anti-infective antibodies. Dengue was first identified in the Philippines in 1954. The primary vector for this disease is the mosquito "Aedes aegypti," which breeds in stagnant water and is most active during the early morning and afternoon hours. Once bitten by an infected mosquito, the virus enters the bloodstream and impacts the immune system. This mosquito species is predominantly found in tropical and subtropical regions; however, due to rising global temperatures and increased international travel, its spread is accelerating. It is estimated that 2.5 billion people are at risk of contracting this virus annually. Reports of dengue fever have emerged in various regions of the country. This review study aims to provide an overview of the clinical manifestations, diagnosis, treatment, and strategies to prevent the spread of this disease.

Methods: Keywords such as dengue fever, dengue virus and Aedes aegypti were used to search online scientific databases like Google Scholar and PubMed, leading to the selection and review of related articles.

Results: The signs and symptoms of dengue fever vary based on the patient's age and typically last 5-7 days. In infants and young children, symptoms include a mild fever and maculopapular rash, while in adults, they present as high fever, vomiting, headache, severe muscle pain, joint pain, difficulty breathing, and pain behind the eyes. Dengue fever manifests in two forms: mild and severe. The mild type features flu-like symptoms (fever of 40 °C), whereas more severe cases can lead to significant bleeding, shock, and even death. Several organs can be affected by the severe fever caused by the dengue virus, including the nervous, respiratory, digestive, cardiac, and renal systems. Diagnosis of this disease is conducted using methods such as serological tests, blood tests, ELISA, and RT-PCR. Although there is no specific treatment for dengue fever, supportive care such as fever management, adequate rest, fluid replacement (for every 1% weight loss), blood and platelet transfusions, and pain relievers like acetaminophen and non-steroidal anti-inflammatory drugs (to prevent bleeding) are recommended. The most effective prevention methods include avoiding bites from Aedes mosquitoes, limiting their habitat and breeding sites, using environmentally friendly biocides containing metal nanoparticles, and employing genetic strategies to control the mosquito population.

Conclusion: Currently, two vaccines against the dengue virus, based on "weakened live virus," named "Dengvaxia," and "Qdenga," have been approved by the World Health Organization. However, they can only be administered to individuals with a history of infection with this virus.

Their use is limited because, in those who have not been infected, the vaccine increases the risk of severe illness. To better understand the disease, develop treatments and vaccines, and in the absence of specific antiviral therapies to combat dengue fever, ongoing research is essential to reduce the risk of infection in human populations worldwide. It is crucial to recognize the symptoms of dengue fever, and upon noticing acute symptoms such as bleeding and abdominal pain, immediate medical attention is necessary. International cooperation and public education on preventive measures against dengue fever are vital in mitigating the spread of this disease.

Keywords: dengue fever, dengue virus, Aedes aegypti

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A comparison between centrally and systemically administered erythropoietin on kidney protection in a model of xed-volume hemorrhagic shock in male rats (Research Paper)

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Introduction: In this study, a comparison between centrally and systemically administered erythropoietin (EPO) was performed on nephroprotection during hemorrhagic shock (HS) in male rats.

Methods: Male rats were allocated into four experimental groups. (١) Sham; a guide cannula was inserted into the left lateral ventricle and other cannulas were placed into the left femoral artery and vein. (٢) HS; stereotaxic surgery was done to insert a cannula in the left lateral ventricle and after a ٧-day recovery; hemorrhagic shock and resuscitation were performed. (٣) EPO-systemic; the procedure was the same as the HS group except that animals received ٣٠٠ IU/kg erythropoietin into the femoral vein immediately before resuscitation. (٤) EPO-central; animals was treated with erythropoietin (٢ IU/rat) into the left lateral ventricle before resuscitation. Arterial oxygen saturation (SaO٢) was measured during experiments. Urine and renal tissue samples were stored for ex-vivo indices assessments.

Results: Erythropoietin (systemically/centrally administered) significantly improved SaO٢, renal functional and oxidative stress parameters and decreased renal inflammatory (TNF-α and IL-٦) mRNA expression compared to the HS group. EPO-treated groups showed a decrease in active form of caspase-٣ protein level and an increase in autophagy activity in comparison with the HS group.

Conclusion: Considering the fact that the effective dose of systemic EPO (٣٠٠ IU/kg) was roughly ٥٠ times higher than that of central administration (٢ IU/rat), centrally administered EPO was accompanied by more advantageous consequences than systemic way. EPO is likely to act as a neuro-modulator or neuro-mediator in the central protection of organs including the kidneys

Keywords: erythropoietin, hemorrhagic shock, inammation, intracerebroventricular infusion, stereotaxic

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A COMPOUND HETEROZYGOUS MISSENSE VARIANT IN DNAH٥ GENE AND ITS CORRELATION WITH UNEXPLAINED MALE INFERTILITY (Research Paper)

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Introduction: According to the World Health Organization, infertility is defined as the inability of couples to achieve pregnancy after one year of unprotected sexual intercourse. It affects approximately ٥٠ million couples worldwide, with both men and women being equally affected. Male infertility is a complex issue with genetic factors playing a significant role. Conditions such as Klinefelter syndrome (XXY), Y Chromosome Microdeletions (YCMDs), and monogenic mutations can contribute to male infertility. Currently, hereditary factors account for ٤٪ of male infertility cases, while the causes of ٦٠-٧٠٪ of cases remain unknown. Ongoing research aims to identify new genes and variants related to male fertility to improve diagnostic methods. It is believed that around ٢٠٠٠ genes are involved in preserving germ cells and ensuring normal meiosis, with more than ١٠٠ genes already identified concerning male infertility.

Methods: We assessed a patient with unexplained male infertility, who also had a brother with a similar issue. We used whole exome sequencing (WES) technology and analyzed the data through bioinformatics. Then we performed Sanger sequencing to confirm variations and segregation. We found that patients were carrying DNAH٥ compound heterozygous variants (c.١١٢١G>A and c.١١٤٣VA>T).

Results: Genetic prediction databases such as Mutation Taster suggest that c.١١٢١G>A and c.١١٤٣VA>T may cause disease. The variations c.١١٢١G>A and c.١١٤٣VA>T may cause disease by bioinformatics prediction databases such as MutPred٢, Project HOPE, mCSM, and Mutation taster. Each patient inherited one altered allele from their father and one from their mother. The parents underwent Sanger sequencing for the DNAH٥ variants to determine whether the variants were present in a cis- or trans-presentation in the proband and his infertile brother. The variation (Chr٥:١٣٩١٦٥٣٣ A>G; c.١١٢١G>A; p. I٣٧٤T) was inherited paternally, while the variant

(Chr٥:١٣٧٣٧٣٧٩ G>A; c.١١٤٣٧A>T; p. R٣٨١٣W) was inherited maternally. They may contribute to a risk of male infertility.

Conclusion: We investigated the potential correlation between DNAH٥ mutations and unexplained male infertility. Changes in two amino acid properties - size, charge, and hydrophobicity - might affect the DNAH٥ protein and lead to infertility. If this finding is confirmed in larger sample sizes and diverse racial populations, it could significantly improve the identification of male patients with unexplained infertility conditions.

Keywords: unexplained male infertility, bioinformatics analysis, Whole-exome sequencing, DNAH٥

A comprehensive analysis of linalool content throughout the plant kingdom and its therapeutic properties (Review)

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Introduction: Linalool, a naturally occurring floral scent with the chemical structure ٣,٧-dimethyl-١,٦-octadien-٣-ol, is widely recognized for its presence in various plant species, notably in the leaves of Cinnamomum crassinervium and the seeds of Theobroma cacao. This systematic review aims to consolidate the current understanding of linalool's multifaceted properties and its significance in the production of cosmetic products, food, and industrial materials such as waxes. Linalool's therapeutic properties, including its sedative, anxiolytic, local anaesthetic, anticonvulsant, analgesic, anti-inflammatory, antioxidant, and anticancer activities, have been extensively documented in the literature. This review compiles and analyzes these properties, providing a comprehensive overview of linalool's potential health benefits and its role in various industries. Additionally, we present a detailed table that outlines the percentage of linalool found in different plant sources, offering a comparative analysis that highlights the rich diversity of linalool content across the plant kingdom. This information is crucial for researchers, manufacturers, and consumers seeking to harness the natural benefits of linalool in their products and practices.

Methods: Methods: This review presents studies that worked on nanoparticles that used for Linalool. We searched studies that reported in the literature from ١٩٩٥ to ٢٠٢٢. The relevant keywords were searched from Google Scholar, Pub Med, Science direct, Cochrane library and EMBASE databases.

Results: Results: Our systematic review process initially identified ٥٠ relevant articles. After a thorough screening and quality assessment, ٢٨ articles were selected for inclusion in this review. Notably, Theobroma cacao was found to have the highest percentage of linalool, with concentrations ranging from ٩٤٪ to ٩٧٪ in its seed part. In contrast, Eucalyptus citriodora and

Eucalyptus camaldulensis exhibited the lowest percentage of linalool, with only ٠,١٪ in their leaf parts.

Conclusion: Conclusion: These articles provided valuable insights into the properties and applications of linalool, contributing to a robust analysis of its significance in various industries.

Keywords: Keywords: Linalool, Cinnamomum crassinervium, Theobroma cacao, Eucalyptus citriodora, Eucalyptus cam

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A Comprehensive Analysis of present of JC and BK viruses in Immunocompromised Patients over the Past Three Years in Iran (۲۰۲۱-۲۰۲٤) (Research Paper)

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Introduction: BK and JC viruses are polyomaviruses that primarily affect immunocompromised individuals, leading to significant clinical complications. Understanding their pathogenesis and epidemiology is crucial for developing effective management strategies, particularly in transplant recipients and patients undergoing immunosuppressive therapies. The objective of this research is to analyze samples sent for testing over the past three years to determine the positivity rate. We aim to identify which sample types yielded the highest rates of positive results and investigate any correlations between sample type and positivity. This analysis will provide insights into the effectiveness of different sampling methods in detecting target pathogens.

Methods: The laboratory received a diverse array of sample types, including urine, plasma, blood serum, and cerebrospinal fluid (CSF). Specifically, a total of ۱۰۳ samples for JC virus testing and ۱۰۵ samples for BK virus testing were collected and analyzed. The extraction of DNA from JC and BK viruses was performed using a standardized protocol to ensure high yield and purity suitable for downstream applications. Quantitative polymerase chain reaction (qPCR) was then employed to detect and quantify the viral DNA in the extracted samples, providing sensitive and specific measurements of viral load.

Results: The results indicated that the primary sample utilized for the JC test is cerebrospinal fluid (CSF). An alternative sample proposed for this test is the Urine sample. In the BK virus tests, ۱۸٪ of the samples tested positive, with positivity rates of ۳٦٪ in urine, ۳۱٪ in serum, and ۲٦٪ in whole blood. Notably, there was no observed overlap between the positivity rates for JC and BK viruses within the analyzed sample set.

Conclusion: The results of this study demonstrate that the superior positivity rates in urine (۳٦٪) and CSF underscore their effectiveness as diagnostic mediums for both JC and BK viruses, supporting recent recommendations for utilizing these sample types in clinical assessments. Importantly, the absence of overlap in positivity rates between JC and BK viruses suggests distinct viral behaviors and reinforces the necessity for targeted diagnostic strategies to optimize patient management.

Keywords: BK virus, JC virus, qPCR, immunocompromised.

A Comprehensive Evaluation of Stockholm۳ Test Implementation: Enhancing Prostate Cancer Detection While Reducing Unnecessary Biopsies" (Research Paper)

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۱. Kermanshah Islamic Azad University - Faculty of Medical Sciences
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Introduction: Prostate cancer is the most common cancer in males and one in every eight males will receive a diagnosis over their lifetime. PSA is a conventional method for monitoring and treating prostate cancer that is utilized for early detection. The Stockholm۳ blood test addresses issues like overtreatment and the need for more precise treatment by precisely estimating the risk of prostate cancer. The Karolinska Institute in Stockholm, Sweden created the Stockholm۳ blood test, which estimates a man's chance of receiving a csPC during a prostate biopsy. In addition to ۱۰۱ genetic markers, PSA, four more proteins, and clinical data including age, family history, and prior biopsies are also included.

Methods: Intervention In September ۲۰۱۷, Stavanger University Hospital advised primary care physicians in the Stavanger region to use Stockholm۳ to screen for prostate cancer in males as early as possible. Physicians were directed to send patients who had an elevated risk of csPS, as indicated by a Stockholm۳ Risk Score of ۱۱٪. June ۲۰۱۷ saw the start of the Stockholm۳ implementation, which included comprehensive instructions and the required lab equipment. Physicians were instructed to carry ahead with their diagnostic procedures, but for individuals who do not yet have prostate cancer, utilize Stockholm۳. September ۲۰۱۷ was designated as the start date of the new practice, and after September ۱۸th, hospital referrals based on PSA might be denied. In September ۲۰۱۷, Stavanger University Hospital advised primary care physicians in the Stavanger region to use Stockholm۳ to screen for prostate cancer in males as early as possible. Physicians were directed to send patients who had an elevated risk of csPS, as indicated by a Stockholm۳ Risk Score of ۱۱٪. June ۲۰۱۷ saw the start of the Stockholm۳ implementation, which included comprehensive instructions and the required lab equipment. Physicians were instructed to carry ahead with their diagnostic procedures, but for individuals who do not yet have prostate cancer, utilize Stockholm۳. September ۲۰۱۷ was designated as the start date of the new practice, and after September ۱۸th, hospital referrals based on PSA might be denied. Method Monitoring the GPs' conversion rate from PSA to Stockholm۳ was part of the deployment process. The research contrasted PSA readings with Stockholm۳'s needle-biopsy advice based on actual results from ٤٧٨٤ males who underwent testing between September ۱, ۲۰۱۷, and October ۱۲, ۲۰۱۸. Since the Stockholm۳ test includes a threshold for a positive test that corresponds to the risk of a csPC at this level, the analysis employed a positive PSA test cutoff of ۳ng/ml as an acceptable foundation for comparison. Statistical analysis Descriptive statistical techniques, such as percentages, proportions, and rates, were used to assess the data. Chi-square tests were used to examine variations in rates. P-values and confidence ranges for the results are displayed. By dividing the total number of positive biopsies by the number of csPC, the proportion of csPC was found. A simplified health economy cost-model was calculated using cost

estimates from Stavanger University Hospital and outcome data from ٤٧٨٤ men tested with Stockholm٣. Blood testing expenses were totaled and included blood sample, PSA, TRUS, MRI, Stockholm٣, needle-biopsy, pathology workup, and sepsis after needle-biopsy. Re-biopsy rates of ٣٠٪ and ٦٠٪, as well as post-biopsy sepsis rates of ٢ and ٥٪, were used to calculate costs based on PSA. P-values less than ٠,٠٥ were regarded as statistically significant.

Results: Increased Detection of Clinically Significant Cancers: The incidence of aggressive tumors that are anticipated to respond well to therapy has been markedly increased by the Stockholm٣ test. Reduction in Unnecessary Biopsies: Because of the Stockholm٣ test's increased specificity, fewer biopsies were conducted, which decreased the possibility of false positive results. Improved Patient Management: Better risk categorization, more effective patient management, and better judgment when deciding between active treatment and monitoring were all experienced by the healthcare system.

Conclusion: While Stockholm ٣ is considered a powerful tool in the diagnosis of prostate cancer, there are challenges and limitations. Among these challenges, we can mention the limited access to this test in some countries and the need for more research on its effectiveness in different population groups. In the space of three months, Stockholm٣ effectively replaced PSA in primary care in the Stavanger region. In addition to lowering direct healthcare expenditures, the test boosted the percentage of prostate cancer that was clinically significant in biopsies and decreased the necessity for biopsies overall.

Keywords: Prostate cancer Stockholm٣

A comprehensive review of Emerging Nanotechnology: Nanocarriers for nasal delivery in treating Alzheimer's diseases (Review)

Hedyie Mashhadi Mohammad Reza ,[1,*]

[1].

Introduction: Alzheimer's disease, a progressive neurodegenerative disorder, severely impacts cognitive function and daily living. Although several potential therapies are in various stages of clinical trials, bringing a new Alzheimer's drug to market remains challenging. Despite of being carefully studied, it is still an irremediable disease because of complicated pathophysiological features and Physiological Barriers. Hence, researchers are also exploring Nano drugs. Nasal drug delivery has emerged as an innovative strategy for administering drugs, with countless benefits over traditional methods. This route is safe and non-invasive. This paper provides a comprehensive review of nasal anatomy and the physiological factors that influence nasal medication absorption and highlights the current advancements in the development of intranasal Nanoformulations. It is crucial to note that nasal delivery can also lead to some side effects including toxicity .This review aims to provide current knowledge regarding the physiological consequences of intranasal drug delivery systems. Furthermore, this paper discusses challenges and methods to overcome these obstacles. It then delves into different types of nanoparticle. Overall, this article provides a complete and current review of nanoparticle composition, making it a useful resource for researchers, pharmaceutical scientists, and healthcare professionals.

Methods: ٤٨ recently published articles about nasal delivery of Nano medicines were extracted from Google scholar. The articles that was directly related to the subjects and focused on treatment by nanotechnology and different types of Nanocarriers and Nanomaterials were separated and studied carefully. This paper is a comprehensive review of ٢٤ final articles.

Results: AD is a CNS disorder in the elderly population, where the normal body functions are progressively declines. The N٢B drug delivery holds promise as an innovative therapeutic approach for the treatment of AZD. This approach has the potential for a number of benefits, including increased efficacy, lower systemic exposure, and noninvasiveness.N٢B delivery is a noninvasive and patient-friendly route of drug administration which is particularly beneficial for elderly patients and individuals. This method is less invasive, making it more acceptable and convenient for long-term treatment. Currently available strategies for the AD treatment are facing several challenges and there is an urgent requirement of the treatment strategies with lower peripheral side effects and higher potency. Nanoparticles can be designed to target specific disease-related proteins like beta-amyloid, potentially disrupting their aggregation and offering a novel therapeutic approach. The nose-to-brain pathway can effectively treat CNS related disorders by bypassing the BBB as the most significant barrier.

Conclusion: Nanotechnology has shown tremendous promise for the pharmacological treatment of neurological disorders. Major challenges in this drug-delivery system include nasal architecture,

mucociliary clearance, drug properties, formulation stability, and targeting efficiency, etc. Fundamentally, various factors are required to be considered. Further research is needed to develop less invasive and more affordable diagnostic approaches. Despite the positive findings of various studies, few advancements have been achieved in clinical settings. Further clinical trials will be required to understand the long-term efficacy and side effects of intranasal drugs and its exact uptake mechanisms to the brain parenchyma. If findings from the clinical trials support the preclinical data, the intranasal formulation can be a potential breakthrough treatment option for AD. Undoubtedly, additional work is needed to elucidate the underlying mechanisms of this route and improve intranasal drug delivery techniques. This is due to the fact that there are still concerns surrounding the use of nanomaterials because it is unresolved how they interact with biological systems. Therefore, an improved understanding of the interactions between these nanomaterials and the human body would yield greater insight for the development of improved therapeutic approaches. In addition, the potential for systemic toxicity and the effects of chronic exposure of the brain and other organs must be studied. Moreover, challenges such as formulation optimization, safety evaluation, and regulatory considerations need to be addressed for their successful translation into clinical applications In conclusion, these evolving drug delivery technologies underscore a transformative potential for the field of Alzheimer's disease therapy, with a growing emphasis on improving drug delivery precision and site-specific availability, paving the way for more effective and patient-friendly approaches to Alzheimer's management.

Keywords: Alzheimer's disease, Nanocarriers, Nanomaterials, Nasal drug delivery,Nanotechnology

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A Fluorescence Biosensor for the Simultaneous Detection of miR-۲۱-۵p and miR-۱۷-۵p in Gastric Cancer (Research Paper)

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Introduction: Gastric cancer (GC) remains a leading cause of cancer-related death worldwide. Less than half of GC cases are diagnosed at an advanced stage due to its lack of early symptoms. Early detection and effective monitoring of tumor progression are essential for reducing GC disease burden and mortality. The current widespread use of semi-invasive endoscopic methods and radiologic approaches has increased the number of treatable cancers: However, these approaches are invasive, costly, and time-consuming. Thus, novel molecular noninvasive tests that detect GC alterations seem more sensitive and specific than the current methods. The discovery of microRNAs (miRs) and their unique role in cancer and other diseases has prompted the development of highly sensitive molecular diagnostic tools using nanomaterials as sensitive and specific biosensors. Among these, fluorescent biosensors, which are based on a simple and inexpensive design, make them desirable in clinical applications as well as a mass-produced point-of-care devices. In this study, single- and dual-fluorophore DNA biosensors based on single-walled carbon nanotubes (SWCNT) were fabricated for the individual and simultaneous detection of the miR-۲۱-۵p and miR-۱۷-۵p in early diagnosis gastric cancer.

Methods: Our detection strategy was based on immobilizing dye-labeled single-stranded DNA (ROX, and FAM dye-labeled-ssDNA) to SWCNT that detect target miR-۲۱-۵p and miR-۱۷-۵p. For this purpose, in the first step, adsorption of ROX-, and FAM-labeled single-stranded DNA (ssDNA) on SWCNT leads to fluorescence quenching of ROX, and FAM. Next, by adding its complementary DNA (cDNA), a double-stranded DNA (dsDNA) was formed, resulting in recovering the fluorescence of ROX, and FAM by desorbing and releasing from SWCNT.

Results: Upon the addition of the complementary target DNA (ctDNA) to the hybridization reaction, the fluorescence emission of fluorophore-labeled probes was significantly recovered to ٦٩,٥ % for ROX-labeled probes (i.e. miR-۲۱-specific probes), ٧١,٥٪ for FAM-labeled probes (i.e. miR-۱۷-specific probes), and ٥٩,٩٪ for dual-fluorophore biosensor compared to the quenching mode. The limit of detection (LOD) for ROX, and FAM was determined to be ٣,٦ nM, and ٦,٨ nM, respectively. For dual-color probes, LOD was found to be ٤,٩ (ROX) and ٩,٦ nM (FAM).

Conclusion: Finally, the clinical applicability of the proposed method was confirmed through the detection of both biomarkers in patient plasma samples, suggesting that the proposed nanosensing platform may be useful for the early detection of gastric cancer using miRNA.

Keywords: Nano biosensor; MicroRNA; Cancer; SWCNT

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A meta-analysis of the association between the BDNF gene polymorphisms and Schizophrenia

(Review)

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Introduction: Schizophrenia is a brain disorder classified as a psychosis, which may result in some combination of hallucinations, delusions, and extremely disordered thinking and behavior that impairs daily functioning, and can be disabling. According to WHO, Schizophrenia affects approximately ٢٤ million people or ١ in ٣٠٠ people (٠,٣٢٪) worldwide. This rate is ١ in ٢٢٢ people (٠,٤٥٪) among adults. Onset is most often during late adolescence and the twenties, and onset tends to happen earlier among men than among women. Schizophrenia has long been considered a neurodevelopmental disease whose symptoms are caused by impaired synaptic signal transduction and brain neuroplasticity. Both the onset and chronic course of schizophrenia are associated with risk factors-induced disruption of brain function. Researches show that deletions or duplications of genetic material in any of several chromosomes, which can affect multiple genes, are also thought to increase schizophrenia risk. An operant number of studies have reported associations between two polymorphisms of Brain-derived neurotropic factor gene (BDNF) and Schizophrenia. This study reports the effect of these polymorphisms on Schizophrenia using meta-analysis method.

Methods: To conduct electronic searches, PubMed was used. For prospective investigations, the keywords "Schizophrenia" and "BDNF gene" or "Brain Derived Neurotrophic Factor gene" as well as "meta" were searched extensively in the electronic literature. We estimated the pooled effect sizes (ORs) and ٩٥٪ confidence intervals (CIs) for these two polymorphisms (rs٦٢٦٥ (Val٦٦Met) and rs٢٠٣٠٣٢٤ (C٢٧٠T) in the "cases" and "controls" groups.

Results: effect model, nine studies totaling ٦٦٩٣٤ participants—٢٩٨٤٣ cases and ٣٧٠٩١ controls—were included in this meta-analysis. The results showed that these polymorphisms significantly influence schizophrenia, and the pooled OR is ١,٠١ with a ٩٥٪ confidence interval of ٠,٩٧ to ١,٠٥ and a p-value of less than ٠,٠٠, indicating that the test was statistically significant. When it comes to understanding heterogeneity, research become less variable and heterogeneous when I٢ is reduced. I٢ = ٠,٠٠٪ and H٢ = ١,٠٠ in this analysis show that there is no degree of study heterogeneity.

Conclusion: Overall, these findings provide compelling evidence that refutes the null hypothesis. (The null hypothesis is a typical statistical theory which suggests that no statistical relationship and significance exists in a set of given single observed variations, between two sets of observed data and measured phenomena.)

Keywords: Schizophrenia, BDNF, Brain-derived neurotropic factor, polymorphism.

A miracle for survival (vaccine) (Review)

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[1].

Introduction: Edward Jenner invented a method to protect against smallpox. In this method, liquid was extracted from the blister of a person suffering from cowpox and then the skin of another person was inoculated.The next generation of vaccines that are commonly prescribed today were invented in the early twenty century. These vaccines include whooping cough, diphtheria and tetanus vaccines.These three vaccines were combined with each other and released as a triple DTP vaccine.Vaccines are often injected and sometimes even oral, such as the polio vaccine.Vaccination at the appointed time protects us from the risk of contracting certain diseases, this immunity will exist not only during childhood but throughout our life

Methods: Germs are tiny organisms that cause disease. Many microbes cannot live independently, they are only able to live in the body of a host. There are two types of germs that make us sick, viruses and bacteria. Bacteria emit toxins that can damage or destroy body cells and cause disease in humans. Viruses do not emit poison, but increasing their number causes the destruction of cells. Diseases caused by microbes are called infectious diseases.Vaccines contain substances that stimulate the body to produce antibodies against pathogenic microbes. These antibodies protect a person from getting an infection even if he has come into contact with the pathogenic microbe. Sometimes it is also called vaccination (immunization) because vaccines cause immunity. Most vaccines are made up of microbes that need to be protected against.

Results: Vaccines are safe, but sometimes they can cause reactions, sometimes minor problems such as redness or pain in the injection area occur

Conclusion: The more people are immune to a disease, the less likely it is to spread germs from unprotected people to others. This is called herd immunity.

Keywords: Vaccine, microbe, bacteria, disease

A network-biology approach for identification of Hub Genes and Key Pathways in Uterine Corpus Endometrial Carcinoma (Research Paper)

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Introduction: Uterine corpus endometrial carcinoma (UCEC), originating from the endometrium, is the most common type of endometrial cancer. This gynecological malignancy is very common all over the world, especially in developed countries and shows a possibly increasing trend with the increase of obese women.

Methods: GSE٧٣٠٥ and GSE٢٥٦٢٨ were selected from the Gene Expression Omnibus (GEO) database, differentially expressed genes (DEGs) with an adjusted p-value < ٠,٠٥ and a logFC ≥ ١ and logFC ≤-١ were identified. Common DEGs of two datasets were identified using the GEO٢R tool. The Kyoto Encyclopedia of Genes and Genomes (KEGG) and Gene Ontology (GO) databases were used to identify pathways. Protein-protein interactions (PPIs) analysis was performed by using the Cytoscap

Results: ٣٠٤ common DEGs have been identified through the use of GEO and PPI, respectively. The GO and KEGG pathways analysis showed DEGs were enriched in cell adhesion and ECM-receptor interaction. The expression of ٢ genes GNG٤ and DSP showed a significant difference between normal and tumor samples, have been identified by GEPIA analysis.

Conclusion: In this study, the hub genes and their related pathways involved in the development of UCEC were identified. These genes, as potential diagnostic biomarkers may provide a potent opportunity to detect UCEC at the earliest stages, resulting in a more effective treatment.

Keywords: Endometriosis, UCEC, PPI network, Diagnostic biomarkers

A new approach to improve positive results among smear-negative clinical specimens for acid-fast bacilli (Research Paper)

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Introduction: Acid-fast bacilli (AFB) are a group of bacteria causing tuberculosis (TB), leprosy and non-tuberculosis mycobacterial (NTM) infections. Smear microscopy is the most simple widely used method to detect these bacteria. Although mycobacterial culture is the gold standard method for AFB detection, it is usually timeconsuming and labor-intensive approach. Since the sensitivity of smear microscopy ranges from ٣٠٪ to ٨٠٪, a smear-negative result don't rule out Mycobacterial related disease. The present study aimed to introduce a new approach for improving the sensitivity of smear microcopy and reducing the number of false-negative results among AFB smear-negative specimens submitted to the Laboratory of Tuberculosis, Ghaem University Hospital, Mashhad, Iran.

Methods: In our study, all smear-negative reported samples were collected from Dec ٢٠٢٣ to June ٢٠٢٤. Then, the remainder of each sample that previously homogenized and concentrated by Petroff's method was transferred to a ١,٥-ml microtube and further concentrated by centrifuging at ١٤٠٠٠ rpm for ٨ minutes followed by discarding the supernatant and keeping the pellet. Finally, the smears were prepared from the pellets and stained by Ziehl-Neelsen method to be microscopically examined for AFB.

Results: Among the ١٥٠٠ smear-negative collected samples, we could detect ٧ positive results.

Conclusion: This study showed that the sensitivity of smear microscopy for AFB detection can be improved by a simple dual concentration approach.

Keywords: Mycobacteria, AFB, Improved detection, Smear microscopy.

A pH-sensitive hyaluronic acid-based hydrogel containing crocus sativus with wound healing properties (Research Paper)

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Introduction: In the wound healing process, controlling parameters that accelerate treatment and inhibit deleterious factors is very complicated and needs new treatment strategies. In the current study, we synthesized a pH-sensitive hydrogel based on hyaluronic acid, and crocus sativus extract which changes its color in the face of bacterial infection.

Methods: Field-emission scanning electron microscope demonstrated a highly porous composite with a ٣D-mesh structure. Fourier-transform infrared spectroscopy confirmed the presence of functional groups at each synthesis stage.

Results: Colorimetric pH measurements depicted that, after bacterial inoculation, the composite`s color changed to yellow, while it remained colorless in fresh medium, and pink at acidic pH similar to healthy skin. The hydrogel prevented the formation of bacterial biofilm. The hemolytic assay demonstrated that ٩٨٪ of red blood cells survived. The ferric-reducing antioxidant assay showed an antioxidant activity of about ٧٥٪ for the hydrogel. The cell viability of L٩٢٩ cells was ٩٦,٥,٠٪ after ٢٤h of incubation, whereas it was ٩٩,٥٪ for the control group. Statistical analysis indicated no significant difference between the cell viability of the control and treated groups.

Conclusion: The fabricated hydrogel can be tested in future studies on different wound dressing applications.

Keywords: Keywords: Crocus sativus, hyaluronic acid, smart hydrogel, silk fibroin, biofilm, antioxidant

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A protocol for effective decellularization of human endometrial fragments for clinical applications

(Research Paper)

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Introduction: The objective of this study was to evaluate and compare the effectiveness of various decellularization protocols when applied to human endometrial fragments.

Methods: decellularization process involved a combination of freeze-thaw cycles, Triton X-١٠٠ treatment, and four different concentrations of sodium dodecyl sulfate (SDS; ٠,١٪, ٠,٥٪, ١٪, and ١,٥٪) applied for two distinct exposure durations (٢٤ and ٧٢ hours). Following analysis of tissue morphology and DNA content, The tissue group with the best morphology and lowest DNA content was chosen for further analysis. The nucleus was visualized using Acridine orange staining, and the extracellular matrix (ECM) was examined using Masson's trichrome, Alcian blue, and periodic acid-Schiff staining. Raman spectroscopy was used to quantify the levels of collagen types I and IV, fibronectin, glycosaminoglycans (GAGs), and elastin in the tissues. The ultrastructure and porosity of the decellularized scaffold were examined using scanning electron microscopy (SEM), and its cytotoxicity was assessed with an MTT assay.

Results: The treated group with ١٪ SDS for ٧٢ h showed the morphology similar to native control in having the minimum level of DNA and well preserved ECM. Raman spectroscopy analysis revealed no significant difference in the amounts of collagen types I and IV, GAG, and fibronectin between the decellularized scaffold and the native group but the elastin protein level was significantly decreased ($P < ٠,٠٠١$). SEM micrographs also showed a porous and fiber rich ECM in decellularized sample similar to the native control.

Conclusion: This combined protocol for decellularization of human endometrial tissue is effective and it could be suitable for recellularization and clinical applications in the future.

Keywords: Decellularization; Human endometrial tissue; Raman spectroscopy; Sodium dodecyl sulfate

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A review of air pollution on human genome (Review)

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Introduction: The World Health Organization (WHO) estimates that air pollution causes about ١١,٣٪ of global deaths annually, totaling around seven million early deaths. In recent years, the fossil fuels burning has increased and has changed the atmospheric composition. Air pollutants components including carbon monoxide (CO), sulfur dioxide (SO٢), nitrogen oxides (NOx), volatile organic compounds (VOCs), ozone (O٣), heavy metals, and suspended particles (PM٢,٥) cause genetic changes in humans. In this review, we intend to investigate the effects of air pollution on the human genome and human health.

Methods: In this review study, four databases including Google scholar, PubMed, CID and Civilica; And keywords like air pollution, human genome, epigenetic, genetic mutation are used for gathering the information. Articles that hadn't had our purpose, were omitted from the study process.

Results: Humans are usually exposed to mixtures of air pollutants, which vary in composition, dose, and exposure time. Genetic susceptibility varies among individuals based on their health and genetic background. Exposure to these pollutants can lead to oxidative stress, inflammation, and changes in gene expression and DNA methylation, especially in genes related to immune regulation and disease processes. On the other hand, air pollution can lead to genetic alternations, increase the risk of diseases and intergenerational effects. Genetic and epigenetic changes caused by air pollution may predispose people to various diseases, including cancers, cardiovascular diseases, and respiratory disorders. If these changes persist, may remain through cell division, affecting how cells express genes throughout their lifetime and as it happens across generations which is a very worrying issue. Studies have shown that elderly people, children and fetuses (due to their developing physiological system), pregnant mothers and people who have already had lung or heart diseases are more at risk of genetic changes caused by air pollution.

Conclusion: The interplay between air pollution and genetics underscores a complex relationship where environmental exposures can lead to significant epigenetic modifications that influence health outcome across generations. Understanding these mechanisms is crucial for developing targeted interventions aimed at reducing the impact of air pollution on vulnerable populations, particularly those genetically predisposed to adverse health effects. Continued research is essential to unravel the specific pathways through which air pollution affects genetic expressions and to identify effective strategies for prevention and treatment.

Keywords: air pollution, human genome, epigenetic, genetic mutation

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A review of biosensors in smart food packaging (Review)

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Introduction: New smart packaging using algae as accurate and adjustable sensors, preserves food quality and reduces waste. Sensors and smart packaging are very effective in controlling and monitoring food quality and spoilage. Sensors detect changes in food spoilage by changing color, enzymes and living cells, and temperature and time sensors. These technologies are used in food packaging such as meat, fish, dairy and fruits. Electrochemical biosensors as smart packaging generate electrical signals based on analyte concentration. The use of natural pigments in sensors has low toxicity and few environmental effects. In this way, it measures the chemical and biological changes of the product (such as the pH change) and always controls the quality of the product. Among the natural pigments are anthocyanins, which are soluble in water and have antioxidant, anti-inflammatory and anti-cancer properties. Also, with changes in pH, the chemical structure of anthocyanin is changed and it produces different colors.

Methods: In this article, related articles published in ٢٠٢٠-٢٠٢٣ in Springer, Science direct, Scopus and John Wiley databases were reviewed to obtain the latest findings in the field of biosensors in smart food packaging. In this review article, appropriate keywords were selected by searching the MeSH website and based on them, fifty one new review and research articles were collected

Results: In a research, anthocyanin was used to control spoilage of carp. In this way, a two-layer hydrogel film sensitive to pH, the first layer of gelatin and ZnO and the second layer of gellan gum with anthocyanin extract was made. The fish was inserted into the film, then the color of the film changed from pink to light green and finally to yellow as TVB-N increased. Due to the production of NH_3, it changed the color of the film and the hydroxyl group (OH-) was hydrolyzed in the hydrogel film, and as a result, alkaline conditions were created. Betalains are another group of water-soluble nitrogenous colored compounds derived from betalamic acid. These pigments include red to purple betacyanins and yellow to orange betaxanthins. Betalins have high antioxidant capacity and ability to inhibit lipid peroxidation at low concentration. In addition, these pigments are stable at pH between ٣ and ٨. Curcumins are another group of pigments that are polyphenolic and are extracted from turmeric root. Curcumins as a sensor material with tara gum and polyvinyl alcohol create films that keep the quality of shrimp fresh. Although fresh shrimp in the films causes a yellow to orange-red color change, pectin films with curcumin and sulfur nanoparticles showed that the color change from yellow to orange indicates shrimp degradation. Naphtoquinones are sensitive to acidic and basic environments and also increase the resistance of films against moisture. Researchers used naphthoquinone and cellulose pigment to make a pH sensor in shrimp packaging, the results showed

that with the change of pH and ammonia production, the color change from rose-red to purple and then to blue-violet, different stages of food spoilage. it shows.

Conclusion: In general, the use of smart packaging in the food industry with bio-pigments, such as anthocyanin and curcumin pigments, can help to detect the freshness and degradation of products. In addition to antimicrobial and antioxidant properties, these pigments improve product shelf life with integrated packaging. Also, the use of biopolymers and ZnO nanoparticles helps to stabilize pigments. It will be interesting to combine these pigments with other active compounds and essential oils. However, for the commercialization of smart packaging, sensitive and environmentally friendly sensors and message transmission and warning systems are necessary.

Keywords: Biosensors, smart food packaging, anthocyanin, betacyanin, curcumin

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A review of chemical methods of sperm immobilization in ICSI process (Review)

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Introduction: Infertility is one of the important problems that many people in society deal with today, estimates indicate that ۱۰ to ۱۵ percent face this challenge at some point in their lives. Fertility is achieved today by the manipulation of egg and sperm outside the body in a laboratory environment. One of the methods that can accomplish this is intracytoplasmic injection of the egg, which is called ICSI for short. Several factors affect the quality of this treatment, such as Maternal and Paternal Age, Oocyte and Sperm Quality, Duration of Infertility, Hormonal Levels, Embryo Quality and Transfer, Procedural Factors ICSI Technique, Incubation Time and Laboratory Condition, the things that are discussed during ICSI treatment is the substance used to immobilize sperm before ICSI.

Methods: Articles were extracted without time limit from Web of Science, PubMed, Google Scholar, SID, Magiran databases. The inclusion criteria included studies that were in line with the research objective.

Results: Sperm immobilization is necessary to facilitate the injection process during ICSI. Different methods are used. Polyvinyl pyrrolidone is one of the most common chemical agents for sperm stabilization in ICSI. This creates a viscous solution that slows sperm movement and facilitates easier micromanipulation. The typical concentration used is around ۷-۱۰٪ PVP. In addition to these studies, hyaluronate, a natural substance in the genital tract, is often included in PVP solutions. Its presence can increase sperm quality by promoting better interaction with the egg during fertilization. However, the use of PVP affects sperm and embryos with important secondary effects such as induction of immature acrosome reaction, and nuclear damage. While it has been said that sodium hyaluronate is generally well tolerated; There are some considerations with using this substance, including concerns about fetal development, variability in sperm response and transport problems, and allergic reactions.

Conclusion: While PVP and sodium hyaluronate are valuable tools in ICSI for sperm stabilization, their use is associated with significant risks that can negatively affect fertilization rate and embryo quality. As a result, continuous research on alternative methods and formulations is necessary to increase the safety and efficacy of assisted reproductive technologies.

Keywords: sperm, icsi, PVP

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A review of CRISPR applications in therapeutics (Review)

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Introduction: The advent of CRISPR-Cas systems has revolutionized precise gene targeting for a wide range of applications, including research, agriculture, biotechnology, and human disease treatment. This technology offers numerous advantages such as ease of design, low cost, high precision, and efficiency. CRISPR enables precise gene addition or deletion in various organisms and cells, allowing for highly accurate genome editing. While these systems have dramatically advanced medical research and gene therapy, it is crucial to address their limitations and potential challenges.

Methods: For this review article, the Google Scholar database was utilized. Articles published from ۲۰۱۹ onwards were included to investigate the applications of CRISPR technology in disease treatment.

Results: The applications and mechanisms of CRISPR technology encompass the development of suitable clinical therapies for a wide range of cancers, such as breast, lung, and colorectal cancer, as well as the discovery of anticancer drugs, the combatting of oncogenic infections, the diagnosis and treatment of genetic blood disorders like sickle cell anemia, the diagnosis and treatment of SARS-CoV-۲, and the treatment of mitochondrial disorders, blindness, Duchenne muscular dystrophy, and neurological diseases. Additionally, its applications extend to agricultural engineering for crop improvement, along with its promising future prospects.

Conclusion: Despite rapid advancements in basic research and clinical trials, CRISPR-Cas systems, as a powerful gene editing approach, face significant challenges including editing efficiency, off-target effects, immunogenicity, and more. Addressing the limitations of this technology is crucial to realizing its full potential.

Keywords: CRISPR-cas۹, treatment, Cancer, gene editing

A review of gut microbiota composition in children with autism spectrum disorder (Review)

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Introduction: Autism spectrum disorder (ASD) is a chronic neurodevelopmental disorder with early onset, which has a prevalence of ١,٧٠,٦٪ among children, and this disorder has been steadily increasing in recent years.

Methods: This systematic review, to identify studies aimed at the effect of gut microbiota in children with autism spectrum disorder, search in Google Scholar, Science Direct, PubMed databases based on keywords Gut microbiota, Autism spectrum disorder, Children Was performed. After reviewing the summary of the articles and checking the title, the irrelevant articles were removed the full text of the articles was searched and the articles related to the topic were included in the study.

Results: According to the studies, people with ASD suffer from neuropsychiatric diseases and intellectual disability, digestive problems (GI), and eating and sleeping disorders. the bacterial characteristics of the intestinal microbiota are unique and different for each person according to age, lifestyle, and eating habits.

Conclusion: Treating the symptoms of autism and associated diseases by adjusting the intestinal microbiota by prescribing probiotics may increase the chances of successful treatment and ensure the quality of people's health.

Keywords: Gut microbiota, Autism spectrum disorder, Children

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A review of psychological interventions in nausea and vomiting caused by chemotherapy in women with breast cancer (Review)

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Introduction: Breast cancer is the most common type of cancer among women, which includes ۳۳٪ of cancers and ۱۹٪ of deaths caused by this cancer. Chemotherapy is an important treatment option for women with breast cancer, however, it has several side effects, the most common of which is nausea and vomiting.

Methods: In this systematic review, to identify studies aimed at psychological interventions in nausea and vomiting caused by chemotherapy in women with breast cancer, Google Scholar, Science Direct, and PubMed databases were searched based on the keywords chemotherapy, breast neoplasms, vomiting, and nausea. After reviewing the summary of the articles and checking the title, the irrelevant articles were removed. The full text of the articles was searched and the articles related to the topic were included in the study.

Results: The results of the studies showed that psychological interventions such as cognitive-behavioral therapy, progressive muscle relaxation exercises, and yoga reduce nausea and vomiting caused by chemotherapy in women with breast cancer.

Conclusion: Breast cancer tumors are one of the psychological interventions that reduce nausea and vomiting caused by chemotherapy in women with breast cancer, and through stress control techniques, breathing and relaxation, and emotional support strategies, the tensions of chemotherapy can be reduced. Facilitate treatment.

Keywords: chemotherapy, breast neoplasms, vomiting, nausea

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A review of stem cells in burn healing (Review)

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Introduction: Burn is a serious health problem with high risk of morbidity and mortality which is divided into three degrees. First-degree burns are not dangerous and are usually treated with home care. Second-degree burns need more care and sometimes they require to follow a treatment because they can be high-risk. Third-degree burns are particularly lethal. In one study, ٦٩٪ of departed patients had second- and third-degree burn. Although there are several treatments available, there is no best cure for them yet. However, stem cell therapy has a very bright prospect in burn's treatment. Stem cells have a fabulous potential, cause their structure gives them the ability to alter to different cell types. They are also one of the most important parts of repairing system.

Methods: In this review study, three databases including google scholar, PubMed and civilica; And keywords like burn, stem cells, burn healing and stem cell therapy are used for gathering the information. Articles that hadn't had our purpose, were omitted from the study process.

Results: The overall researches proved that stem cell therapy has amazingly improved burn healing rate, with no consideration of transplant type, burn area, and treatment method in compared to traditional treatments. Studies indicated that stem cells can accelerate wound healing by enhancing the synthesis of extracellular matrix components, reducing inflammation, and promoting angiogenesis which is crucial for delivering nutrients to healing tissues. Analyses indicated that hair follicle stem cells seemed to exert more positive effects on animals with burn wounds, in comparison with other stem cells. There were some similar researches that analyses ٢٠ studies of Mesenchymal Stem Cells (MSCs) therapy in burn wounds in animals, where stem cell treatment improved closure, reduced wound area, and improved vascularization of the tissues. Most useful ways of Stem cell applications were intradermal injections in the wound edge or wound bed. There are also potential ways of cell application; however, that do not involve injection: topical cells alone, cells encrusted in dressings, and topical treatment with an ointment, or intravascular treatment. A mass group of studies achieved a statistically remarkable improvement in wound healing in groups of animals treated with stem cells from different origins and with various forms of administration.

Conclusion: Although stem cell therapy has worked amazingly so far, it is in the level of experimental studies. Because of limited evidence and randomized studies, the routine use of stem cells in the cure of a burn wound cannot be suggested. Further studies on more patients should be performed to analyze the safety and efficiency of stem cells in burn wound management as well as to establish the most appropriate cell type, origin, and way of application. So, more researches are needed to be expanded.

Keywords: burn, stem cells, burn healing, stem cell therapy

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A review of the application of nanoparticles in the treatment of cutaneous leishmaniasis (Review)

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Introduction: Introduction: Cutaneous leishmaniasis (CL) caused by Leishmania spp. is the most significant endemic disease in Iran, with nearly ٢٠,٠٠٠ new cases of CL reported annually. Unfortunately, despite the substantial prevalence of cutaneous leishmaniasis in Iran, there is still no adequate method for prevention, control, or treatment. Moreover, the development of disfiguring and long-lasting sores on various parts of the body, such as the face, and the potential for secondary infections make the treatment of this disease even more essential. Although pentavalent antimonial compounds remain the first-line treatment for this disease, they present several limitations, including severe side effects, the need for daily injections, and drug resistance. Consequently, the use of nanocomposite drugs in the treatment of this disease has garnered significant attention from researchers. The present study aims to review the effects of nanoparticles studied in relation to leishmaniasis.

Methods: Materials and Methods: In this study, data collection was carried out using keywords related to the role of nanoparticles in the treatment of cutaneous leishmaniasis, such as "Cutaneous leishmaniasis", "Leishmania major", "In vivo", "In vitro", "nanoparticles" and "treatment" in the PubMed, ProQuest, Scopus, Embase, Google Scholar, Science Direct, and Wiley databases.

Results: Findings: The review of various studies indicated that some nanoparticles, including Gold, Silver, Cobalt Oxide, Chromium Oxide, Nickel Oxide, and Bimetallic Gold-Silver, showed significant effects for reducing the symptoms of cutaneous leishmaniasis. For example, ON-AuNPs were found active against Leishmania tropica (KMH٢٣) promastigotes (IC٥٠= ١٢,٥٦ and ٢١,٥٢ µg/mL) and amastigotes (IC٥٠= ١٧,٤٤ and ٤٢,٢٠ µg/mL). Also, Silver nanoparticles produced with the aqueous extract of Zingiber officinale reduced Leishmania major amastigotes at an IC٥٠ of ٢,٣٥ ppm. In another study, results showed that silver nanoparticles coated with curcumin demonstrated strong anti-leishmanial activity with an IC٥٠ of ٥٨,٩٩ µg/mL against promastigotes and an EC٥٠ of ٥٨,٩٩ µg/mL against amastigotes, as well as the Nickel oxide (using floral extracts of Callistemon viminalis) and zinc oxide (leaf extracts of Elaeagnus angustifolia) nanoparticles reduced L. tropica promastigotes at IC٥٠ values of ٣٧ and ٢٤,٩ (µg·mL −١) , respectively.

Conclusion: Conclusion: Unlike typical drugs with high side effects and low efficacy using in the treatment of cutaneous leishmaniasis, studies have shown that nanoparticles can be useful in treating this disease, with low toxicity and high efficacy.

Keywords: Keywords: Leishmania spp., Cutaneous leishmaniasis, Nanoparticles.

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A review of the effects of probiotics on metabolic syndrome (Review)

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Introduction: Obesity is increasing all over the world, which is associated with the development of metabolic syndrome (Mets) and can lead to a series of cardiovascular risk factors and metabolic diseases.

Methods: To identify studies aimed at the effect of probiotics on metabolic syndrome, this systematic review was conducted in Science Direct, Google Scholar, and PubMed databases based on the keywords Probiotics, Metabolic syndrome, and Obesity. After reviewing the summary of the articles and checking the title, the irrelevant articles were removed. The full text of the articles was searched and the articles related to the topic were included in the study.

Results: Changing the composition of the gastrointestinal tract microbiota can contribute to insulin resistance associated with obesity. In addition, consuming probiotics in MetS patients improves body mass index, blood pressure, and glucose metabolism. Also, probiotics positively affect the adhesion of soluble vascular cells.

Conclusion: Probiotics can be used as an adjuvant treatment to improve some clinical features of metabolic syndrome and inflammatory biomarkers. Also, from a clinical point of view, cardiovascular risk may be different in women than in men with this syndrome.

Keywords: Probiotics, Metabolic syndrome, Obesity

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A review of the role of the human microbiome in the pathogenesis of pain (Review)

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Introduction: The intestine has the most populous and diverse anaerobic and aerobic micro-photosystem. Living organisms in the human body are mainly composed of bacteria, however, yeasts, archaea, or parasites that live in a large area of the digestive tract often play a secondary role.

Methods: To identify studies aimed at the role of the human microbiome in the pathogenesis of pain, this systematic review was conducted in the databases of Science Direct, and PubMed Google Scholar, based on the keywords Microbiome, Pain, and Treatment. After reviewing the summary of the articles and checking the title, the irrelevant articles were removed. The full text of the articles was searched and the articles related to the subject were included in the study.

Results: According to the studies, the growing evidence related to the microbiome with stress, anxiety, depression, neurological diseases, and brain functions under the influence of microorganisms can cause pain intensification. gut microbiota covers pain and is a new and promising therapeutic approach for pain management.

Conclusion: Recent studies show that the human microbiome may be an essential component of the pathogenesis of various types of pain. Also, further molecular studies can create new targets for painkiller treatment, significantly improving many patients' quality of life.

Keywords: Microbiome, Pain, Treatment

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A review of the transplantation of human umbilical cord mesenchymal stem cells for the treatment of premature ovarian failure (Review)

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Introduction: Premature ovarian failure (POF) is one of the problems and diseases for women's reproductive health, the frequency of which has increased in recent years. Premature ovarian failure is one of the main causes of female infertility, which is identified before the age of ٤٠.

Methods: In this systematic review, to identify studies aimed at the effect of human umbilical cord mesenchymal stem cell transplantation for the treatment of premature ovarian, search in Science Direct, PubMed, and Google Scholar databases based on keywords Premature ovarian failure, stem cell, umbilical cord was done. After checking the title and abstract of the articles, irrelevant articles were removed. The full text of the articles was searched and the articles related to the topic were included in the study.

Results: The causes of POF are unknown in ٩٠٪ of cases, but studies have shown that treatment with stem cells is an effective method for treating infertility. Several environmental factors such as viral infections, and smoking can cause infertility and POF, and smoking extensively changes ovarian function.

Conclusion: Premature ovarian failure strongly affects the mental and physical health of young women. Women with this disease usually use hormones to treat the symptoms of estrogen deficiency, which is not very effective. We should look for better alternatives to treat most diseases, where treatment with stem cells is more effective than other methods.

Keywords: premature ovarian failure, stem cells, umbilical cord

A review on signaling pathways of Propolis as a nutrition adjuvant in cancer therapy (Review)

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Introduction: Introduction:Cancer is still a global complication which is a major burden for societies. Propolis, is a promising plant-based substance with diverse chemical compounds. Recently, it has been noticed by medical researchers due to extensive therapeutic capacities,. Nowadays, the low side effect therapeutic strategies are necessary in order to alleviate the complications of conventional therapies like surgery, : chemotherapy, and radiotherapy. Therefore, clinical application of propolis as an adjuvant, is hopeful. Anti cancer compounds of propolis trigger different signaling cascades leading to apoptosis and cancer cells death.

Methods: Method: In this review, during the last ١٠ years, anti-cancer and adjuvant potential of propolis, is well-established based on extensive studies.

Results: Result: One of the major mechanisms which is failed in cancer, is programmed cell death (apoptosis). Propolis, can regulate both intrinsic and extrinsic pathways in apoptosis. It was found that ethanolic extract of propolis (EEP) might induce various cascades, including the tumor necrosis factor related apoptosis inducing ligand (TRAIL) pathway, Bcl-٢ associated X protein (Bax) and p٥٣ pathway, and downregulate extracellular signal regulated kinases (ERK١/٢) signaling pathway. The epithelial mesenchymal transition (EMT) plays a crucial role in metastasis. Key pathways such as Wnt, Hedgehog, and Notch are involved in cell motility, invasion, and migration. Additionally, overexpression of Mortalin, a highly conserved heat shock chaperone, in cancer cells contributes to metastasis. CAPE(caffeic acid phenethyl ester) as a well-known anticancer constituent of propolis, can reduce the expression of mortalin, vimentin, MMP٢, MMP٩, β-catenin, Wnt٣α, and TGFβ in breast cancer cells (MDA-MB-٢٣١ and MCF-٧). Angiogenesis inhibitors impede the formation of blood vessels by targeting proteins known as angiogenesis activators, such as vascular endothelial growth factor (VEGF). In tumors, the balance between activators and inhibitors is skewed due to the dominance of pro angiogenic factors. Propolis and some of its components have shown anti angiogenic activity. Caffeic acid (CA) acts as an anti angiogenic compound by inhibiting HIF-١ (hypoxia-inducible factor ١), leading to a reduction in phosphorylated JNK-١ (c-Jun N-terminal kinases). CAPE also inhibits the production of VEGF, MMP-٢, and MMP-٩. One of the main characteristics of tumor cells is their failure to regulate the cell cycle, resulting in uncontrolled cell proliferation. Mechanisms such as Cyclins, which bind and activate cyclin-dependent kinases (CDKs),

control cell division at the appropriate time. CDKs phosphorylate specific targets/molecules that are properly activated during the cell cycle. Propolis and its components regulate cyclin D, CDK٢/٤/٦, and their inhibitors, and upregulate p٢١ and p٢٧, thereby arresting the cell cycle in the G٢/M or G٠/G١ phases. In U٩٣٧-a leukemia cell line- it was found that a methanol extract of propolis increased cell accumulation to ٣٢,٨٪ and ٣٧,٧٪ in the G٢/M phase due to the downregula¬tion of cyclin A, B, CDK٢, and high levels of p٢١ and p٢٧ proteins. Another important protein in cell cycle arrest is p٥٣, which is activated after DNA damage. P٢١, activated by p٥٣, is responsible for the p٥٣ dependent checkpoint and G١ arrest. CAPE and Art C (artepillin C) disinte¬grate the mortalin-P٥٣ complex, leading to P٥٣ activation. In addition to anticancer characteristics of propolis, Synergistic effects with anti cancer drugs reduces the required doses of drugs and their associated side effects. The use of doxorubicin and epirubicin in chemotherapy presents side effects such as liver damage due to oxidative stress via ROS. During oxidative stress, ALT and AST, two key hepatic enzymes, are increased. The antioxidant effects of propolis prevents hepatocyte damage secondary to lipid peroxidation induced by doxorubicin and epirubicin.

Conclusion: Conclusion: The various effective components of propolis are involved in the different biological pathways including critical cell signaling pathways in the onset, progression, and metastasis of cancer cells. The pathways affected by propolis are apoptosis, PI٣k / AKT / mTOR, NF-κB, JAK-STAT, TLR٤, VEGF, and TGFβ path¬ways. The majority of the studies demonstrated the cytotoxicity activity of propolis and its bioactive compounds against various cancer cells. Some studies also investigated the potential synergistic activity of propolis with other therapeutics. Numerous in vitro and in vivo studies, have verified anticancer and adjuvant potential of propolis as a promising drug for further investigation in clinical trials.

Keywords: Keywords: Propolis, anticancer, signaling pathways, apoptosis, anti-proliferation.

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A study of Teriflunomide's effect on alpha-synuclein(۹CK۳) by molecular docking method

(Research Paper)

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Introduction: Parkinson's disease is a chronic, progressive neurodegenerative disease that affects mobility and muscle control.Over the last ۲۰ years, there has been a sharp increase in both the incidence and frequency of this condition. a-Synuclein is a presynaptic neuronal protein associated neuropathologically and genetically with Parkinson's disease (PD). secreted a-synuclein may have harmful effects on neighboring cells such as causing aggregation, which could lead to the propagation of the disease. More specifically, in Parkinson's disease (PD), neuronal dysfunction and degeneration are linked to α-Syn aggregation. Teriflunomide is the second oral agent approved for MS. It can reduce the activity of proliferating T-lymphocytes and B-lymphocytes which can lead to diminishing the overall inflammatory response. This investigation aims to determine whether Teriflunomide can bind to the alpha-synuclein protein as a ligand

Methods: The docking strategy is an analytical descriptive technique and for using this method the ۳D structure of alpha-synuclein was downloaded first from the Protein data bank. The necessary modifications were then made using the Chimera software(version ۱,۱۷,۱), including the removal of solvents, and the evacuation of water molecules The next step was to download the ۳D structure of Teriflunomide from the PubChem site. Afterward, teriflunomide was assigned as a ligand, and alpha-synuclein fibrils were assigned as a receptor using Pyrex software (version ۸). Both data were selected separately and the docking process started. The data output was checked as an Excel file.

Results: According to the docking process, the results were as follows. Ligand Binding Affinity rmsd/ub rmsd/lb finalprp_۹CK۳_۵٤٦۸٤۱٤۱_uff_E=۳٤٦,۸۱_uff_E=۳٤٦,٤۸ -٦,۸ ۰ ۰
finalprp_۹CK۳_۵٤٦۸٤۱٤۱_uff_E=۳٤٦,۸۱_uff_E=۳٤٦,٤۸ -٦,۸ ۱۸,۵٤ ۱۷,۹۵۳
finalprp_۹CK۳_۵٤٦۸٤۱٤۱_uff_E=۳٤٦,۸۱_uff_E=۳٤٦,٤۸ -٦,۸ ۵,۰۹ ۳,۳٦۲
finalprp_۹CK۳_۵٤٦۸٤۱٤۱_uff_E=۳٤٦,۸۱_uff_E=۳٤٦,٤۸ -٦,٦ ٤,٦۵۸ ۳,۱٦۵
finalprp_۹CK۳_۵٤٦۸٤۱٤۱_uff_E=۳٤٦,۸۱_uff_E=۳٤٦,٤۸ -٦,٦ ۷,۹۵۳ ٤,۹۳۸
finalprp_۹CK۳_۵٤٦۸٤۱٤۱_uff_E=۳٤٦,۸۱_uff_E=۳٤٦,٤۸ -٦,٦ ۷,٤ ۵,۱٤۸
finalprp_۹CK۳_۵٤٦۸٤۱٤۱_uff_E=۳٤٦,۸۱_uff_E=۳٤٦,٤۸ -٦,٦ ۱۸,۵۲۷ ۱۸,۰۸
finalprp_۹CK۳_۵٤٦۸٤۱٤۱_uff_E=۳٤٦,۸۱_uff_E=۳٤٦,٤۸ -٦,٦ ۲۰,٤۲۹ ۱۹,۱۲۵
finalprp_۹CK۳_۵٤٦۸٤۱٤۱_uff_E=۳٤٦,۸۱_uff_E=۳٤٦,٤۸ -٦,۵ ۷,٦۰۷ ٤,٦۹۵

Conclusion: alpha-synuclein is one of the key proteins in Parkinson's disease, on which many studies are conducted. As claimed by docking results, we found that there is a probability of binding Teriflunomide to the alpha-synuclein fibril, therefore the clinical trial period of this drug can begin in the field of Parkinson's disease.

Keywords: alpha-synuclein protein, Teriflunomide, Docking method, Parkinson's disease

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A Systematic Review on Strategies for Biofilm Prevention and Control of Listeria monocytogenes in Food Processing Environments (Review)

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Introduction: Listeria monocytogenes is among the most significant pathogens associated with foodborne diseases and is a major concern in the food industry due to its ability to form biofilms, which are resistant to conventional antimicrobial measures and facilitate cross-contamination and possible outbreaks. There is a growing need to explore new strategies for biofilm prevention and control, as current traditional measures are inefficient in eliminating these biofilms. This systematic review critically reviews the current state-of-the-art research on new approaches to combating L. monocytogenes biofilms, including new sanitizers, surface modifications, and enzymatic disruption of biofilm matrices.

Methods: Comprehensive electronic databases, including PubMed, Web of Science, and Scopus, were searched in an attempt to retrieve studies on L. monocytogenes biofilm prevention and control. The search strategy employed the most pertinent keywords and MeSH terms related to "Listeria monocytogenes," "biofilms," "prevention," "control," "sanitizers," "surface modifications," and "enzymatic disruption." Studies published in English between ٢٠١٠ and ٢٠٢٤ were included in the search. All eligible studies subjected the studies to a review to perform assessments of new strategies for preventing or controlling L. monocytogenes biofilms in food processing environments or equivalent laboratory models.

Results: The first search yielded ١,٢٤٧ records. Duplicate records and irrelevant studies were eliminated. An additional ٦٨ publications were included in the final review. These studies examined various strategies for biofilm prevention and control, including the following: Novel sanitizers: Plant-derived antimicrobials, bacteriocins, nanoparticles, and synergistic sanitizer combinations showed promising results in destroying L. monocytogenes biofilms. Surface modifications: Anti-fouling coatings, integration of antimicrobial agents into surface materials, and micro-patterned surfaces showed promise for biofilm prevention or aiding in removal. Enzymatic disruption: Proteases, glycosidases, DNases,. This review, therefore, recommended conducting deep study on molecular mechanisms that regulate biofilm formation and persistence so that these regulatory pathways or their adhesion mechanisms may be targeted to inhibit biofilm formation or to destabilize biofilms that already exist.

Conclusion: This systematic review aims to bring out an overview of the state-of-the-art research work done in the development of strategies that can help in the prevention and control of L. monocytogenes biofilm in food processing. The promising approaches that have come forth so far do require further research to help decide whether these are effective, cost-effective, and workable

in a real-world setup of food production. A partnership between academia, industry, and regulatory bodies will be pivotal to help translate this into practical solutions that work in the domain of food safety and minimizing the risk of L. monocytogenes contamination.

Keywords: Listeria monocytogenes, biofilms, novel sanitizers, surface modifications, food safety

Abdomen Computed Tomography-based Radiomics and Machine Learning for Bone Mineral Density Evaluation: A review (Review)

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Introduction: The evaluation of bone mineral density (BMD) is crucial for diagnosing and managing osteoporosis and other metabolic bone diseases. Traditional methods, such as dual-energy X-ray absorptiometry (DXA), have limitations in accessibility and precision. Recent advancements in radiomics and machine learning (ML) offer promising alternatives. This review explores the application of abdomen computed tomography (CT)-based radiomics combined with ML techniques for BMD evaluation, highlighting their potential to enhance diagnostic accuracy and clinical outcomes.

Methods: A comprehensive literature search was conducted across multiple databases, including PubMed and Scopus focusing on studies published between ٢٠١٠ and ٢٠٢٣. Keywords included “abdominal CT,” “radiomics,” “machine learning,” and “bone mineral density.” Selected studies were assessed for methodological quality and relevance. Data extraction focused on the type of radiomics features used, ML algorithms applied, and the performance metrics reported. Comparative analyses were performed to evaluate the efficacy of CT-based radiomics and ML models against traditional DXA measurements.

Results: The review identified ٢٥ relevant studies that utilized abdomen CT-based radiomics and ML for BMD evaluation. Commonly extracted radiomics features included texture, shape, and intensity-based metrics. ML algorithms such as support vector machines (SVM), random forests, and deep learning models demonstrated high predictive accuracy, with some studies reporting area under the curve (AUC) values exceeding ٠,٩٠. Comparative analyses indicated that CT-based radiomics and ML models provided comparable or superior BMD assessments relative to DXA, particularly in detecting early-stage osteoporosis and assessing fracture risk.

Conclusion: Abdomen CT-based radiomics combined with ML techniques represents a promising approach for BMD evaluation. The integration of advanced imaging features and sophisticated ML algorithms can potentially overcome the limitations of traditional methods, offering enhanced diagnostic precision and early detection capabilities. Future research should focus on standardizing

radiomics feature extraction, optimizing ML models, and validating these approaches in larger, diverse populations to facilitate clinical translation and widespread adoption.

Keywords: Bone Mineral Density, Computed Tomography, Radiomics, Machine Learning

Adherence to the ٢٠١٨ AHA cholesterol management guideline in hyperlipidemia treatment among adults in an outpatient setting (Research Paper)

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Introduction: Although evidence-based guidelines and effective treatments exist for dyslipidemia, a significant disparity remains between guidelines and clinical practice. In this study, we investigated adherence to statin therapy per the ٢٠١٨ ACC/AHA Guideline recommendations

Methods: This is a retrospective, descriptive-analytical study involving ١,٢٢٤ individuals who presented to the laboratories located in Birjand, Eastern Iran, from June ٢٠٢٢ to March ٢٠٢٣. Analyses were conducted on ٧٠٠ patients. Data collection utilized a checklist and serum value measurements of laboratory factors deemed necessary for the study

Results: Treatment was administered per the guidelines for ٣٤٨ out of the ٧٠٠ patients (٤٩,٧٪). With ٦٠,٧٪, the diabetes group exhibited the highest level of adherence to guidelines. In the atherosclerotic cardiovascular disease (ASCVD) group, ٣١,٧٪ followed the recommendations. The lowest adherence rates were in groups with a ١٠-year ASCVD risk score of ≥٢٠٪ and severe hypercholesterolemia, respectively (٠٪ and ٢,٨٪). In our study, atorvastatin was the most frequently prescribed statin, with the majority of patients consuming a moderate-intensity statin. None of the severely hypercholesterolemic patients achieved the LDL goal. Moreover, LDL-C goal achievement was low among the ASCVD group and those with an ASCVD risk score of ≥٢٠٪.

Conclusion: Patients with hypercholesterolemia adhere inadequately to the AHA Guideline. Consequently, training courses are needed to inform medical doctors, particularly general practitioners, of the latest dyslipidemia treatment recommendations as the AHA advises

Keywords: statin, AHA Guideline, diabetes, ASCVD, hyperlipidemia

Advancements and Future Outlook in Single-Cell Analysis (Review)

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Introduction: Single-cell sequencing is an approach to detect the gene sequence information at single-cell level, yielding a new understanding of the gene expression profiling of an individual cell between heterogeneous populations. It has been proved that both eukaryotic and prokaryotic cell populations are heterogeneous. This is to say individual cells in populations differ dramatically in size, protein levels, and expressed RNA transcripts. Hence it is not far enough to analyze the physiological characteristics on the level of homogenized cell population, which may ignore the critical changes occurring in individual cells. Single-cell analysis is performed to analyze the genomics, transcriptomics, proteomics, and metabolomics at the single-cell level, enabling it possible to discover mechanisms not seen when studying a bulk population of cells.

Methods: Here's a brief overview of a typical single-cell RNA sequencing (scRNA-seq) workflow: Sample Preparation: Isolate single cells from the tissue or culture of interest. This can be done using methods like fluorescence-activated cell sorting (FACS) or microfluidics. Cell Lysis and RNA Capture: Lyse the cells to release their RNA. Capture the RNA using specialized beads or plates that contain oligonucleotides designed to bind RNA molecules. Reverse Transcription and Amplification: Convert the captured RNA into complementary DNA (cDNA) using reverse transcription. Amplify the cDNA to generate enough material for sequencing. Library Preparation: Prepare sequencing libraries from the amplified cDNA. This involves adding adapters and barcodes to the cDNA fragments to enable sequencing and identification of individual cells. Sequencing: Sequence the prepared libraries using high-throughput sequencing platforms like Illumina. Data Analysis: Process the sequencing data to align reads, quantify gene expression, and identify cell types and states. This step requires advanced bioinformatics tools and expertise. Interpretation: Analyze the results to gain insights into cellular heterogeneity, gene expression patterns, and potential biological mechanisms.

Results: The advances of single-cell analysis over the past ٥ years have happened at a lightning pace, and the potential for their use in various fields is high. However, the novelty of these single-cell techniques also implies various limitations. Due to the heterogeneity present in cell populations, it is necessary to analyze the function of individual cells at high resolution. Single-cell function analysis provides a novel understanding of the function of an organ or tissue or system and the interaction of single cells on a global scale. For example, single tumor cell function analysis helps to explain the different responses of different patients to the same anti-cancer drug and the mechanism of anti-cancer drug resistance, promoting to develop more effective therapeutic strategies.

Conclusion: Single-cell analysis, while incredibly powerful, comes with several challenges like Technical Complexity, the procedures involved, such as isolating individual cells and preparing them for analysis, require highly specialized equipment and expertise. This can make the process time-

consuming and costly. Despite these challenges, ongoing advancements in technology and methodology are continually improving the robustness and accessibility of single-cell analysis.

Keywords: RNA-Seq, single cell, Data Analysis, Sequencing

Advancements in Tissue Engineering and Stem Cell Therapy for Optic Nerve Regeneration: The Role of Nfe۲ (Research Paper)

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Introduction: Optic nerve damage, resulting from conditions such as glaucoma or traumatic injuries, leads to irreversible vision loss due to the limited regenerative capacity of retinal ganglion cells (RGCs). Traditional treatments have been largely ineffective in restoring vision, highlighting the need for innovative approaches. Recent advancements in tissue engineering and stem cell therapy offer promising solutions for optic nerve regeneration. This paper explores the potential of Nuclear Factor Erythroid ۲ (Nfe۲) in promoting the regrowth of optic nerve fibers, presenting a novel avenue for restoring vision in affected individuals. Tissue engineering and stem cell therapy are pivotal strategies in regenerative medicine. Biomaterial scaffolds that mimic the extracellular matrix provide a supportive environment for cells to attach, grow, and differentiate, while releasing growth factors to enhance regeneration. Techniques have been developed to convert stem cells, such as induced pluripotent stem cells (iPSCs) and embryonic stem cells (ESCs), into retinal ganglion cells (RGCs) capable of replacing damaged cells. Additionally, gene therapy can improve the survival and integration of transplanted cells. Tools like CRISPR/Cas۹ enable the modification of stem cells to express neuroprotective factors, further enhancing their regenerative potential. Nfe۲ is a crucial protein for optic nerve regeneration. Research has shown that stimulating Nfe۲ production in adult mice with crushed optic nerves leads to significant regrowth of nerve fibers without adverse effects. Gene therapy techniques that stimulate Nfe۲ production have demonstrated successful regeneration of nerve fibers in damaged optic nerves. The effectiveness of Nfe۲ in promoting optic nerve regeneration suggests its potential in treating other nerve injuries in the brain and spinal cord, making it a promising target for developing therapies for neurodegenerative diseases and traumatic injuries. Tissue engineering and stem cell therapy are pivotal strategies in regenerative medicine. Biomaterial scaffolds that mimic the extracellular matrix provide a supportive environment for cells to attach, grow, and differentiate, while releasing growth factors to enhance regeneration. Techniques have been developed to convert stem cells, such as induced pluripotent stem cells (iPSCs) and embryonic stem cells (ESCs), into retinal ganglion cells (RGCs) capable of replacing damaged cells. Additionally, gene therapy can improve the survival and integration of transplanted cells. Tools like CRISPR/Cas۹ enable the modification of stem cells to express neuroprotective factors, further enhancing their regenerative potential. Nfe۲ is a crucial protein for optic nerve regeneration. Research has shown that stimulating Nfe۲ production in adult mice with crushed optic nerves leads to significant regrowth of nerve fibers without adverse effects. Gene therapy techniques that stimulate Nfe۲ production have demonstrated successful regeneration of nerve fibers in damaged optic nerves. The effectiveness of Nfe۲ in promoting optic nerve regeneration suggests its potential in treating other nerve injuries in the brain and spinal cord, making it a promising target for developing therapies for neurodegenerative diseases and traumatic injuries.

Methods: Experimental models, particularly rodents, are used to study the effects of Nfe۲ on optic nerve regeneration. These models involve inducing optic nerve injury through controlled crush injuries and subsequently administering Nfe۲ gene therapy using viral vectors. Biomaterial scaffolds are developed and characterized to support cell growth and differentiation. Pluripotent stem cells (iPSCs and ESCs) are cultured and induced to differentiate into RGCs. Gene editing tools like CRISPR/Cas۹ are employed to enhance the expression of neuroprotective factors in stem cells. Delivery of Nfe۲ genes to target cells is achieved using viral vectors, such as adeno-associated viruses (AAVs). Quantitative PCR and Western blotting are used to confirm gene expression levels.

Results: Significant regrowth of nerve fibers was observed in animal models treated with Nfe۲ gene therapy. Histological analysis using immunohistochemistry showed that the regenerated fibers exhibited proper orientation and connectivity with target tissues. The density of regenerating axons was significantly higher in the Nfe۲-treated group compared to controls. Behavioral tests, such as the optokinetic response (OKR) and visual cliff test, indicated partial recovery of visual function in treated animals. These tests demonstrated that the regenerated fibers were not only structurally intact but also functionally active. The biomaterial scaffolds were found to be biocompatible, with no signs of chronic inflammation or immune rejection. The gene therapy approach did not result in tumor formation or other adverse effects, as confirmed by long-term monitoring and histopathological analysis. Nfe۲ gene therapy showed superior results compared to other regenerative factors, such as BDNF and CNTF, in terms of both nerve regrowth and functional recovery. Statistical analysis using ANOVA and post-hoc tests confirmed the significance of these findings.

Conclusion: Combining tissue engineering, stem cell therapy, and the application of Nfe۲ represents a significant advancement in optic nerve regeneration. These approaches offer a promising way to restore vision and improve the quality of life for individuals with optic nerve damage. Future research should focus on optimizing these techniques and translating them into clinical therapies. The potential of Nfe۲ in treating other forms of nerve injuries in the brain and spinal cord also warrants further investigation.

Keywords: Optic nerve regeneration, tissue engineering, stem cell therapy, Nfe۲

Advances and potential of immunotherapy against malignant Glioblastoma multiforme (Review)

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Introduction: Primary brain cancer that is most commonly aggressive is called glioblastoma multiforme (GBM). Gliomas (tumors arising from glial cells) and non-gliomas are the two categories into which brain malignancies are classified. Astrocytomas, ependymomas, and oligodendrogliomas are the three sub-classes of gliomas that are further classified based on the kind of glial cell involved in the creation of the tumor. GBM is classified as a stage IV high-grade malignant astrocytoma. Though it is a rare tumor type with a global prevalence of fewer than ١٠ cases per ١٠٠,٠٠٠ individuals, GBM has an extremely unfavorable prognosis. Although GBM can develop at any age, it is typically detected in older adults, with a median diagnostic age of ٦٥. Males are more likely than females to be diagnosed with GBM. The aim of this study was Advances and potential of immunotherapy against malignant Glioblastoma multiforme.

Methods: The present study is titled Advances and potential of immunotherapy against malignant Glioblastoma multiforme which was done by searching scientific databases such as Science Direct, Springer, Google Scholar and PubMed.

Results: Activated immune cells can be injected intravenously into the patient's body or implanted and inserted into the tumor cavity as part of cell-based immunotherapy, sometimes referred to as adaptive immunity. The first cells employed in glioblastoma patients' clinical trials and investigations were natural killer cells triggered by lymphocytes. These cells are taken from interleukin-٢-cultured peripheral blood lymphocytes. Cytotoxic T cells and cells with the ability to invade and assault targets systematically are produced as a result of this process; nevertheless, they do not exclusively target glioblastoma cells. This method's initial phase of clinical studies has mainly failed. The findings of a review of ٣٦ individuals who received autologous activated natural killer cell lymphokine were published by Dillman et al. At one year, ٧٥٪ of patients had an average survival of ٢٠ months. Another strategy is to collect lymphocytes from peripheral blood and lymph nodes after peripheral injection of autologous tumor cells that have been rendered inactive by radiation and GM-CSF. These lymphocytes are then stimulated by autologous tumor cells, which can be used as an antigenic source in clinical trials. After being reactivated in vitro, these cells were reinjected into the patients.

Conclusion: GBM still has significant therapeutic obstacles in spite of advancements in techniques including brain surgery, radiation, and chemotherapy. One area of research that is making headway is the targeted targeting of host immune system stimulation to kill brain tumor cells without damaging healthy surrounding tissue. Aggression and the fact that the tumor always develops are two features of GBM. According to recent research, immunotherapy techniques may be able to locate and eradicate GBM cell invasion in the brain. Special Remarks Furthermore, immunotherapy using tumor T cells holds significant promise for treating GBM as it can completely eradicate tumor

recurrence. They can be applied in addition to existing therapies. Although several effective strategies in animal models have been clinically proven in human GBM, these studies have not yet reached the testing stage.

Keywords: Glioblastoma multiforme, Cytotoxic T cells, immunotherapy

Advances in Biotechnology for Disease Diagnosis and Treatment (Review)

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Introduction: Biotechnology has emerged as a transformative field in healthcare, revolutionizing both the diagnosis and treatment of diseases. The integration of biotechnology with artificial intelligence, molecular diagnostics, and personalized medicine has provided clinicians with more accurate, efficient, and timely tools to manage various diseases. This review aims to explore recent advancements in biotechnology, particularly focusing on its role in disease diagnosis and therapeutic development. Several groundbreaking approaches, such as gene editing, molecular diagnostics, and (bio)printing, are now at the forefront of modern medicine.

Methods: This review is based on an extensive analysis of recent literature, focusing on key articles that have contributed to our understanding of biotechnological advancements in medicine. The primary articles used include those published in peer-reviewed journals addressing innovations such as AI-assisted diagnostics, advances in personalized medicine, and novel therapeutic techniques. Key sources include: ١. Advances in AI and manufacturing in biotechnology. ٢. Personalized medicine through bioprinting technologies. ٣. Recent developments in gene therapy. The review synthesizes the methodologies discussed in these articles to understand the broader trends in the field.

Results: Recent studies show significant progress in several areas of biotechnology: ١. Artificial Intelligence and Diagnostics AI and machine learning are increasingly integrated into diagnostic platforms. Algorithms can now analyze complex datasets such as medical images or genetic sequences, allowing for early detection of diseases such as cancer. According to recent studies , AI models have achieved higher accuracy in diagnosing conditions like breast cancer from imaging data than traditional methods. These technologies are also used to predict disease progression, enabling earlier interventions. ٢. Molecular Diagnostics Biotechnology has expanded the scope of molecular diagnostics, which use biomarkers to detect diseases at the molecular level. This technology is especially critical in diagnosing genetic disorders, cancers, and infectious diseases. In a ٢٠٢٣ study , molecular diagnostics played a pivotal role in the early detection of COVID-١٩, reducing mortality rates through rapid intervention. Innovations such as CRISPR-based diagnostics are set to become commonplace in clinical settings. ٣. Personalized Medicine and (Bio)Printing One of the most promising advances is personalized medicine, where treatments are tailored to individual patients based on their genetic profile. ٣D bioprinting technology has enabled the creation of patient-specific tissues and organs for transplantation, offering a more precise and effective therapeutic strategy. A ٢٠٢٤ study highlights that (bio)printing technologies are critical in developing personalized treatments for diseases such as liver and kidney failure, where donor organs are scarce. ٤. Gene Therapy Gene editing technologies like CRISPR have opened new frontiers in treating genetic diseases. These methods allow for direct modification of faulty genes responsible for conditions like cystic fibrosis or muscular dystrophy. Research has shown promising results, with gene therapies

curing diseases previously considered untreatable . Furthermore, advancements in gene therapy are now expanding into cancer treatment, where genetic modifications are made to enhance the patient's immune system to target cancer cells.

Conclusion: The integration of biotechnology in medical diagnostics and treatment is reshaping the landscape of modern healthcare. From AI-driven diagnostic tools to personalized medicine and gene therapy, the advances discussed in this review highlight the potential of biotechnology to not only improve the accuracy and efficiency of disease diagnosis but also to offer more effective, patient-specific treatments. As research continues, it is likely that these technologies will become even more refined, leading to a new era in healthcare where precision medicine becomes the standard of care. Further exploration and funding into these areas will be crucial in realizing the full potential of biotechnology in improving patient outcomes.

Keywords: Biotechnology, Molecular Diagnostics , Personalized Medicine and (Bio)Printing ,Gene Therapy

Advances in cancer treatment using anticancer vaccines (Review)

sina kazemi dogolsar,[1,*]

١.

Introduction: Cancer, as one of the major health challenges of today, due to the biological complexities and variety of tumors, its effective treatment has become a global problem. Conventional treatment methods include surgery, chemotherapy, radiotherapy, and targeted therapies, each of which has its own advantages and disadvantages and may be associated with significant side effects. In particular, surgery and chemotherapy face certain limitations and often require careful management of side effects. In this regard, anti-cancer vaccines have been considered as a new therapeutic approach. These vaccines are divided into two main categories: preventive vaccines, which are designed to prevent cancer in high-risk individuals, and therapeutic vaccines, which are used to stimulate the body's immune response to fight cancer cells in cancer patients. This article examines recent advances in the field of anti-cancer vaccines, including benefits, challenges and problems in this field, and analyzes the performance of various vaccines and strategies to improve their effectiveness. The aim of this review is to provide an overview of the current status and future prospects in the use of anticancer vaccines as a complementary and novel therapy.

Methods: Introduction: Cancer is one of the most complex and life-threatening human diseases, resulting from genetic and epigenetic changes in cells. These changes disrupt normal cellular processes such as cell division, differentiation, and apoptosis. Cancer occurs when the body's cells begin to proliferate uncontrollably, forming malignant tumors. In this process, cancer cells escape the natural mechanisms of cellular control and circumvent the body's defense systems to promote their own growth. ١. Mechanisms of Cancer Formation Cancer is a multi-stage disease arising from numerous alterations in the genome of cells. These changes may be caused by environmental factors (such as carcinogenic chemicals, radiation, and viruses) or internal factors (such as inherited genetic mutations). The genes involved in cancer are generally classified into three categories: ١,١. Oncogenes: Oncogenes are mutated versions of normal genes called proto-oncogenes, which are naturally involved in biological processes like growth and cell division. Mutations or overexpression of these genes can lead to their abnormal activation and tumor development [١]. ١,١,١. Mechanisms of Oncogene Action Oncogenes contribute to cancer through several mechanisms: Point mutations: These mutations may lead to changes in the amino acid sequence of proteins, resulting in abnormal activity. For instance, a mutation in the RAS gene can lead to the continuous production of active RAS proteins, sending constant growth signals [٢]. Overexpression: Increased expression of an oncogene can lead to the overproduction of proteins responsible for cell division and growth. Genes such as MYC and HER٢ exemplify this mechanism [٣]. Gene fusion: In some cases, fusion of oncogenes with other genes can result in abnormal proteins. For example, gene fusions in leukemia (e.g., BCR-ABL) produce fusion proteins with abnormal activity [٤]. ١,٢. Role of Oncogenes in Cancer Oncogenes play various roles in different cancers: Breast cancer: The HER٢/neu oncogene is one of

the most important in breast cancer, promoting increased growth and proliferation of cancer cells. Targeted therapies like trastuzumab (Herceptin) have been designed to inhibit the activity of this protein [٥]. Lung cancer: Genes such as RAS and EGFR play critical roles in non-small cell lung cancer (NSCLC). Alterations in these genes can lead to disease progression and resistance to standard therapies [٦]. Leukemia: In blood cancers such as acute myeloid leukemia (AML), mutations in the FLT٣ gene contribute to the development and progression of the disease [٧]. ٢. Tumor Suppressor Genes: Tumor suppressor genes are key regulators that control cell growth and division, preventing cancer development. These genes generally function in two ways: first, by producing proteins that help control the cell cycle and prevent abnormal cell division; second, by repairing DNA damage to avoid the genetic changes that may lead to cancer [٨]. ٢,١. Key Tumor Suppressor Genes p٥٣ Gene: The p٥٣ gene is one of the most crucial tumor suppressor genes, often referred to as the "guardian of the genome" [٩]. The p٥٣ protein helps regulate the cell cycle and induce apoptosis (programmed cell death). When DNA damage occurs, p٥٣ halts cell proliferation, facilitating DNA repair, and if unsuccessful, it induces apoptosis [١٠]. BRCA١ and BRCA٢ Genes: These genes are also recognized as important tumor suppressors that help repair DNA damage. Mutations in BRCA١ and BRCA٢ are associated with increased risks of breast and ovarian cancers. These genes encode proteins involved in DNA repair processes [١٢]. PTEN Gene: PTEN is another tumor suppressor gene that regulates cellular signaling pathways, especially the PI٣K/Akt pathway [١٣]. PTEN mutations are linked to various cancers, including prostate, breast, and thyroid cancers [١٥]. ٣. DNA Repair Genes: DNA repair genes play a crucial role in maintaining genetic integrity and preventing harmful mutations. These genes are responsible for identifying and repairing DNA damage caused by environmental, internal, or natural replication errors [٢٠]. Dysfunction in these genes can lead to various diseases, including cancer [٢١]. ٤. The Role of the Immune System in Cancer Defense One of the body's first lines of defense against cancerous cells is the immune system, which consists of components like lymphocytes, macrophages, and natural killer (NK) cells that play a role in recognizing and destroying abnormal cells. Specifically, T cells are crucial in identifying cancer cells by recognizing cancer antigens on their surfaces and initiating the destruction process [٣٠]. Cancer Immune Evasion Mechanisms Cancer cells can employ various mechanisms to evade immune detection: Reduced antigen presentation: Cancer cells may reduce the expression of antigens recognized by the immune system. In particular, the downregulation of MHC class I molecules on the surface of cancer cells may result in decreased recognition by T cells [٣١]. Suppression of immune responses: Cancer cells can secrete chemicals like tumor growth factors and cytokines that suppress immune activity. These substances may induce regulatory T cells (Tregs), which naturally inhibit immune responses and reduce the body's ability to fight cancer [٣٢]. Expression of inhibitory proteins: Cancer cells often express proteins such as PD-L١, which bind to inhibitory receptors like PD-١ on T cells, preventing their activation. This is one of the primary mechanisms through which cancer evades the immune system [٣٣]. Cancer Vaccines One significant advancement in the fight against cancer is the development of cancer vaccines, aimed at boosting the immune system to recognize and destroy cancer cells. Unlike traditional vaccines that protect against viral or bacterial infections, cancer vaccines are categorized into preventive and therapeutic vaccines. These vaccines are designed to stimulate the immune system to recognize specific cancer cell antigens and activate immune cells for

targeted action. Types of Cancer Vaccines Cancer vaccines are broadly classified into several categories, each employing different mechanisms to stimulate an immune response against cancer cells: Neoantigen-based vaccines Dendritic cell vaccines DNA and RNA vaccines Peptide vaccines Oncolytic virus vaccines Protein-based vaccines Tumor cell vaccines Liposome-based vaccines Chimeric antigen receptor (CAR) vaccines Nanoparticle-based vaccines Hybrid vaccines Epitope-based vaccines Microbiome-based vaccines The article will further explore some of these vaccine types.

Results: Introduction: Cancer is one of the most complex and life-threatening human diseases, resulting from genetic and epigenetic changes in cells. These changes disrupt normal cellular processes such as cell division, differentiation, and apoptosis. Cancer occurs when the body's cells begin to proliferate uncontrollably, forming malignant tumors. In this process, cancer cells escape the natural mechanisms of cellular control and circumvent the body's defense systems to promote their own growth. ١. Mechanisms of Cancer Formation Cancer is a multi-stage disease arising from numerous alterations in the genome of cells. These changes may be caused by environmental factors (such as carcinogenic chemicals, radiation, and viruses) or internal factors (such as inherited genetic mutations). The genes involved in cancer are generally classified into three categories: ١,١. Oncogenes: Oncogenes are mutated versions of normal genes called proto-oncogenes, which are naturally involved in biological processes like growth and cell division. Mutations or overexpression of these genes can lead to their abnormal activation and tumor development [١]. ١,١,١. Mechanisms of Oncogene Action Oncogenes contribute to cancer through several mechanisms: Point mutations: These mutations may lead to changes in the amino acid sequence of proteins, resulting in abnormal activity. For instance, a mutation in the RAS gene can lead to the continuous production of active RAS proteins, sending constant growth signals [٢]. Overexpression: Increased expression of an oncogene can lead to the overproduction of proteins responsible for cell division and growth. Genes such as MYC and HER٢ exemplify this mechanism [٣]. Gene fusion: In some cases, fusion of oncogenes with other genes can result in abnormal proteins. For example, gene fusions in leukemia (e.g., BCR-ABL) produce fusion proteins with abnormal activity [٤]. ١,٢. Role of Oncogenes in Cancer Oncogenes play various roles in different cancers: Breast cancer: The HER٢/neu oncogene is one of the most important in breast cancer, promoting increased growth and proliferation of cancer cells. Targeted therapies like trastuzumab (Herceptin) have been designed to inhibit the activity of this protein [٥]. Lung cancer: Genes such as RAS and EGFR play critical roles in non-small cell lung cancer (NSCLC). Alterations in these genes can lead to disease progression and resistance to standard therapies [٦]. Leukemia: In blood cancers such as acute myeloid leukemia (AML), mutations in the FLT٣ gene contribute to the development and progression of the disease [٧]. ٢. Tumor Suppressor Genes: Tumor suppressor genes are key regulators that control cell growth and division, preventing cancer development. These genes generally function in two ways: first, by producing proteins that help control the cell cycle and prevent abnormal cell division; second, by repairing DNA damage to avoid the genetic changes that may lead to cancer [٨]. ٢,١. Key Tumor Suppressor Genes p٥٣ Gene: The p٥٣ gene is one of the most crucial tumor suppressor genes, often referred to as the "guardian of the genome" [٩]. The p٥٣ protein helps regulate the cell cycle and induce apoptosis (programmed

cell death). When DNA damage occurs, p٥٣ halts cell proliferation, facilitating DNA repair, and if unsuccessful, it induces apoptosis [١٠]. BRCA١ and BRCA٢ Genes: These genes are also recognized as important tumor suppressors that help repair DNA damage. Mutations in BRCA١ and BRCA٢ are associated with increased risks of breast and ovarian cancers. These genes encode proteins involved in DNA repair processes [١٢]. PTEN Gene: PTEN is another tumor suppressor gene that regulates cellular signaling pathways, especially the PI٣K/Akt pathway [١٣]. PTEN mutations are linked to various cancers, including prostate, breast, and thyroid cancers [١٥]. ٣. DNA Repair Genes: DNA repair genes play a crucial role in maintaining genetic integrity and preventing harmful mutations. These genes are responsible for identifying and repairing DNA damage caused by environmental, internal, or natural replication errors [٢٠]. Dysfunction in these genes can lead to various diseases, including cancer [٢١]. ٤. The Role of the Immune System in Cancer Defense One of the body's first lines of defense against cancerous cells is the immune system, which consists of components like lymphocytes, macrophages, and natural killer (NK) cells that play a role in recognizing and destroying abnormal cells. Specifically, T cells are crucial in identifying cancer cells by recognizing cancer antigens on their surfaces and initiating the destruction process [٣٠]. Cancer Immune Evasion Mechanisms Cancer cells can employ various mechanisms to evade immune detection: Reduced antigen presentation: Cancer cells may reduce the expression of antigens recognized by the immune system. In particular, the downregulation of MHC class I molecules on the surface of cancer cells may result in decreased recognition by T cells [٣١]. Suppression of immune responses: Cancer cells can secrete chemicals like tumor growth factors and cytokines that suppress immune activity. These substances may induce regulatory T cells (Tregs), which naturally inhibit immune responses and reduce the body's ability to fight cancer [٣٢]. Expression of inhibitory proteins: Cancer cells often express proteins such as PD-L١, which bind to inhibitory receptors like PD-١ on T cells, preventing their activation. This is one of the primary mechanisms through which cancer evades the immune system [٣٣]. Cancer Vaccines One significant advancement in the fight against cancer is the development of cancer vaccines, aimed at boosting the immune system to recognize and destroy cancer cells. Unlike traditional vaccines that protect against viral or bacterial infections, cancer vaccines are categorized into preventive and therapeutic vaccines. These vaccines are designed to stimulate the immune system to recognize specific cancer cell antigens and activate immune cells for targeted action. Types of Cancer Vaccines Cancer vaccines are broadly classified into several categories, each employing different mechanisms to stimulate an immune response against cancer cells: Neoantigen-based vaccines Dendritic cell vaccines DNA and RNA vaccines Peptide vaccines Oncolytic virus vaccines Protein-based vaccines Tumor cell vaccines Liposome-based vaccines Chimeric antigen receptor (CAR) vaccines Nanoparticle-based vaccines Hybrid vaccines Epitope-based vaccines Microbiome-based vaccines The article will further explore some of these vaccine types.

Conclusion: conclusion At the end of this article, it can be concluded that anti-cancer vaccines have shown high potential as a new treatment strategy in dealing with different types of cancers. Considering the challenges in traditional treatments such as chemotherapy and radiotherapy that may face severe side effects and drug resistance, anti-cancer vaccines can play an effective role as a

complementary or alternative method in the management of cancer diseases. Among the most important advantages of anti-cancer vaccines is their ability to be personalized based on the genetic characteristics of each patient. These vaccines can be designed based on specific neoantigens that are produced in cancer cells and directly stimulate the body's immune system to recognize and destroy cancer cells. This feature increases the efficiency of treatment and reduces side effects. In this context, neoantigen vaccines are one of the most promising strategies in personalized immunotherapy due to their ability to stimulate strong immune responses. Another effective strategy in anti-cancer vaccines is the use of dendritic cells. Dendritic cells play a key role in the activation of T cells due to their high ability to absorb and process antigens. These vaccines can help fight cancer cells by strengthening the body's immune system. Although the production of these vaccines is complex and expensive, they have shown promising results in the treatment of various cancers, including melanoma and prostate cancer. However, there are many challenges in the development and application of these vaccines. One of these challenges is the cost and time-consuming process of producing vaccines due to the need for genomic sequencing and bioinformatics analysis. Also, the immune response to these vaccines may vary among different patients, which requires further research to optimize processes and increase the effectiveness of treatments. In general, anti-cancer vaccines as a new and complementary strategy in the treatment of cancers have shown great potential and have a bright future in the field of cancer treatment. Nevertheless, there is still a need for more research and improvement of the production and application processes of these vaccines in order to achieve a significant improvement in the control and treatment of cancer.

Keywords: conclusion At the end of this article, it can be concluded that anti-cancer vaccines have shown hig

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Advances in CRISPR-Cas Technology: Implications for the Treatment of Cancer and RNA Virus Infections (Review)

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Introduction: CRISPR-Cas, which stands for "Clustered Regularly Interspaced Short Palindromic Repeats," is recognized as a bacterial defense system that bacteria use to protect themselves against viral infections. In recent years, CRISPR has emerged as a powerful tool for gene editing in more complex organisms, including humans, animals, and plants. This technology enables scientists to make precise and targeted changes to the genome. Bacteria use CRISPR to cut and destroy the DNA of viruses that attack them. This system includes a guide RNA segment and an enzyme called Cas٩, which cuts the DNA at specific locations.

Methods: The present review study explores the role of CRISPR-Cas in the treatment of various diseases such as cancer and RNA viruses, as well as recent technological advancements in this system. Relevant documents were sought through searches in databases such as PubMed, Google Scholar, and ScienceDirect using keywords including CRISPR-Cas٩, gene editing, and gene therapy. ٤٠ articles were selected within the timeframe of ٢٠١٩ to ٢٠٢٤. After analyzing the sources, ٢٨ articles that were more comprehensive and closely related in topic, were selected for inclusion in this paper.

Results: The high precision and efficiency of the CRISPR-Cas system have enabled it to target and edit specific genes associated with the growth and proliferation of cancer cells, aiding in the control of this disease. One of the important applications of CRISPR-Cas in cancer treatment is immunotherapy. In this approach, the patient's T cells are engineered using CRISPR, enhancing their ability to identify and attack cancer cells. This strategy has shown promising results in treating cancers such as leukemia and advanced melanoma. Additionally, CRISPR-Cas is effective in treating infections caused by RNA viruses. This technology can eliminate the genome of the HIV virus from infected cells, potentially leading to a cure for this disease. In response to the COVID-١٩ pandemic, efforts have been made to use CRISPR-Cas to destroy the RNA of the SARS-CoV-٢ virus and reduce the severity of the infection. Technological advancements also include the use of CRISPR-Cas for epigenetic editing and controlling gene expression without altering the DNA sequence. This new approach can serve as a powerful tool for scientific research and disease treatment.

Conclusion: CRISPR-Cas, as a powerful gene editing tool, holds tremendous potential for treating various diseases, especially cancer and viral infections. With continuous advancements in this technology, it is expected that its clinical applications will expand, potentially leading to a major breakthrough in medical science. The findings from this study indicate that CRISPR-Cas is not only impactful in basic research but also in clinical applications, paving the way for its acceptance as a standard therapeutic approach in the near future.

Keywords: CRISPR-Cas, Genome editing, Gene therapy, Cancer treatment

Advances in Medical Genetics: Transforming Diagnosis and Treatment (Review)

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Introduction: Medical genetics is a branch of medicine that focuses on the genetic basis of health and disease. It involves the study of genetic disorders, the development of genetic tests, and the application of genetic knowledge to improve patient care. With the advent of advanced genomic technologies, medical genetics has become a pivotal field in modern medicine, offering insights into the diagnosis, treatment, and prevention of various diseases. Genetic Disorders Genetic disorders are conditions caused by abnormalities in an individual's DNA. These abnormalities can be inherited from parents or occur spontaneously. Some well-known genetic disorders include: - Cystic Fibrosis: A condition caused by mutations in the CFTR gene, leading to severe respiratory and digestive problems. - Sickle Cell Anemia: A blood disorder caused by a mutation in the HBB gene, resulting in misshapen red blood cells. - Huntington's Disease: A neurodegenerative disorder caused by a mutation in the HTT gene, leading to progressive brain damage.

Methods: Genetic Testing Genetic testing involves analyzing an individual's DNA to identify genetic mutations that may cause disease. These tests can be used for: - Diagnosis: Confirming the presence of a genetic disorder. - Risk Assessment: Evaluating the likelihood of developing certain conditions. - Carrier Testing: Determining if an individual carries a gene for a hereditary disorder. Personalized Medicine Personalized medicine is an innovative approach that tailors medical treatment to the individual characteristics of each patient, often based on their genetic profile. This approach allows for: - Targeted Therapies: Developing treatments that specifically target genetic mutations. - Optimized Drug Dosing: Adjusting medication dosages based on genetic factors to minimize side effects and maximize efficacy. - Preventive Strategies: Implementing lifestyle changes and monitoring to prevent disease onset. Ethical Considerations The rapid advancement of genetic technologies raises important ethical issues, such as: - Privacy: Ensuring the confidentiality of genetic information. - Discrimination: Preventing genetic discrimination in employment and insurance. - Informed Consent: Ensuring individuals understand the implications of genetic testing.

Results: Conclusion on Medical Genetic Testing Medical genetic testing plays a crucial role in the diagnosis, management, and prevention of genetic disorders. These tests allow for the identification of genetic mutations that may lead to various health conditions, providing valuable information for patients and their families. Early diagnosis through genetic testing can facilitate timely interventions, personalized treatment plans, and informed reproductive choices. Furthermore, the insights gained from genetic testing can contribute to a better understanding of disease mechanisms and progression, paving the way for novel therapeutic approaches. However, it is essential to consider the ethical implications and potential psychological impacts associated with genetic testing, including concerns about privacy, discrimination, and the emotional burden of uncertain results. In summary, while medical genetic testing offers significant benefits and holds great promise for

advancing healthcare, it must be conducted with careful consideration of ethical standards and patient support to ensure that the advantages are maximized while minimizing potential drawbacks.

Conclusion: Conclusion on Medical Genetics Medical genetics is a transformative field that bridges the gap between genetic research and clinical practice. It offers profound insights into the understanding of genetic disorders and the development of innovative diagnostic and therapeutic strategies. As genomic technologies continue to advance, the potential for personalized medicine becomes increasingly attainable, allowing for treatments tailored to individual genetic profiles. However, the field also presents ethical challenges that must be addressed to ensure responsible use of genetic information. By balancing scientific progress with ethical considerations, medical genetics holds the promise of significantly enhancing healthcare outcomes and improving the quality of life for individuals with genetic conditions.

Keywords: ١. Genetic Testing ٢. Medical Genetics ٣. Genetic Disorders ٤. Diagnosis ٥. Personalized Medicine

Advances in Microfluidic Technology for Breast Cancer Diagnosis (Review)

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Introduction: Breast cancer continues to pose a considerable public health concern on a global scale, thereby necessitating the development of innovative diagnostic methodologies. Microfluidic technology, characterized by its precision and operational efficiency, presents significant advancements in the early identification and diagnosis of breast cancer. Microfluidics encompasses the manipulation of fluids at the microscale, facilitating the meticulous control and examination of diminutive samples. This technological paradigm is particularly advantageous in medical diagnostics due to its capability to execute intricate laboratory procedures on a singular microchip.

Methods: A comprehensive literature search was conducted using PubMed and Google Scholar to identify relevant studies on microfluidic applications in breast cancer diagnosis. Key terms included "microfluidics," "breast cancer," "diagnosis," "circulating tumor cells," "exosomes," and "ctDNA." A total of ۲۷ articles were identified with the intention of conducting a thorough examination and analysis of this topic.

Results: Microfluidic devices have demonstrated significant potential in various aspects of breast cancer diagnosis: Circulating Tumor Cells (CTCs): Microfluidic platforms can efficiently isolate and analyze CTCs from blood samples, providing valuable insights into tumor progression. Aptamer-Based Sensors: These sophisticated sensors utilize aptamers to selectively bind and identify CTCs, thereby providing exceptional sensitivity without necessitating the use of labeling agents. Exosome Analysis: Microfluidic techniques enable the isolation and characterization of exosomes, extracellular vesicles released by cancer cells, which contain biomarkers associated with breast cancer. Immunoaffinity-Based Methods: Microfluidic platforms can effectively isolate exosomes through the application of antibodies, facilitating the examination of their molecular composition. Cell-Free Tumor DNA (ctDNA): Microfluidic devices can detect ctDNA, a non-invasive biomarker for early cancer detection and monitoring.

Conclusion: Microfluidic technology offers a promising paradigm for breast cancer diagnosis, providing enhanced sensitivity, specificity, and early detection capabilities. This technology also enhances the accuracy of cancer biomarker identification when compared with conventional assays. By enabling the analysis of circulating tumor cells, exosomes, and ctDNA, microfluidic devices have the potential to revolutionize the management of breast cancer. However, further research and standardization are necessary to fully realize their clinical potential.

Keywords: Microfluidics, Breast Cancer, Diagnosis

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Advancing Breast Cancer Diagnosis and Treatment with Gold Nanoparticle-Based Nanosensors

(Review)

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Introduction: Breast cancer remains a formidable global health issue, underscoring the urgent necessity for innovative approaches to enhance early diagnosis and treatment strategies. Gold nanoparticle-based nanosensors have emerged as promising tools in this arena due to their unique physical and chemical properties, which facilitate the precise identification of cancer biomarkers and the targeted delivery of therapeutic agents. This study investigates the mechanisms by which these nanosensors function, focusing on their application in breast cancer diagnostics and therapy.

Methods: Searching and reading articles in NCBA, Scopus, Gigalib, Google Scholar

Results: Breast cancer continues to represent a considerable global health concern, highlighting the need for novel strategies for early diagnosis and efficient treatment. In this context, gold nanoparticle-based nanosensors have been recognized as promising instruments, capitalizing on their distinctive characteristics to facilitate the accurate identification of biomarkers as well as the targeted administration of therapeutic compounds. This study explores the intricate mechanisms involved in the utilization of gold nanoparticle-based nanosensors for the detection and treatment of breast cancer. Gold nanoparticle-based nanosensors utilize diverse mechanisms for the sensitive detection of biomarkers associated with breast cancer. These nanoparticles are functionalized with ligands, including antibodies or DNA probes, that are specifically designed to target biomarkers such as HER۲/neu and BRCA۱. The recognition of these targets occurs through interactions such as antigen-antibody binding or complementary base pairing. When the nanoparticles bind to the target biomarkers, they exhibit changes in their localized surface plasmon resonance (LSPR) properties, leading to observable modifications in optical signals. These variations in signal intensity or wavelength are indicative of the presence of breast cancer biomarkers, allowing for sensitive and specific detection, even at low concentrations. Gold nanoparticle-based nanosensors present significant adaptability across multiple imaging techniques utilized in the diagnosis of breast cancer. In the context of photoacoustic imaging, these nanoparticles absorb near-infrared radiation and transform it into acoustic signals, facilitating high-resolution and high-contrast imaging of deep tissues. Furthermore, surface-enhanced Raman scattering (SERS) imaging leverages the distinctive enhancement of Raman signals provided by gold nanoparticles, enabling the sensitive identification of molecular-level biomarkers. Plasmonic imaging leverages the pronounced resonant properties of gold nanoparticles to improve the contrast in optical imaging methodologies. This enhancement enables the acquisition of detailed molecular information regarding breast cancer lesions. Gold nanoparticle-based nanosensors have demonstrated significant potential as carriers for targeted drug delivery in the treatment of breast cancer. The functionalization of these nanoparticles with targeting ligands allows for selective binding to receptors that are overexpressed on breast cancer

cells, thereby enabling the accurate delivery of therapeutic agents. Furthermore, gold nanoparticles can be engineered to respond to specific external stimuli, such as changes in pH, temperature, or light, which facilitates the controlled release of therapeutic compounds. This design strategy enhances the precision of targeting cancer cells and reduces the likelihood of unintended effects on healthy tissues. Gold nanoparticle-based nanosensors are instrumental in assessing therapeutic responses in breast cancer treatments. By functionalizing these nanoparticles with specific biomarkers that reflect treatment effectiveness, it becomes possible to monitor cellular responses in real-time. These nanosensors enable the detection of variations in the levels of proliferation and apoptotic markers, thereby offering critical information regarding the effectiveness of the treatment and informing personalized therapeutic strategies.

Conclusion: In summary, the exploration of gold nanoparticle-based nanosensors marks a significant advancement in breast cancer diagnosis and treatment. These nanoparticles exhibit unique properties that make them excellent tools for detecting key biomarkers, including HER٢/neu and BRCA١, through techniques like localized surface plasmon resonance and sophisticated imaging approaches. Beyond mere detection, these nanosensors facilitate targeted drug delivery, minimizing side effects on healthy tissues and improving therapeutic efficacy. They also allow for real-time monitoring of treatment responses, enhancing the precision of breast cancer management and enabling personalized treatment strategies tailored to individual patient needs. This research underscores the potential of these nanosensors to improve patient outcomes, ultimately contributing to higher survival rates and better quality of life for breast cancer patients. Continuing advancements in gold nanoparticle technologies are anticipated to drive further innovations in cancer diagnostics and treatment, highlighting their essential role in modern oncological care.

Keywords: Gold nanoparticle-based nanosensors, Breast cancer detection, Biomarker recognition, HER٢/neu, BRCA١

Advancing Breast Cancer Research: The Role of BRCA١ Mutations and Organoid Models (Review)

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Introduction: Breast cancer holds a significant status among the most widespread malignancies globally, with mutations in the BRCA١ gene representing a pivotal element in its pathogenesis and progression. The role of the BRCA١ gene is significant in addressing DNA double-strand breaks, using homologous recombination as its operational technique. Mutations that impair BRCA١ disrupt this vital repair process, resulting in genomic instability and an increased vulnerability to cancer. Conventional models utilized to investigate BRCA١ mutations possess inherent limitations, thereby necessitating the development of more precise and representative experimental frameworks. Tumor organoids obtained from patients (PDTOs) signify a creative and encouraging pathway for investigating cancer. These three-dimensional cultures preserve the histological and genetic attributes of the parent tumors, thereby furnishing a more physiologically relevant environment for exploring cancer biology and evaluating therapeutic interventions.

Methods: The establishment and maintenance of organoids involved the procurement of fresh tissue specimens from breast cancer patients harboring BRCA١ mutations. These specimens underwent enzymatic digestion and mechanical dissociation to yield cell suspensions, which were subsequently encapsulated in Matrigel and cultured under meticulously formulated media conditions. The organoids were systematically monitored and passaged to guarantee their continued growth and viability. The study also integrated a variety of assays aimed at assessing the responses of organoids to therapeutic treatments. Drug dose-response assays were performed to determine the efficacy of diverse therapeutic agents. We engaged in the examination of the expression rates of crucial proteins tied to DNA repair operations and cell cycle oversight by employing immunohistochemical evaluations along with Western blotting procedures. The implementation of EdU incorporation assays, alongside RNA extraction and subsequent RT-qPCR, was crucial for the investigation of cellular proliferation and shifts in gene expression. Live cell imaging employing specific peptides enabled the elucidation of protein interactions within the organoids.

Results: The organoid models derived from BRCA١-mutated breast cancer tissues displayed genetic and phenotypic attributes that closely resembled those of the original tumors, thereby affirming their applicability as a representative model for this cancer subtype. The use of PARP inhibitors, for instance talazoparib, in organoids that have BRCA١ mutations caused a notable rise in DNA damage and cytotoxicity when compared to the wild-type variants. Merging PARP inhibitors with substances that damage DNA, like temozolomide, has produced a significantly better interaction, illustrating their synergistic relationship. The investigation further demonstrated that elevated levels of mutant p٥٣ (mtp٥٣) and PARP expression were associated with heightened sensitivity to the combined

treatment regimen. This dual biomarker strategy holds significant potential for predicting and optimizing treatment outcomes for patients afflicted by BRCA\ mutations.

Conclusion: The employment of organoid models derived from breast cancer tissues characterized by BRCA\ mutations signifies a significant advancement in the investigation of the underlying mechanisms that drive tumorigenesis and the evaluation of novel therapeutic interventions. These models retain the intricate architecture and genetic diversity of the original tumors, thereby providing a more accurate representation when compared to traditional cell lines. The findings of the investigation underscore the potential advantages of a synergistic methodology that incorporates PARP inhibitors alongside DNA-damaging therapies to enhance patient management for individuals with BRCA\ mutations. Future research initiatives should focus on the enhancement of organoid models to encompass a wider array of genetic backgrounds and the exploration of additional combinatorial therapies to further improve patient outcomes.

Keywords: Breast Cancer, BRCA\, Organoid

Advancing Cancer Treatment Through the Utilization of Organoids: A review (Review)

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Introduction: Cancer treatment remains a significant challenge due to the heterogeneity of tumors and the variability in patient responses to therapy. Traditional models for studying cancer often fail to capture the complexity of human tumors, leading to ineffective treatments. Organoids, which are ۳D cultures derived from patient tumor cells, have emerged as a promising solution. They accurately replicate the architecture and functionality of actual tumors, offering a more reliable platform for studying cancer biology and testing therapeutic interventions. This review aimed to explore the latest developments in organoid technology and its implications for cancer treatment.

Methods: The review was conducted through a systematic literature search using databases such as PubMed, Scopus, and Web of Science. Keywords such as "organoids," "cancer treatment," "personalized medicine," and "drug testing" were utilized to identify relevant articles. Selected studies were critically analyzed to summarize key findings regarding organoid development, therapeutic applications, and biomarker identification. The review also examined case studies and clinical trials that have demonstrated the integration of organoids into oncology practice. The findings will be useful to present a cohesive understanding of the role of organoids in advancing cancer

Results: This review provided a comprehensive overview of the advancements in organoid technology and its applications in cancer treatment. It highlighted the potential of organoids to facilitate personalized therapy, improve drug screening processes, and deepen our understanding of tumor biology. By identifying current challenges and limitations, the review will also offer insights into future research directions, paving the way for the clinical adoption of organoid-based approaches in oncology.

Conclusion: The proposed review on advancing cancer treatment through the utilization of organoids aimed to provide a critical assessment of the current state of research and its implications for personalized medicine. By providing existing literature and identifying future directions, this review contributed to understanding how organoids can transform cancer therapy and improve patient outcomes. This comprehensive revirew will serve as a valuable resource for researchers, clinicians, and policymakers in the oncology research field.

Keywords: Organoids, Cancer Treatment, Tumor Biology, Patient-Derived Models

Advancing Early Detection and Management of Triple-Negative Breast Cancer: A Systematic Review of Liquid Biopsy Applications (Review)

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Introduction: Triple-negative breast cancer (TNBC) is a particularly aggressive form of breast cancer with the absence of estrogen receptor (ER), progesterone receptor (PR), and HER٢ expression. The lack of targeted therapies leads to its poor prognosis and limited treatment options. Due to rapid progression and high metastasis rate in TNBC, early detection is crucial for improving its outcomes. Liquid biopsy, a non-invasive diagnostic tool that analyzes biomarkers such as circulating tumor DNA (ctDNA) and circulating tumor cells (CTCs), offers a promising approach for early detection and management of TNBC. This systematic review aims to evaluate the role of liquid biopsy in the early detection of TNBC, focusing on the effectiveness of ctDNA and CTCs in identifying the disease at an early stage, monitoring disease progression, and guiding personalized treatment.

Methods: This systematic review was conducted by searching multiple databases, including PubMed, Embase, and Cochrane Library, for studies published between ٢٠١٥ and ٢٠٢٤. Included studies were selected based on the following criteria: (١) clinical trials, observational studies, meta-analyses, and systematic reviews evaluating the application of liquid biopsy in TNBC, (٢) research focusing on ctDNA and CTCs detection methods, and (٣) studies reporting on diagnostic accuracy, prognostic value, and early detection capabilities. Exclusion criteria comprised case reports, case series, and studies not focused on TNBC or lacking relevant outcome data.

Results: The review analyzed ٢٥ studies involving ١,٢٠٠ TNBC patients. Findings revealed that liquid biopsy is highly effective for early-stage detection of TNBC. Sensitivity rates for ctDNA detection ranged from ٦٠٪ to ٨٥٪, while specificity varied from ٧٠٪ to ٩٠٪, depending on the detection method and the tumor's genetic profile. Studies using digital PCR and next-generation sequencing (NGS) demonstrated higher sensitivity compared to the conventional methods. CTCs were also detected in early-stage TNBC patients, with sensitivity ranging from ٥٠٪ to ٧٥٪. The presence of CTCs correlated strongly with a higher risk of metastasis and poorer prognosis. Additionally, liquid biopsy proved valuable in monitoring minimal residual disease (MRD) after treatment, with ctDNA levels serving as an early indicator of potential recurrence. The ability to identify actionable mutations through liquid biopsy facilitated personalized treatment approaches, although the effectiveness varied based on the tumor's molecular characteristics and the technology used.

Conclusion: Liquid biopsy represents a significant advancement in the early detection and management of TNBC. The ability to detect ctDNA and CTCs provides a non-invasive method for identifying the disease at the early stages, which is crucial for improving patient outcomes. The review highlights the effectiveness of ctDNA analysis in detecting TNBC-specific mutations and monitoring disease progression, with higher sensitivity and specificity observed with advanced techniques such as digital PCR and NGS. CTC detection also offers valuable prognostic information, correlating with metastatic risk and treatment response. Despite its promising potential, challenges remain in standardizing liquid biopsy methods and improving sensitivity, particularly for early-stage disease. Further research and technological advancements are essential to overcome these challenges and integrate liquid biopsy into routine clinical practice. Overall, liquid biopsy shows great promise for enhancing early detection, personalizing treatment, and improving the management of TNBC, offering new hope for patients with this aggressive cancer subtype.

Keywords: Triple Negative Breast Cancer, Liquid Biopsy, Circulating Tumor DNA, Circulating Tumor Cells

Advancing Medical Genetics: The Role of CRISPR-Cas۹ in Treating Genetic Disorders (Review)

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Introduction: CRISPR-Cas۹, a groundbreaking gene-editing technology, has revolutionized the field of medical genetics, offering unprecedented possibilities for treating genetic disorders. This technology allows for precise modifications of the DNA sequence, enabling the correction of mutations that cause various inherited diseases. As research progresses, CRISPR-Cas۹ is increasingly being explored as a tool for developing personalized therapies, potentially providing cures for conditions previously considered untreatable.

Methods: This review examines recent studies focused on the application of CRISPR-Cas۹ in treating human genetic diseases. We conducted an extensive search of literature from the past decade, selecting studies that demonstrate the use of CRISPR-Cas۹ in correcting genetic mutations in diseases such as cystic fibrosis, sickle cell anemia, and Duchenne muscular dystrophy. These studies were analyzed to identify key trends, methodological advancements, and challenges in translating gene-editing technology from the laboratory to clinical practice.

Results: Our analysis reveals significant progress in the application of CRISPR-Cas۹ for gene therapy. For instance, several studies have successfully corrected genetic defects in preclinical models, demonstrating the potential of CRISPR-Cas۹ to cure hereditary diseases. Moreover, the development of enhanced delivery systems has improved the efficiency and specificity of gene editing. However, the field still faces challenges, such as off-target effects, ethical concerns regarding germline editing, and the need for robust regulatory frameworks.

Conclusion: CRISPR-Cas۹ holds immense promise for the future of personalized medicine by providing targeted treatments for genetic disorders. To fully realize its potential, continued research and careful consideration of ethical implications are essential as the technology moves closer to clinical application.

Keywords: Medical Genetics , CRISPR-Cas۹ , Gene Editing , Genetic Disorders , Personalized Medicine

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Aeronautical Physiology and High Altitude Training (Review)

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Introduction: Hypoxia refers to the lack of oxygen available for normal tissue metabolism. If hypoxia is severe enough, it can disrupt nerve activity and sometimes even lead to coma.

Methods: Adaptability to hypoxia: An astronaut or a pilot never stays at high altitude for long enough to adapt to its conditions. But climbers and athletes who train at high altitudes make enough compromises to be able to survive and train at altitudes that are several thousand meters above sea level. Compromise is usually done in the following ways: ۱- Increasing pulmonary ventilation: the oxygen deficiency mechanism in the control of pulmonary ventilation normally only increases the ventilation rate by ٦٥٪, but after the person stays at a high altitude for several days, this mechanism becomes more and more effective. Increases ventilation up to ٤٠٠٪. Therefore, more oxygen is provided to the bubbles. ۲- Increase in red blood cells and hemoglobin: When a person stays at a high altitude for at least ۲ weeks, hypoxia causes a sharp increase in the production of red blood cells. If an athlete starts training at altitude, based on the reduction of oxygen pressure and the body's need for it during sports activities, especially endurance activities, a hormone called erythropoietin is secreted from the kidneys and stimulates the bone marrow. With the increase of red blood cells, hemoglobin increases, and as a result, the decrease in oxygen pressure at altitude is compensated by the increase in the amount of hemoglobin, and the athlete can continue his training without feeling a lack of oxygen. One of the advantages of this work is that if such a person, who has trained for at least two weeks at an altitude of ۲۳۰۰ meters, is transferred to a lower place, as long as the adaptation effect is not lost, he has a higher oxygen transport capacity. and as a result will be more successful in endurance competitions.

Results: The main problem at altitude is the reduction of oxygen pressure. An ordinary person often gets sick at an altitude of ۳,۰۰۰ to ٤,۰۰۰ meters above sea level and his level of consciousness drops. At an altitude of ٥,٥۰۰ meters, a person's senses are disturbed so much that he loses the power of recognition, and at an altitude of ۷,۰۰۰ meters, if pure oxygen does not arrive, he will go into a coma within ۲۰ to ۳۰ minutes.

Conclusion: Oxygen therapy is used to improve some types of hypoxia. For example, this method is used to treat hypoxia caused by the reduction of oxygen in the atmosphere, reduction of pulmonary ventilation and diffusion disorders from the respiratory membrane. In any case, an increase in oxygen concentration causes an increase in oxygen pressure in the alveoli, and as a result, increases the release of oxygen into the blood. In different types of hypoxia, the main problem may be the reduction of oxygen transfer to the tissues or the reduction of the use and consumption of oxygen in the cells. In this case, oxygen therapy may not have much effect.

Keywords: Hypoxia , Oxygen , High Altitude , Red Blood Cells

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Allograft Pericardium Membrane; An Appropriate Candidate for Heart Surgeries (Research Paper)

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Introduction: Regenerative medicine is an emerging interdisciplinary field of research and clinical application, focusing on the repair, replacement, or regeneration of cells, tissue, or organs. Patches prepared from autologous, allogeneic, or xenogeneic tissues are widely used to repair heart defects. An allogenic extracellular matrix (ECM) is the ideal graft to minimize immunogenicity after recipient implantation. Nevertheless, decellularization of allogenic tissues aims at reducing the immunogenic reaction that might trigger inflammation and tissue calcification over time, as reported for allogenic cardiac tissues. In this project, an allograft pericardium membrane fabricated by the Iranian Tissue Product (ITP) company was evaluated in case of its structure and decellularization. It was assumed that the pericardium membrane would present appropriate structural characteristics. Also, the membranes would not be expected to cause any immune reactions.

Methods: After completion of donor screening, the pericardium tissue was dissected to remove any additional tissue such as fat. Then, it was decellularized using H_2O_2 and segmented into certain dimensions. Finally, the samples were lyophilized by freeze-dryer and gamma irradiated with the dose of ٢٥ kGy. A scanning electron microscope (SEM) has been used to evaluate the microstructure of the allograft. Also, to examine its biocompatibility, the cell viability after ٧٢ hours was investigated through ٣-(٤,٥-dimethylthiazol-٢-yl)-٢,٥-diphenyl-٢H-tetrazolium bromide (MTT) assay. To validate the decellularization process, hematoxylin and eosin (H&E) colorimetric staining was used.

Results: According to the obtained results, the porous structure of the graft was preserved after the procedure, and due to the interconnectivity of the pores, the prepared pericardium membrane may provide a favorable microenvironment for the initiation of cellular activities (such as migration, growth, proliferation, and differentiation) and eventually, regeneration of the damaged area. The output of the MTT assay also indicated the survival of more than ٨٠٪ of the cells and demonstrated the lack of toxicity within the structure. Prior to decellularization, numerous thick bundles of mature collagen fibers admixed with several fibroblasts and fibrocytes are obvious in the tissue. In the decellularized tissue, some bundles of collagen fibers admixed with some scattered fibroblasts and fibrocytes can be observed. Therefore, the acceptable decellularization of the pericardium tissue without destructive impact on its native structure was validated.

Conclusion: Regarding the notable results of the structural and biological characteristics of the decellularized product, it can be claimed that the prepared allograft pericardium is a desirable candidate for repairing the defects in the heart with minimum risks of immunogenicity.

Keywords: Allograft, Pericardium membrane, Heart surgery.

Ameliorative effects of melatonin on sperm biochemical parameters during cryopreservation in the asthenozoospermic men: an invitro study (Research Paper)

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Introduction: Sperm motility is crucial for the ability of sperm to penetrate the oocyte and achieve fertilization. According to the World Health Organization (WHO) ٢٠٢١ guidelines, less than ٤٢ percent of motility is called asthenozoospermia, which is one of the most common causes of male infertility. Reactive oxygen species (ROS), generated during cryopreservation, can impair sperm function. Melatonin, has antioxidant activities and can reduce the amount of ROS in the cell, so it may protect sperm from ROS- related damage. This study aims to evaluate the impact of melatonin on sperm biochemical parameters during cryopreservation in asthenozoospermic men.

Methods: ٣٠ semen samples were collected from Asthenozoospermic patients. Each sample was divided into three groups: Control (fresh), Freeze (treated with cryo-protectant), and Freeze+ Melatonin (treated with cryo-protectant+ ١mM Melatonin solution). In each sample, the level of sperm Malondialdehyde (MDA) and sperm antioxidant enzymes, including Total Antioxidant Capacity (TAC), Catalase (CAT), Glutathione (GSH), and Superoxide dismutase (SOD) were analyzed using Enzyme-linked immunosorbent assay (ELISA).

Results: Our results showed a significant decrease in sperm antioxidant enzyme levels and TAC, also significant increase in sperm MDA levels in the freeze group compared to the control group ($P<٠,٠٥$). In contrast, the Freeze+ Melatonin group showed a significant increase in sperm antioxidant enzymes and TAC levels, as well as a significant decrease in sperm MDA levels compared to the freeze group ($P<٠,٠٥$).

Conclusion: This study indicates that melatonin supplementation may serve as an effective strategy approach to enhance the quality of cryopreserved sperm in asthenozoospermic men. By reducing ROS levels and protecting sperm from oxidative damage, melatonin has the potential to improve sperm function and increase the likelihood of successful fertilization. Additional research is needed to validate these results and investigate the mechanisms behind melatonin's positivs impact on sperm quality.

Keywords: Asthenozoospermia, Biochemical Parameters, Cryopreservation, melatonin.

Amyotrophic Lateral Sclerosis (ALS): The Role of Key Genetic Mutations in Disease Progression

(Review)

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Introduction: Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease that leads to the weakening and wasting of voluntary muscles. Despite recent research, the diagnostic and treatment options remain unsatisfactory. About ۹۰٪ of ALS cases are sporadic (sALS), while around ۱۰٪ are familial (fALS). So far, ۱۷ genes have been associated with ALS, with mutations in four key genes—SOD۱, TARDBP, C۹ORFV۲, and FUS—accounting for a large percentage of familial cases. Research has shown that the C۹ORFV۲ gene plays a significant role in ALS. Expansion of a GGGGCC hexanucleotide repeat in the noncoding region of this gene has been associated with behavioral and memory issues, as well as neurodegenerative disorders like ALS. It has been found that about ٤٧٪ of fALS patients and ٥٪ of sALS patients have this repeat expansion, making it the most frequent genetic cause of ALS so far. Another important gene in ALS is SOD۱, which encodes a protein found in various tissues like the liver and the central nervous system. Mutations in SOD۱ are responsible for roughly ۲۰٪ of fALS cases. There have been more than ۱۸۰ mutations of SOD۱ identified, accounting for about ۳٪ of all ALS cases. These mutations cause the protein to misfold, leading to the formation of insoluble aggregates that spread between neurons, which contributes to the disease progression and nerve damage. The FUS gene is another crucial gene in ALS. Although the exact mechanism of how FUS mutations cause neurodegeneration is still unclear, some evidence suggests that these mutations might affect processes like DNA repair, metabolism, and axonal transport, all of which could contribute to the progression of ALS. Similarly, the TARDBP gene, which encodes the TDP-٤۳ protein, is important for RNA metabolism. Mutations in TARDBP are linked to an increased risk of ALS and its progression. Abnormal TDP-٤۳ has been found in all ALS cases, except in those with SOD۱ and FUS mutations. Misfolded TDP-٤۳ proteins form amyloid fibrils, which are a hallmark of ALS pathology.

Methods: To better understand how these genetic mutations contribute to ALS, we used model organisms such as fruit flies, zebrafish, and mice that were genetically modified to carry mutations in ALS-associated genes. We mainly focused on the processes of protein misfolding and aggregation. Using advanced microscopy and biochemical techniques, we observed the formation and spread of misfolded proteins in the neurons of these models. We also conducted behavioral tests to connect these molecular changes with functional impairments in the animals. These experiments were designed to compare the findings in animal models with the clinical features observed in human ALS patients.

Results: The main goal of these studies was to identify the genetic mutations that drive ALS progression. By using these animal models, we confirmed that a wide range of gene mutations, such as those in SOD۱, TARDBP, C۹ORFV۲, and FUS, play critical roles in ALS development. Mutant

SOD١ proteins were found to spread from one neuron to another in a prion-like manner, which accelerates the progression of the disease. Furthermore, C٩ORFV٢ mutations were shown to lead not only to motor impairments but also to cognitive and behavioral abnormalities, which resemble the complex clinical symptoms observed in human ALS cases. Our findings further confirmed that SOD١ mutations are a significant cause of familial ALS. We also demonstrated that C٩ORFV٢ mutations are linked to both familial and sporadic ALS, emphasizing the diverse mechanisms underlying this complex disease.

Conclusion: In summary, the results of our research highlight the crucial role of genetic mutations in driving protein misfolding and aggregation in ALS. Mutations in genes like SOD١, TARDBP, C٩ORFV٢, and FUS each affect different molecular pathways but all lead to the same devastating outcome—neurodegeneration. Understanding these pathways is critical for developing future therapies aimed at targeting these misfolded proteins. Further research should focus on therapies that either prevent protein misfolding or stop the spread of aggregates between neurons. Translating these findings from animal models to human clinical treatments could pave the way for better therapeutic strategies for ALS patients in the future.

Keywords: Amyotrophic Lateral Sclerosis (ALS), SOD١, TARDBP, C٩ORFV٢, FUS

An elderberry-supplemented diet improves spermatogenesis in mice with busulfan-induced azoospermia (Research Paper)

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Introduction: Approximately ٤٠–٥٠٪ of all infertility cases are due to male infertility, and one of the most important causes of infertility is azoospermia. This study aimed to evaluate the potential effect of elderberry on the spermatogenesis process in the azoospermia mice model

Methods: Thirty adult male mice were randomised into three groups: control; busulfan (٤٥mg/kg); and busulfan+elderberry (٢٪), ٦mL orally per animal. Sperm samples were collected from the tail of the epididymis, and testis specimens were also collected and then subjected to sperm parameters analysis, histopathological evaluation, reactive oxygen species (ROS), and glutathione (GSH) measurement to determine the mRNA expression and hormonal assay

Results: The results indicated that the total sperm count in the control group was significantly higher compared to the busulfan (P < ٠,٠٠٠١) and busulfan + elderberry (P < ٠,٠٠٠١) groups. Our results showed that the treatment by elderberry had a significant impact on serum testosterone level in mice induced by busulfan. The results revealed that the serum testosterone level in the busulfan group was significantly decreased com-pared to control and busulfan + elderberry groups.

Conclusion: It can be concluded that the elderberry diet may be considered a complementary treatment to improve the spermatogenesis process in busulfan-induced azoospermic mice. Implications. Considering some limitations, the elderberry diet can be an alternate option for improving testicular damage following chemotherapy.

Keywords: azoospermic mice, elderberry diet, spermatogenesis busulfan

An Evaluation of the Safety and Effectiveness of Tyrosine Kinase Inhibitors Targeting EGFR in Glioma Patients: A Comprehensive Systematic Review and Meta-Analysis (Review)

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Introduction: Gliomas, especially glioblastoma, present significant treatment challenges and are associated with a poor prognosis. Although tyrosine kinase inhibitors (TKIs) that target the epidermal growth factor receptor (EGFR) have shown potential, their effectiveness in gliomas has not been thoroughly validated. This study sought to systematically review and conduct a meta-analysis on the safety and efficacy of TKIs in patients with glioma.

Methods: A thorough literature search was performed across databases including PubMed, Embase, Scopus, and Web of Science, concluding on December ٢٦, ٢٠٢٣. The inclusion criteria encompassed randomized controlled trials and observational studies that assessed TKIs in glioma patients. The primary outcomes measured were overall survival (OS), progression-free survival (PFS), and the incidence of adverse events. A random-effects meta-analysis was utilized to aggregate the results.

Results: A total of ٢,٤٢٤ patients from various studies were analyzed. The pooled mean OS was determined to be ١٢,٦٨ months (٩٥٪ CI: ٦,٢٩-١٩,٠٨), with ١-year and ٢-year OS rates of ٤٣٪ (٩٥٪ CI: ٣٤٪-٥٢٪) and ١٤٪ (٩٥٪ CI: ٨٪-٢٠٪), respectively. The mean PFS was recorded at ٩,٦١ months (٩٥٪ CI: ٤,٨٣-١٤,٣٨). The overall response rate was found to be ١٩٪ (٩٥٪ CI: ١٪-٣٦٪). Adverse events classified as grade ≥٣ were reported in ٣٥٪ of patients (٩٥٪ CI: ١٣٪-٥٧٪). Subgroup analyses indicated that combination therapies yielded better outcomes compared to TKI monotherapy, with certain newer TKIs, such as vandetanib, demonstrating enhanced efficacy.

Conclusion: TKIs offer modest yet significant advantages in the treatment of gliomas, particularly when used in conjunction with other therapeutic modalities. Although initial improvements in survival rates are noted, long-term outcomes continue to pose challenges. Additional research is essential to develop more effective, brain-penetrant TKIs and to refine combination treatment strategies to enhance patient outcomes in glioma cases.

Keywords: Glioma, TKI, Tyrosine Kinase Inhibitor, EGFR

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An herbal bioactive drug compound with a delayed release curve in a PEGylated cationic nano-niosome formulation for cancer cells (Research Paper)

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Introduction: This study aimed to PEGylated cationic nano-niosomes formulation containing curcumin (CUR) for drug delivery to MCF-٧ breast cancer cell lines and slow release of encapsulated CUR to reduce drug side effects on other healthy cells and increase drug effect on cancer cells.

Methods: In this applied/in vitro study, PEGylated cationic nano-niosomes containing curcumin as herbal anticancer drug in MCF-٧ cell line were prepared in laboratory through lipid phase mixing, phosphate buffer addition to a lipid thin film, and the production of nano-niosomes by sonication and dialysis process. Curcumin-containing niosomes were produced using the lipid phase by thin film fabrication method and reduced to a nanometer size by sonication. The average diameter (٨٥,٤ nm) of drug-carrying nano-niosomes was determined using a nano-sizer

Results: Our results includes acquisition of technical knowledge of fabricating nano-niosomes containing a herbal bioactive ingredient as a nanosystem with the herbal medicine curcumin, proper loading of curcumin (with anticancer effect) at > ٩٥٪ inside nano-niosomes with a size of < ١٠٠ nm to intensify the effectiveness of this medicine in cancer treatment, and preparation of PEGylated cationic nano-niosomes containing a body-compatible herbal bioactive substance with a slow release curve and good stability in terms of size and surface loading after ٢ months of production.

Conclusion: The produced curcumin-carrying liposomal nano-carrier has a slow-release curve and body biocompatibility that can be used in preparation of drug delivery systems containing similar hydrophobic drugs as an effective approach in treatment of various cancers, and agriculture, as well as in various pharmaceutical, medical, health, and environmental industries.

Keywords: Drug delivery, MCF-٧ cell lines, MCF-١٠A cell Lines, Cancer cells, Herbal bioactive, Nano-niosomes

An in-depth look at the new plans for Gastric Cancer (GC) treatment (Review)

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Introduction: Gastric cancer (GC) is one of the most common malignancies worldwide. Gastric Cancer is caused by an uncontrolled growth of cells that starts in the stomach. GC is a multifactorial disease in which environmental and genetic factors can influence its occurrence and development. Today, almost the only preventive method aimed at early detection of tumors is cancer screening. The first way to diagnose GC is to observe the symptoms of the disease in a person. Vomiting blood, seeing blood in the stool, sudden, severe and unwanted weight loss, indigestion and feeling pain and bloating in the upper abdomen, feeling full early after eating are symptoms of GC. But typically sampling or biopsy is the surest way to detect GC. Endoscopy, blood tests, CT scans, PET scans, tumor marker tests, stool blood tests and breath tests are other ways to diagnose GC. Treatment of GC depends on many factors, but generally a combination of techniques is used. Common treatments include surgery to remove the tumor, chemotherapy to kill cancer cells, compression to kill cancer cells, and targeted molecular treatments to inhibit the growth of cancer cells. Complementary therapies such as radiotherapy and hormone therapy can also be used. The aim of the study was to take an in-depth look at new programs for GC treatment.

Methods: The present paper is a review study. In this study,٤٩ articles published from ٢٠١٨ to٢٠٢٤, which were in the form of quantitative studies, meta-analysis and original research and systematic review were examined. Entry criteria included: Availability of full text and articles published between ٢٠١٨ and ٢٠٢٤, and exit criteria included: Case Report studies. The MeSH terms were " Gastric cancer " OR " H. Pylori " OR " Hyperthermic Intraperitoneal Chemotherapy (HIPEC)".

Results: Most GC are found when the disease has spread beyond the stomach, when a cure is less likely. A new approach to treating GC called hyperthermic intraperitoneal chemotherapy (HIPEC) delivers heated liquid chemotherapy directly to the abdomen where it can target the cancer. During a HIPEC treatment, the abdominal cavity is bathed with hot chemotherapy to kill any microscopic cancer cells. The chemo can stay locally in that region, the abdomen, and then it can continue to work even past the procedure. And then that allows us to use really high concentrations of the chemo directly where the cancer is. HIPEC has been used as a treatment for other cancers for several decades, but just recently has been adapted to GC. The outcomes have been significantly better than those achieved with traditional chemotherapy. chemotherapy combined with surgery prolongs the survival of patients with other localized metastases in the future. The development of

new treatment strategies, including new chemotherapeutic agents and regimens, could improve the survival outcomes of patients with oligometastatic from gastric cancer.

Conclusion: GC is a heterogeneous disease that affects a large number of people annually and remains an unmet clinical problem. GC severely affects the population of developing countries. Improvements in hygiene and eradication of H. Pylori significantly improved these gastric cancer statistics in developing countries. According to our studies gastric cancer accounts for about ٦٪ of cancers worldwide and is the fifth most frequently diagnosed malignant cancer and the third leading cause of cancer-related death. With the development of genomics, the updating of modern imaging technology and the emergence of artificial intelligence and big data, GC surgical treatment has gradually entered medicine. Advances have been made in understanding the pathogenesis and Molecular Biology of gastric cancer and optimizing available treatment options and methods. In the future, however, the focus should be on exploring more gastric cancer classification, fine-tuning treatment strategies and developing new drugs for patients with advanced gastric cancer. As the research progresses, I hope there will be more progress in discovering more effective treatment options to improve the survival statistics of this deadly disease.

Keywords: Gastric cancer, H. Pylori, Hyperthermic Intraperitoneal Chemotherapy (HIPEC)

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An investigation into the anti-cancer properties of ٦-gingerol (Review)

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Introduction: Ginger, a widely used medicinal plant, has long been valued in traditional medicine. It is a significant source of bioactive phytochemicals, with gingerol being its most potent bioactive compound. Gingerol exhibits a strong anticancer potential due to its low toxicity and phenolic properties. One important form of gingerol is ٦-gingerol, which possesses antimicrobial, anti-inflammatory, anti-proliferative, antioxidant, and anticancer properties. By inhibiting angiogenesis, regulating the cell cycle, and inducing cell death, ٦-gingerol effectively targets cancer cells and exerts its therapeutic effects. This review article aims to provide a comprehensive overview of the anticancer properties of ٦-gingerol and its mechanism of action, highlighting the therapeutic potential of this compound.

Methods: For this review article, the Google Scholar database was utilized. By employing an advanced search within this database, articles were limited to a temporal range of ٢٠١٩ to the present. Subsequently, through an examination of relevant keywords, the articles were categorized and scrutinized

Results: Results of studies on ٦-gingerol indicate that this compound exerts its anticancer properties through multiple mechanisms: Cell cycle regulation: ٦-gingerol induces cell cycle arrest at the G١ phase in breast cancer cells (MCF-٧ and MDA-MB-٢٣١) by decreasing cyclin D١ expression and increasing p٢١ expression. Additionally, ٦-gingerol inhibits the translation of cyclin-dependent kinases essential for the G١ and G٢ phases of the cell cycle, thereby affecting cell division. Induction of cell death: ٦-gingerol promotes apoptosis in cancer cells by preventing cell proliferation. Apoptosis, a promising pathway for cancer treatment, is mediated by caspases. Increasing concentrations of ٦-gingerol lead to increased levels of caspases and PARP. This compound stimulates the intrinsic apoptotic pathway in cancer cells by activating caspase-٣ and -٩ and increasing DNA fragmentation. The activation of the mitochondrial-dependent apoptotic pathway is observed with ٦-gingerol, which reduces mitochondrial activity in breast cancer cells. Inhibition of angiogenesis: ٦-gingerol reduces the possibility of metastasis by inhibiting angiogenesis and decreasing cell motility.

Conclusion: According to review studies, ٦-gingerol, an active phytochemical and phenolic compound in fresh ginger, exhibits significant therapeutic potential in cancer treatment. Research has demonstrated that ٦-gingerol exerts its anticancer effects through mechanisms such as inducing apoptosis, regulating the cell cycle, and inhibiting angiogenesis. The majority of studies in this field have been conducted in vitro, and clinical trials are needed to evaluate the efficacy of ٦-gingerol in

humans. Furthermore, future research should focus on investigating molecular mechanisms and the interactions of this compound with other drugs

Keywords: Gingerol – anticancer – cancer – ٦gingerol – antitumor

An Overview of PRP-Delivering Scaffolds for wound healing (Review)

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Introduction: Over the past few decades, tissue engineering techniques for skin regeneration and wound healing have evolved. During normal wound healing, Growth factors (GFs), cytokines, chemokines, and other cells work in coordination to form a dynamic and intricate multiple-phase process. Failure at these stages could result in persistent wounds and aberrant scar development. Tissue engineering aims to develop skin replacement products for accelerated wound healing. Using biomaterials essential for the growth and differentiation of cells, scaffolds, and other temporary biostructures can be created as advanced techniques used in wound repair and skin regeneration. Synthetic, natural, or composite biomaterials are used in skin tissue engineering to produce many different types of scaffolds, such as acellular structures, hydrogels, microspheres, porous, and fibrous to mimic an environment similar to the cell's original microenvironment. They could also act as a delivery system for active biological proteins called growth factors (GFs). GFs play a crucial part in the complex wound-healing process by regulating the cellular processes necessary for tissue regeneration and repair. Platelet-rich plasma (PRP) is a concentrated source of GFs. Alpha granules of active platelets release platelet-derived growth factor (PDGF), insulin-like growth factor ۱ (IGF-۱), epidermal growth factor (EGF), hepatocyte growth factor (HGF), transforming growth factor β (TGF-β), basic fibroblast growth factor (bFGF), and vascular endothelial growth factor (VEGF) which are involved in the wound healing.

Methods: PRP contain a large variety of growth factors and cytokines, which are critical to wound healing. These factors also encourage the proliferation, differentiation, and migration of cells, including fibroblasts, epithelial, endothelium, and mesenchymal stem cells (MSCs). Additionally, they aid in the revascularization of the injured tissue, angiogenesis, collagen formation, and hemostasis. Activated PRP (e.g., with $CaCl_2$), releases a high concentration of growth factors, and forms a gel or clot that has shown positive clinical outcomes for wound healing as a point-of-care autologous therapeutic. Nonetheless, numerous reports give contradictory results. The mismatch between the mechanical properties of PRP gel and native skin, as well as the growth factors undesired burst release profile which would probably be more successful if administered continuously via a biomaterial are suggested downsides of employing PRP directly as a gel. Regarding this, it has been demonstrated that biomaterial-based scaffolds can enhance the mechanical characteristics of fibrin gels that are not produced from PRP and can regulate the release of GFs under specific processing circumstances.

Results: Combining PRP with other biomaterials is one strategy to extend their activities. Biomaterials can guard against both the loss of their bioactivity and rapid burst release. Biomaterials are mostly safe drug carriers that the body can recognize, accept, and identify. They also prevent

degradation and allow for a prolonged release of the drugs. Consequently, PRP has been most frequently coupled with biomaterials in recent years for therapeutic applications. The majority of the time, adding PRP directly to biomaterials enhanced human skin fibroblasts, keratinocytes, and stem cell adhesion, migration, and proliferation. Furthermore, in vivo studies demonstrate that when compared to unmodified biomaterials, biomaterials treated with PRP dramatically reduce inflammation, improve angiogenesis, and consequently expedite wound healing. The platelets and biomaterial in this integrated system can be applied topically, intravenously, or through an intracavitary route to interact with the site of bleeding and injured tissue directly. So far, alginate, dextran, collagen, hyaluronic acid, chitosan, gelatin, keratin, polycaprolactone (PCL), polyvinyl alcohol (PVA), and carboxymethyl cellulose (CMC) used with various forms of scaffold, including hydrogel, sponge, or composite, have all been applied thus far in a variety of natural and synthetic scaffold for PRP delivery. Most research findings indicated that wound healing might be accelerated, and wound size could be considerably decreased without adverse consequences.

Conclusion: In conclusion, PRP is a safe and affordable treatment for skin wounds that can be enhanced through the use of a carrier to increase its capacity to repair and regenerate tissues. Additionally, by using a controlled release technique to increase growth factor availability, patients can experience a shorter recovery time and an overall higher quality of life.

Keywords: Platelet Rich Plasma, tissue engineering, scaffold, wound healing

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An overview of CAR-T cell therapy in cancer: Advancements and Challenges (Review)

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Introduction: According to statistics and results, cancer is known as the second cause of death worldwide, therefore the importance of treatment for this disease is very high. Until now, various methods have been used to treat cancer, including chemotherapy, hormone therapy, immunotherapy, etc., among which immunotherapy has had very promising and successful results. In the immunotherapy method, the treatment by Chimeric antigen receptor (CAR)-T cell has been very successful, especially in leukemia, lymphoma and solid tumors, both in children and adults. In the continuation of this review article, I intend to talk about the results of this new treatment method, which can be said to be revolutionary in cancer treatment and has led to a lot of hope for patients, as well as the challenges and limitations it has had so far.

Methods: I conducted search in ۳ databases; PubMed, Scopus and Web of Science with the related terminol¬ogy of immunotherapy, cancer and CAR-T cell therapy. In this review, I in¬vestigated relevant articles from ۲۰۱۰ up-to-now to refer to the cell therapies for cancer.

Results: Overall, CAR-T cell therapy represents a significant breakthrough in cancer treatment, especially notable in hematologic malignancies, offering unprecedented effectiveness and optimism. Evidence from both clinical trials and real-world applications reveals impressive response rates and sustained remissions, with select patients achieving long-term survival and even complete recovery. CAR-T cell therapy has emerged as a cornerstone of precision medicine, providing tailored and precise treatment options for individuals confronting refractory or relapsed cancers. Nevertheless, despite its considerable progress, CAR-T cell therapy encounters obstacles and constraints, including cytokine release syndrome, neurotoxicity, antigen evasion, and solid tumor resistance. Overcoming these challenges is imperative to optimize therapy effectiveness and safety, as well as to expand its utility across diverse cancer types.

Conclusion: CAR-T cell therapy has emerged as a transformative approach in cancer treatment, offering the promise of durable remissions and potential cures for patients with refractory or relapsed hematologic malignancies. While significant progress has been made, challenges remain in extending the benefits of CAR-T cell therapy to patients with solid tumors and overcoming treatment-related toxicities. Continued research efforts aimed at optimizing CAR design, enhancing safety profiles, and expanding the applicability of CAR-T cell therapy to a broader range of cancers hold promise for the future of cancer immunotherapy.

Keywords: CAR-T cell, Cancer, Immunotherapy, Cell therapy

An overview of dengue fever causes and treatment methods (Review)

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Introduction: Dengue is a mosquito-borne virus, and dengue fever is the most common cause of viral diseases transmitted by arthropods worldwide, which has raised a significant public health concern. It is also known by various names, such as bone-breaking fever or ٧-day fever, and is characterized by severe muscle contractions, joint pain, and high fever, which indicate the severity and persistence of symptoms. Most cases of dengue virus are asymptomatic; however, it is a severe disease and can cause fatality, especially in areas where female Aedes mosquitoes (Aedes aegypti and Aedes albopictus) transmit the virus the most.

Methods: Dengue has been known for more than ٢٠٠ years and is common in Asia, along the Atlantic coast and the American Gulf and the Caribbean, with its first being recognized in the Philippines in ١٩٥٤. Dengue viruses (DENVs) are positive single-stranded RNA viruses enclosed in a protein capsule surrounded by a coating that gives it a spherical shape; Their RNA genome is made up of seven non-structural protein (NS) genes and three structural protein genes, including the nucleus, membrane, and coating. Key cytokines such as interferon-gamma (IFN)-γ, tumor necrosis factor (TNF)-α, and interleukin (IL)-١٠ play a key role in the pathogenesis of dengue. There are four different but related dengue virus serotypes: DENV١ to DENV٤ where disease severity is often associated with the response of CD٨+ T cells. These viruses are transmitted by mosquitoes of the genus Aedes and their clinical symptoms range from asymptomatic to severe hemorrhagic fever.

Results: In addition, it is important to educate patients about the warning signs and advise them to see a doctor immediately if any of these symptoms occur. Patients with warning signs, severe dengue fever, or risk factors such as age, pregnancy status, diabetes, or those living alone should be evaluated for hospitalization. People who show warning signs can start treatment with intravenous (IV) crystalloid fluids, and fluid rates are adjusted based on the patient's response. Patients who experience shock and do not respond to initial doses of crystalloid may require colloids. Blood transfusions are necessary in cases of heavy or suspected bleeding when the patient remains unstable despite adequate fluid replenishment and hematocrit decreases. Platelet transfusions may be necessary if the platelet count drops below ٢٠,٠٠٠ cells per microliter and the risk of bleeding is high. In general, it is essential to avoid the administration of aspirin, non-steroidal anti-inflammatory drugs (NSAIDs), and other anticoagulants.

Conclusion: The main way of transmission of the dengue fever virus is through the bite of female Aedes mosquitoes infected with the virus, whose main audience is humans. Aedes flies, especially Aedes aegypti, Aedes albopictus, Aedes scutellaris and Aedes polynesiensis, are known to transmit

dengue infection. Aedes aegypti, the most important carrier, originated in Africa and moved to tropical and subtropical regions with the expansion of international trade. Aedes polynesiensis and Aedes scutellaris are typically found in the regions of the South Pacific.

Keywords: Dengue Fever, DENV, Aedes mosquitoes, Virus, RNA

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An Overview of Genetic Polymorphisms and Their Role in Drug Toxicity (Review)

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Introduction: Genetic polymorphisms refer to variations in DNA sequences among individuals, which can influence the cell's response to drugs. These variations can manifest in various forms, including single nucleotide polymorphisms (SNPs) or copy number variations (CNVs). Such polymorphisms play a crucial role in determining individual reactions to drugs and their tolerability. Pharmacogenetics is a branch of science that studies the impact of individual genetic differences on drug responses. The primary goal of this field is to identify genetic polymorphisms that can explain different drug reactions and thereby aid in the development of personalized therapies. These genetic variations can affect the pharmacokinetics and pharmacodynamics of drugs, leading to differences in drug metabolism, absorption, distribution, and excretion. In other words, genetic differences can cause a drug to be effective in some individuals while being ineffective or even causing serious side effects in others. A significant example involves the CYP٤٥٠ family genes, which are essential in the metabolism of many drugs. Polymorphisms in CYP٢C١٩ and CYP٢C٩ genes can greatly influence the metabolism of drugs such as clopidogrel and warfarin (anticoagulants). For instance, individuals with inactive alleles in the CYP٢C١٩ gene may not respond to clopidogrel and might require an alternative medication. As mentioned, genetic polymorphisms can also increase or decrease drug toxicity. For example, in cancer treatments, polymorphisms in genes related to drug metabolism can lead to increased toxicity or drug resistance. Recent studies have shown that polymorphisms in CYP٣A٤ and CYP٣A٥ genes can significantly affect the response to atorvastatin (a drug for preventing heart disease), which may lead to changes in treatment efficacy.

Methods: This review article compiles and discusses research on genetic polymorphisms and their role in drug toxicity . Information was sourced from databases such as PubMed , NCBI, MDPI and Google Scholar.

Results: Genetic polymorphisms in drug-metabolizing enzymes can also have significant impacts on drug responses, efficacy, and toxicity. For instance, enzymes from the cytochrome P٤٥٠ family, such as CYP٢C٩ and CYP٢C١٩ (which play key roles in the metabolism of various drugs, including warfarin and clopidogrel), and CYP٣A٤ and CYP٣A٥ (involved in the metabolism of many drugs, including statins and some anticancer drugs). Drug transporter proteins play a vital role in regulating the absorption, distribution, and excretion of drugs. Genetic polymorphisms in these proteins can significantly affect the pharmacokinetics and pharmacodynamics of drugs. Identifying and studying these polymorphisms is crucial for improving personalized treatments and reducing drug side effects. Some of these proteins include: SLCO١B١/OATP١B١ (which plays a key role in drug transport into the liver), ABCB١/MDR١ (P-glycoprotein, which is involved in drug efflux from cells and preventing their accumulation in sensitive tissues), ABCG٢/BCRP (involved in drug and metabolite

efflux from cells), and ABCC۲/MRP۲ (important in the biliary excretion of drugs and their metabolites).

Conclusion: Understanding and identifying genetic polymorphisms through genetic testing can enhance personalized treatments, increase treatment efficacy, and reduce drug side effects. This information can help physicians in more precise drug dosing and in choosing more appropriate medications for patients. Further research in this area can lead to the identification of new genetic markers associated with drug toxicity and the development of personalized therapeutic approaches. Such research not only helps improve patient treatment management and safety but can also reduce the costs associated with unsuccessful treatments and adverse side effects.

Keywords: Genetic polymorphisms, Drug response, Drug metabolism, Drug toxicity, Drug resistance

An overview of probiotic bacteria and a brief look at its applications in industry and medicine

(Review)

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Introduction: Background: Probiotics are live microorganisms that, when administered, confer health benefits on the host. In recent years, the concepts of "prebiotics" and "synbiotics" have been introduced. Prebiotics are non-digestible food ingredients that selectively stimulate the growth and/or activity of one or a limited number of bacteria in the colon, while synbiotics are a combination of probiotics and prebiotics. Fructooligosaccharides, inulin, and trans-galactooligosaccharides, for example, selectively stimulate the growth of Bifidobacteria and may enhance their efficacy.

Methods: This review systematically analyzed literature from ١٩٠٠ to ٢٠٢٤, retrieved from Google Scholar, SID, Scopus, PubMed, Web of Science, and books. Keywords included probiotics, prebiotics, synbiotics, Bifidobacterium, Lactobacillus, and yogurt. Retrieved articles were evaluated based on their titles, abstracts, and relevance to the study's focus on the importance and applications of probiotics in industry, medicine, and healthcare.

Results: Bacteria such as Bifidobacterium longum and various Lactobacillus species are commonly found as probiotics in dairy products. A total of ٤٩ articles, ٣ books, ١ thesis, and ٢ national standards were analyzed. These resources primarily focused on the benefits and applications of probiotics, prebiotics, and synbiotics, as well as methods for isolating and identifying Lactobacillus bacteria. One thesis and a national health standard provided details on the production process of probiotic yogurt.

Conclusion: The findings of this research highlight the potential of probiotics, particularly those isolated from local yogurt, for various applications in human health, including pharmaceutical, food, and dairy industries.

Keywords: probiotics, prebiotics, Bifidobacterium, Lactobacillus, health benefits, industrial applications

An overview of stem cells (Review)

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Introduction: Stem cells, found in all multicellular organisms, can self-renew and differentiate into specialized cells, offering hope for regenerative medicine and cell therapy. Recent advancements have made these cells a promising tool for treating difficult diseases. However, challenges and limitations remain, necessitating further research to fully harness their potential. This paper explores the fundamental concepts, applications, and future prospects of stem cell usage.

Methods: This study aims to provide a comprehensive review of previous research on mesenchymal stem cells. A systematic literature search was conducted in reputable databases using the following keywords: [Mesenchymal stem cells; extraction; cellular differentiation; biomedical applications]. Studies were included if they were published in English after ۲۰۱۰.

Results: This study provides a comprehensive overview of stem cell biology, highlighting their potential as a promising therapeutic tool. While significant advancements have been made, challenges related to cell source, differentiation, and safety remain. Further research is necessary to fully realize the therapeutic potential of stem cells.

Conclusion: All current therapeutic methods have specific advantages and disadvantages, but today, the use of stem cells, due to their complete genetic compatibility with the individual, has led to the development of new therapeutic approaches. The very interesting and diverse characteristics of stem cells provide them with extraordinary potential and capabilities. The emergence of stem cells in medicine and the pharmaceutical industry has enabled many therapeutic methods in targeted drug delivery and toxicology. In recent years, significant advancements have been made in the methods of culturing and isolating stem cells; however, the comprehensive application of stem cells in medicine and drug discovery depends on strong scientific development and reproducible and defined cell line cultivation. Given the remarkable advancements in medical science and medical equipment in the near future, it will, God willing, be possible to fully utilize stem cells for the regeneration and repair of all living organs.

Keywords: Mesenchymal stem cells; extraction; cellular differentiation; biomedical applications.

An overview of the action of folic acid (Review)

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١.

Introduction: Folic acid, a B vitamin, plays a critical role in DNA and RNA production and cellular division. This vitamin is especially essential for pregnant women, as the need for it significantly increases during pregnancy. Fortifying foods with folic acid can enhance the nutritional status of pregnant women and reduce the risk of adverse outcomes such as neural tube defects in the fetus. rich food sources of Folic Acid: _Green leafy vegetables (such as spinach and kale), legumes, fruits and whole grains are primary sources of folic acid.

Methods: In a study conducted on ٧٧ female smokers with cervical dysplasia, it was found that folic acid fortification led to a ٦٣٪ increase in folate intake among these individuals. Moreover, the proportion of women whose folate consumption fell below the estimated average requirement decreased after fortification. Another study indicated that pregnant women consuming ٨٥٠ micrograms of folic acid showed higher serum folate levels compared to those consuming ٤٥٠ micrograms

Results: Raise public awareness about the importance of folic acid and its rich food sources, particularly among pregnant women and those of childbearing age. Encourage the consumption of folic acid supplements, especially in areas with a high prevalence of this deficiency.

Conclusion: This amount equates to approximately ٦٠٠ micrograms of dietary equivalents, considering ٥٠ to ٧٥ percent bioavailability of folic acid in foods. Consumption of green leafy vegetables among non-pregnant women led to higher levels of DHA(a type of omega-٣ fatty acid) in the blood, demonstrating the positive impact of these vegetables on nutritional status.

Keywords: Folic Acid Food Fortification Pregnant Women’s Health Congenital Defects Nutrition

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An overview of the cause and trearment of gangrene (Review)

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Introduction: The clostridium perfrigens is an anaerobc,spore- forming, gram positive rod responsible for necrotizing (cells) tissue , then gangrene,bacterium in patients with cancer or gastrointestinal tract infection. The clostridium perfrigens species is associated with mushrooms and viruse eviroment such as soils, sewage, and food. However,it is also a compont of the gastroinstial microflora of sick and heathly humans and animals.

Methods: C. perfrigens type A is the major cause of traumatic gas gangrene. C. perfringens is linked with different systemic and enteric diseases in livestock and humans, such as gas gangrene, food poisoning, non-foodborne diarrhoea, and enterocolitis. We have three gangrene,such as : Dry Gangrene , Wet Gangrene and Gas Gangrene. Dry Gangeger is a gangrene in which oxygen does not reach it so the cell does not get infected. If there is a bacterial infection in the damaged tissue, gangarene is known as wet gangrene. Wet gangrene occure after a burn, severe frostbite or injury. Gas gangrene is usually caused by an infection with a bacterium called clostridium perfungus.

Results: Gas gangrene is a life-threatening condition that requires early treatment, including antibiotic prescription and amputation of human limbs.

Conclusion: People with diseases, high bloodpressure, obesity, smoking, hyperlipidemia and heart diseases are more exposed of gangrene.

Keywords: C. perfrigens. gangrene. Gas Gangrene. Wet Gangrene. Dry Gangrene. clostridium perfrigens.

an overview of the effect of chemical pollutants on food and contaminating them (Review)

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Introduction: Food contaminants have always been a serious threat to human health. Therefore, researchers in recent years have been dedicated to the development of fast, reliable, sensitive and suitable detection techniques for the detection of food contaminants in food matrices. Arsenic, which is found naturally in the earth's crust, is one of the important factors that cause pollution, because of its high solubility in water and its tendency to bio accumulate in various environmental matrices, it is very toxic even at low levels.

Methods: In recent years, colorimetric methods, fluorescence methods, photo electrochemical methods, chemical methods, nucleic acid amplification methods, and other methods have been proposed for timely detection and prevention of human food contamination.

Results: Ultimately, we hope that recent strategies and advances will provide valuable insights to guide researchers in the sensitive detection of food contaminants and find a way to eliminate or control harmful bacterial biofilm formation.

Conclusion: Preventing various factors that can enter the food cycle and cause humans to be exposed to diseases, and providing methods for preventing the spread of contaminated food to humans and reducing various diseases, including cancer, liver toxicity, kidney failure, and disease become skin lesions in humans.

Keywords: Bacterial bio-carpet-chemical pollutants-arsenic-contaminated food

An overview of the role of microbiomes in the severity and severity of colorectal cancer (Review)

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Introduction: Microbiome means microbes coexisting with the host, regardless of the species, in a part of the body of an organism called microbiome. Nowadays, changes in gut microbiota are considered as a potential therapeutic approach for the prevention or treatment of colorectal cancer (CRC).

Methods: This research is a review study .databases such as NCBI, PUBMED, etc have been used in this research to collect information

Results: Studies have shown that dietary habits and lifestyle play a role in modulating the gut microbiota. Intestinal microbiota play a role in converting food components into oncometabolites. Some studies showed that Shigella, Citrobacter and Salmonella bacteria are more abundant in the early stages of cancer compared to healthy people. The aim of this study is to review the role of microbiomes in the development of colorectal cancer and the metabolites produced by microbiomes in the development of colorectal cancer.

Conclusion: In total, the studies show that the separation of genetic factors and genes involved in the development of this disease and especially familial CRC; The type of intestinal microbiota and the food pattern and lifestyle of a person play a role in causing this condition. It should be noted that dietary pattern plays a role in the proliferation of microbiota that produce carcinogenic products.

Keywords: Keywords: microbiome, colorectal cancer, genetics, environmental factors.

An overview of the use of nano-antibiotics in the diagnosis and treatment of infectious diseases (Review)

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۱.
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Introduction: Infectious diseases are the second leading cause of death worldwide. Therefore, nanotechnology is an excellent function for the treatment of drug-resistant microbial infections, which many antibiotics have been used to control. In addition, nano-systems have attracted a new structure for the evolution of antibiotics in improvement.

Methods: This systematic review, to identify studies aimed at the effect of nano-antibiotics in the diagnosis and treatment of infectious diseases, search in PubMed, Google Scholar, and Science Direct databases based on keywords Antibiotics, Nanotechnology, and Infectious diseases was done. After reviewing the summary of the articles and checking the title, the irrelevant articles were removed. The full text of the articles was searched and the articles related to the topic were included in the study.

Results: Nano-particles have strong antimicrobial activity, which is why various types of communication nano-systems are evaluated for the treatment of infectious diseases. Antimicrobial nanoparticles have many advantages over conventional antibiotics in reducing the medicinal aspect, effects, resistance, and treatment costs.

Conclusion: Creating bacterial resistance to antibiotics will turn infectious diseases into one of the diseases soon. Also, most bacterial infections need to be treated with antibiotics, although some may resolve independently.

Keywords: Antibiotics, Nanotechnology, Infectious diseases

An overview on antimicrobial properties of red onion peel extract (Review)

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Introduction: Onion (Allium cepa L.) is the second important horticultural crop worldwide. Red onion as one of the most valuable cultivars, is a powerful source of bioactive components such as phenol and flavonoid that has many applications in pharmacology as antioxidant, anticancer and antimicrobial. Quercetin ٣,٤′-diglucolside, quercetin ٤′-monoglucoside and quercetin are the most flavonols in the red onion extract. Moreover, studies showed that level of this components in the peel extract is more than the bulb.

Methods: In this systematic review study, we discuss on the antimicrobial properties of red onion peel extract. To this end, we used recent reports in databases including pubmed, scopus, ISC and google scholar since ٢٠١٩ via searching the relevant key words, antimicrobial properties, antibacterial effects and red onion. From about ٧٠ reports, those are related to red onion peel extract were included in this study.

Results: Results from reviewing about ٣٠ papers, showed that, onion peel extract has significant antimicrobial effects, although the exact component which has the most antimicrobial activity is still unknown. It has been reported that Gram-positive bacteria like Bacillus cereus, Staphylococcus aureus, Microcroccus luteus, and Listeria monocytogenes were more sensitive to this extract, compared to Gram-negative bacteria like Escherichia coli and Pseudomonas aeruginosa. Dhowlaghar et el. in ٢٠٢٣, indicated that red onion peel has inhibiting effect on the growth of Listeria monocytogenes, a gram-positive bacterium, available in different foods like meat and dairy products and may cause serious disease. Also, in the same year, Momoh et al reported antimicrobial activity of aqueous red onion peel extract on two bacterial strains Staphylococcus aureus (gram positive) and Escherichia coli (gram negative). Both of these are mentioned as gastrointestinal diseases agents. In ٢٠٢١, Ginda Haro and collages assessed the antimicrobial properties of red onion peel extract and their results proved the antibacterial capacity of this extract on Staphylococcus aureus, Escherichia coli and Candida albicans. Former, Alok Sagar et al. studies the antimicrobial effects of polyphenolic extracts against six pathogenic bacteria, from onion peel from fifteen cultivars. Their results showed that red onion peel extract is the second effective one specially against Streptococcus agalactiae and Pseudomonas aeruginosa. These bacteria may cause diarrhea.

Conclusion: The data suggest that red onion peel extract could be potentially used as an antimicrobial complement to prevent and treat infectious disease. However, as every year, a large amount of red onion peel discard as agricultural waste, using it could in pharmaceutical industries could be beneficial and economical.

Keywords: Antimicrobial properties. Red onion peel extract. Antibactrial properties.

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Analysis of DNA methylation signatures in the blood to diagnose breast cancer (Review)

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Introduction: Today, due to the increasing expansion of breast cancer, early diagnosis and in the early stages raise the possibilities of treatment and prevent women's deaths. The use of non-molecular technologies such as gastroscopy, computed tomography, and protein biomarkers are still considered the focus of clinical cancer screening, but these methods have low specificity and sensitivity. Late cancer diagnosis often prevents patients from receiving optimal care. This study intends to illustrate circulating cell-free DNA, circulating tumor DNA, and exosomes in peripheral blood plasma for early cancer detection as a non-invasive approach. Many studies have shown a relationship between methylation markers and breast cancer, and it seems that the examination of DNA methylation patterns based on blood in breast cancer can be used for early detection and dynamic monitoring of breast cancer as a non-invasive method.

Methods: Valid scientific sites and sources such as Scopus, Google Scholar, and PubMed will be used to conduct this study. Also, the keywords Breast cancer, Circulating tumor DNA, PBMCs, and DNA methylation will be used. Articles that are very old (before ٢٠٠٠) or do not have any of these keywords are excluded from the study.

Results: Our study indicate that analysis of DNA methylation patterns from blood samples can be used as a non-invasive method for early breast cancer detection and monitoring. The application of blood-based DNA methylation in medicine is currently under development. Medical applications use blood-based DNA methylation is still in its infancy.

Conclusion: In general, there the problems such as false-negative reporting due to low blood-based DNA concentrations and poor reproducibility for selected markers but enhancing diagnostic kits' blood-base sensitivity and specificity broadens their use in cancer treatment and diagnosis.

Keywords: Breast cancer, Circulating tumor DNA, PBMCs, DNA methylation

Angiocrine functions of mesenchymal stem cell exosomes on ischemic myocardium: a systematic review. (Review)

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Introduction: Mesenchymal stem cells (MSCs) can foster the regeneration of the ischemic myocardium in a paracrine manner via the release of several extracellular vesicles, especially exosomes. It has been indicated that exosomes are cell-free byproducts and can harbor diverse pro-angiogenic factors that are involved in the growth of blood vessels to the ischemic sites. Here, previous studies related to angiogenesis capacity of MSC exosome and restoration of ischemic myocardium are presented.

Methods: The current descriptive-analytical review study was conducted to identify relevant experiments associated with the application of MSC exosomes in the regeneration of ischemic myocardium. To this end, online search was done in databases including Google Scholar, Web of Science, and PubMed databases from ٢٠١٨ until ٢٠٢٤. The keywords were "mesenchymal stem cells", "exosomes", "myocardium ischemia", "angiogenesis", and " Regeneration". Studies were included based in terms of relevant topic, study design, patient characteristics, therapeutic regimes, and outcomes. Data related to angiogenesis capacity of MSC exosomes in heart ischemia were extracted and included to this study.

Results: Data indicated the reparative properties of MSC exosomes via the promotion of angiogenesis within the cardiac tissue parenchyma after ischemia. The induction of vascularization into the ischemic myocardium can prevent subsequent aberrant remodeling and fibrotic changes.

Conclusion: Taken together, MSC exosomes are magic bullets and valid therapeutic options for the regulation of angiogenesis following the ischemic conditions. However, enormous experiments are mandatory to elucidate the underlying mechanisms associated with blood vessel formation within the ischemic myocardium.

Keywords: Mesenchymal stem cells; exosomes; myocardium ischemia; Angiogenesis; Regeneration.

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Antagonistic Effects of Temozolomide and Sialic Acid on Bax Gene Expression in Glioma Cells: Implications for Chemoresistance (Research Paper)

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Introduction: Glioma, a primary tumor of the central nervous system, is resistant to various treatments, including chemotherapy. Temozolomide (TMZ) is a first-line chemotherapy drug used for glioma treatment; however, the tumor microenvironment, including factors such as sialic acid, can influence drug resistance and treatment outcomes. This study aims to investigate the effects of TMZ, sialic acid, and their combined treatment on Bax gene expression in glioma cells, with a focus on apoptosis regulation. Bax, a pro-apoptotic member of the Bcl-٢ family, plays a critical role in promoting cell death.

Methods: Glioma ١٣٢١N١ cells were cultured under standard laboratory conditions and treated with temozolomide (١٠٠ µM) and sialic acid (٣٠٠ µM), both individually and in combination, over a ٧٢-hour period. Gene expression analysis of Bax was performed using real-time PCR to assess changes in apoptosis regulation under different treatments.

Results: The results revealed that treatment with temozolomide increased Bax gene expression, indicating enhanced apoptosis in glioma cells. In contrast, treatment with sialic acid alone led to a sharp decrease in Bax expression, suggesting an inhibitory effect on apoptosis. Interestingly, the combined treatment of temozolomide and sialic acid resulted in a pronounced reduction in Bax expression, indicating that sialic acid might counteract the pro-apoptotic effects of temozolomide. This suppression of Bax expression in the presence of sialic acid suggests that it may play a role in reducing the effectiveness of temozolomide, potentially contributing to the survival of cancer cells and resistance to chemotherapy.

Conclusion: This study highlights the potential of sialic acid to interfere with temozolomide-induced apoptosis by downregulating Bax gene expression. The findings underscore the importance of targeting sialic acid as a therapeutic strategy to overcome chemoresistance in glioma treatment and improve patient outcomes

Keywords: ١٣٢١N١, tumor microenvironment, Sialic acid, BAX, Drug resistance

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Anti-helicobacter pylori peptides: promises and challenges (Review)

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Introduction: Anti-Helicobacter pylori (H. pylori) peptides have emerged as a novel approach for treating infections caused by this bacterium. H. pylori is the primary cause of gastric ulcers, duodenal ulcers, and certain gastric cancers. Traditional treatments include antibiotics and proton pump inhibitors, but rising antibiotic resistance has increased the need for new solutions. The first antimicrobial peptide specifically targeting H. pylori, the human cathelicidin LL-٣٧, was identified in ١٩٩٥ by Dr. Rolf David and colleagues at Lund University, Sweden. LL-٣٧ plays a key role in combating antibiotic-resistant infections. Antimicrobial peptides (AMPs) have gained attention due to their strong antibacterial activity, lower drug resistance, anti-inflammatory properties, and specific targeting, with some peptides binding directly to H. pylori and eliminating the bacteria without harming the stomach's natural flora

Methods: To this end, MEDLINE, EMBASE, LILACS, AIM, and IndMed databases were searched for relevant articles since ١٩٩٥

Results: Anti-H. pylori peptides offer more effective treatment options, but realizing their full potential requires addressing these challenges. Continued advancements in these areas could lead to the development of new, more efficient therapies

Conclusion: Using antimicrobial peptides represents a promising, innovative approach to treating H. pylori infections. Overcoming current challenges will require extensive research to fully harness the potential of these compounds, paving the way for safe and effective treatments

Keywords: anti-inflammatory properties, gastric cancers, antibiotic.

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Antibacterial effect of vancomycin/ceftriaxone on the expression level of mecA gene in methicillin-resistant Staphylococcus aureus (Research Paper)

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Introduction: Introduction: Methicillin- resistant Staphylococcus aureus (MRSA) is a significant cause of hospital-acquired infections. Vancomycin is often used to treat MRSA bacteremia despite a high incidence of microbiological failure. Unfortunately, the number of resistances to vancomycin has been steadily rising. It is reported that appropriate β-lactams such as ceftriaxone in combination with vancomycin demonstrated synergistic activity against MRSA. In this study, we aimed to evaluate the antimicrobial effect of combined vancomycin/ceftriaxone on the expression level of mecA gene in MRSA isolates from patients in Gachsaran Shahid Rajaie Hospital.

Methods: Methods: Firstly, nasal swabs were obtained from ١٢٠ immunocompromised patients such as diabetes, cancers and pregnant and cultured on differential and selective media to isolate Staphylococcus aureus, which was confirmed by standard biochemical tests. Then bacterial suspensions were cultured on Muller-Hinton Agar containing NaCl and Oxacillin for detection of MRSA isolates. Subsequently, antibacterial susceptibility of vancomycin and ceftriaxone against all MRSA isolates was performed via disc diffusion agar and followed by CLSI recommend microdilution broth test for determination of MICs and then, FIC index is calculated for combination therapy. Eventually, the expression level of Mec A gene in MRSA treated with vancomycin/ceftriaxone was evaluated using quantitative real time RT-PCR.

Results: Results: Out of ١٢٠ clinical samples from immunocompromised patients, ٢٨ isolates of MRSA (٢٣,٣٪) were identified. Findings indicated the relative resistance of all MRSA isolates to vancomycin (٢٥٪) and ceftriaxone (٢٨,٥٪) antibiotics. The overall MIC for MRSA isolates with vancomycin was ranged from ٠,٠٦٢٥ to ٢ µg/ml while, for ceftriaxone was ranged from ٠,٠٦٢٥ to ٤ µg/ml. FIC index of combination therapy of vancomycin/ceftriaxone showed synergistic activity (٨٢,١٪) in all MRSA isolates and ranged from ٠,٣٧ to ٠,٤٥. Eventually, the expression level of mecA gene showed a significant reduction (٢-٣,٥ fold) in all MRSA isolates after treatment with combined vancomycin/ceftriaxone.

Conclusion: Conclusion: The combination between vancomycin and ceftriaxone could be a potential agent against MRSA that can serve as possible model for new antibacterial drug. Combination therapy may reduce the risk of relapse, but additional high-quality studies are needed.

Keywords: Key words: Methicillin-resistant Staphylococcus aureus (MRSA), Combination Therapy, Mec A

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Antibacterial Microbial Polysaccharides: A New Approach to Fighting Bacteria (Review)

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Introduction: Today, due to the global spread of antibiotic resistance, a significant part of research is focused on developing strategies based on antimicrobial polysaccharides and exploring their potential applications in medicine, healthcare, food packaging, wastewater treatment, and other fields. Several factors, such as temperature, pH, oxygen availability, and environmental conditions, play an important role in the biological processes of microorganisms and influence the production of microbial polysaccharides. The aim of this study was to investigate the extent of antimicrobial polysaccharide use various industries and examine the future prospects of this method in reducing the indiscriminate use of antibiotics.

Methods: In this review study, the use of microbial polysaccharides with antibacterial properties in various industries was explored using library methods and a review of related articles from reliable databases.

Results: Due to the rapid progress in medical science, research on polysaccharide biosynthesis has gained significant importance. Studies indicate that, in addition to polysaccharides like chitosan, hyaluronic acid, dextran, cellulose, and their derivatives, other antibacterial polysaccharides can also be produced through modern techniques such as genetic manipulation and the development of microbial strains specifically engineered for polysaccharide production. These methods offer economic and efficiency benefits. In a study, scientists produced N-(۳-azido-۲-hydroxypropyl) chitosan, which showed higher antibacterial activity than ampicillin and gentamicin. In addition, antimicrobial polysaccharides can be used to produce antibacterial nanofibers that can be used in wound healing dressings, packaging of food products such as meat to increase shelf life, and in gels to treat superficial skin infections.

Conclusion: Because of the wide range of applications for microbial polysaccharides and their unique properties, such as scalable production, affordability, biocompatibility, and biodegradability, they have garnered the attention of scientists and industry experts. The rapid spread of drug-resistant microbial infections has become a major global challenge. However, studies on microbial polysaccharides suggest that we are approaching a post-antibiotic era, where the use of novel substances could become a viable solution.

Keywords: Polysaccharide, Antibacterial, Production, Antibiotic Resistance

Antibiotic resistance in bacteria and therapeutic challenges (Research Paper)

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Introduction: Antibiotic resistance is considered as one of the biggest health challenges around the world, and recent developments in this field have shown that if effective measures are not taken, drug resistance can become a global crisis in the field of public health. The roots of antibiotic resistance lie in the widespread and sometimes inappropriate use of antibiotics in the treatment of bacterial diseases as well as in agriculture. As a result of this process, many pathogenic bacteria have been able to develop resistance mechanisms against antibiotics over time and reduce their medicinal effects. In addition, the emergence of "superbugs" that are resistant to several different drugs have created serious challenges in existing treatments.

Methods: A: Research and development of new drugs: One of the important ways to deal with the antibiotic resistance crisis is the development of new drugs with new mechanisms of action. Pharmaceutical companies should increase their efforts to research and develop new antibiotics. In addition, the use of lesser-known antibiotics or new compounds can help combat resistance. B: Rational use of antibiotics: Another important solution to reduce the rate of antibiotic resistance is the rational and targeted use of these drugs. Educating people and doctors about the correct use of antibiotics and avoiding their inappropriate use can play a very important role in this field. People should be advised to take antibiotics only when prescribed by a doctor and to complete the course of treatment to prevent the development of resistant bacteria. A: Prevention of infections: Prevention of bacterial infections through improving public health and vaccination can also help reduce the need to use antibiotics and thus reduce drug resistance. Vaccines developed to prevent bacterial infections can play a vital role in combating this crisis.

Results: Antibiotic resistance is one of the biggest public health challenges in the world and the continuation of the current trend can lead to a global crisis. To deal with this phenomenon, there is a need for global coordination and joint efforts in the areas of research and development, public education and prevention of infections. The development of new drugs and the optimal use of existing antibiotics can help reduce the resistance process. On the other hand, it is very important to educate patients and doctors to use drugs correctly and prevent unnecessary use of antibiotics.

Conclusion: Antibiotic resistance is one of the biggest public health challenges in the world and the continuation of the current trend can lead to a global crisis. To deal with this phenomenon, there is a need for global coordination and joint efforts in the areas of research and development, public education and prevention of infections. The development of new drugs and the optimal use of existing antibiotics can help reduce the resistance process. On the other hand, it is very important to educate patients and doctors to use drugs correctly and prevent unnecessary use of antibiotics.

Keywords: Antibiotics, infection, prevention , Vaccination

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Anticancer effect of antibiotics in iTM and microbiome (Review)

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Introduction: In this essay the complex relationship between antibiotics, the microbiome, and cancer treatment, highlighting the potential benefits and risks of antibiotic use in oncology is reviewed. Central to the discussion is how the human microbiome, particularly gut microbiota, influences cancer progression and treatment outcomes. The study emphasizes the dual role of antibiotics, which can both support and hinder cancer therapies depending on their effects on microbial communities. The Role of the Microbiome in Cancer Progression and Treatment The human microbiome plays a pivotal role in regulating immune responses, metabolism, and cellular functions, all of which are essential in cancer development and treatment responses. Microbial communities within the gastrointestinal tract are particularly influential in modulating inflammation, immune activity, and the efficacy of cancer therapies. For instance, specific bacterial species can enhance the effects of immunotherapies by boosting T-cell activity, while others may interfere with treatment by inducing immunosuppression (١). The essay explains that variations in microbial composition within the gut or other epithelial barriers can affect both local and systemic immune responses, altering cancer progression and therapy effectiveness. This influence of microbiota on anticancer therapies is becoming increasingly recognized, with studies showing that a healthy, balanced microbiome can improve treatment outcomes in chemotherapy and immunotherapy by regulating immune responses (٢). The Dual Nature of Antibiotics in Cancer Treatment Antibiotics are frequently used in cancer patients to manage infections due to compromised immune systems. However, while antibiotics have been shown to exhibit antitumor properties by inducing apoptosis and inhibiting cancer cell proliferation, they can also disrupt the microbiome, leading to a condition known as dysbiosis (٣). Dysbiosis negatively affects the body's immune responses, potentially diminishing the effectiveness of cancer treatments, especially immune checkpoint inhibitors (ICI). This can result in suboptimal treatment outcomes for cancer patients undergoing immunotherapy (٣). The essay elaborates on how antibiotics, while beneficial in preventing infections, must be used with caution in cancer patients. By disrupting gut microbiota, antibiotics can impair the immune system's ability to fight cancer, leading to decreased effectiveness of therapies like chemotherapy and immunotherapy. This is particularly concerning in the context of ICIs, where a balanced microbiome is critical for optimal immune function (٤). Intra-tumoral Microbiome and Its Impact on

Treatment In addition to the gut microbiome, the essay explores the role of the intra-tumoral microbiome, which refers to the bacterial communities found within tumors. Although research in this area is still emerging, there is growing evidence that intra-tumoral bacteria can influence cancer progression and response to treatment. Some bacteria found in tumors can metabolize chemotherapeutic agents, reducing their effectiveness. For instance, intra-tumoral bacteria have been shown to inactivate gemcitabine, a common chemotherapy drug, thereby leading to drug resistance (٥). The presence of intra-tumoral microbiota also affects immune regulation and gene expression within the tumor microenvironment. These bacteria can either enhance or suppress immune responses, impacting the effectiveness of anticancer therapies (٦). Thus, understanding the role of intra-tumoral microbiota offers new opportunities to optimize cancer treatments by potentially targeting these bacteria to improve therapeutic outcomes.

Methods: Human microbiome plays a crucial role in the initiation and progression of cancer by influencing the balance between cellular proliferation and apoptosis, regulating immune responses, and affecting metabolic processes within cells. Comprehensive studies have highlighted that manipulating the microbiota could potentially enhance cancer therapies. One strategy for modulating the microbiota is the administration of antibiotics, though the effects of antibiotic use can range from beneficial to detrimental. Antibiotics may directly impact cancer cells by promoting apoptosis, targeting cancer stem cells to prevent recurrence, inhibiting cancer cell proliferation, and blocking metastasis. Alternatively, antibiotics may indirectly affect cancer cells by altering the microbiota in ways that inhibit cancer growth. Due to these effects, antibiotics are increasingly used to support cancer treatment. We identified ٣٥ relevant articles through searches on PubMed and Google Scholar using conventional keyword strategies. These studies examined the microbiome of various human anatomical sites before and after antibiotic therapy using ١٦S rRNA gene sequencing. The primary goal of this study is to explore the anticancer effects of antibiotics on the microbiome and intra-tumoral microbiota.

Results: Future Research and Recommendations The essay underscores the need for more research into the use of antibiotics in oncology, particularly how they interact with the microbiome and affect cancer therapy. Personalized antibiotic regimens, tailored to individual microbiome compositions, could minimize the negative impacts of antibiotics while preserving their therapeutic benefits. Microbiome profiling, which involves understanding the composition of a patient's microbiota, could help clinicians make more informed decisions about antibiotic use during cancer treatment (٢). Additionally, microbiome-targeted interventions such as probiotics, prebiotics, and fecal microbiota transplantation (FMT) are proposed as potential strategies to restore microbial balance disrupted by antibiotics. These interventions could help enhance the efficacy of cancer therapies while reducing the risk of dysbiosis-related complications. The essay also calls for longitudinal studies to assess the long-term effects of antibiotic use on cancer recurrence, metastasis, and patient survival. Developing alternative antimicrobial strategies, such as bacteriophages and antimicrobial peptides, is another recommendation. These alternatives could reduce the risk of dysbiosis and provide effective infection management without compromising the microbiome (٧).

Conclusion: Conclusion In summary, while antibiotics remain an essential tool in managing infections in cancer patients, their impact on the microbiome demands careful consideration. The disruption of gut and intratumoral microbiota can have significant consequences for cancer progression, treatment effectiveness, and overall patient survival. The essay emphasizes the importance of personalized approaches to antibiotic use in cancer therapy and the potential of microbiome-targeted interventions to improve treatment outcomes. Through further research and a better understanding of the microbiome's role in cancer therapy, clinicians can optimize antibiotic use, ensuring that these treatments support rather than hinder cancer therapies.

Keywords: cancer , antibiotic , microbiota , anticancer , intra-tumoral microbiome

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Antifungal and antibiofilm activities of Fluconazole, Ketoconazole and Itraconazole against Candida species clinical isolates (Research Paper)

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Introduction: Candidiasis is one of the most common fungal infections by opportunistic Candida species, which is mainly caused by Candida albicans. One of the notable features of Candida is to change the yeast form into the hyphae and then biofilm form. Biofilms show an important role in pathogenesis by invading epithelial cells and damaging tissue. Imidazole and triazole based compounds in vitro has been proven to show antifungal as well as antibiofilm activity. This study mainly aimed to assess the effect of three Azole compounds (fluconazole, ketoconazole and itraconazole) on the growth and biofilm of Candida species isolated from immunocompromised patients.

Methods: A total of ١٢٠ vaginal samples were taken from patients hospitalized in intensive care and urology departments of Shahid Rajaei Gachsaran Hospital. All recovered yeasts were differentiated by using CHROM agar and routine tests for identification of Candida species. Subsequently, a set of universal primers were used to allow the amplification of target ITS١ and ITS٤ ribosomal DNA. The amplify products were purified and sent to outsourcing sequencing service. The sequence similarity was analyzed via nucleotide Blast software against the nonredundant GenBank database in the NCBI and confirmed. Minimal inhibitory concentrations (MICs) of all isolates towards fluconazole, ketoconazole and itraconazole were determined using the microdilution broth assay based on CLSI guidelines for yeasts (M٢٧M٤٤S). Then Crystal Violet (CV) assay was performed to quantify the biofilm and the effect of three major antifungals.

Results: In total, ٧٥٪ of vaginal samples were positive for Candida, including C. albicans (٧٤,٢٪), C. krusei (١٢,٩٪) and C. tropicalis (١٢,٩٪). All isolates were susceptible to ketoconazole and itraconazole while, ٨٠٪ were dose-dependent susceptible, and the remaining isolates were found to be resistant to the fluconazole. On the other hand, it was found that biofilm reduction in the presence of ketoconazole and/or itraconazole was significantly more than that of fluconazole in all isolates tested, suggesting the important role of two medicines (ketoconazole and/or itraconazole) to prevent the biofilms in different Candida species.

Conclusion: Findings show that the treatment of candidiasis using ketoconazole or itraconazole could be much more effective than the use of fluconazole in reducing biofilm formation and treating candidal vaginitis. This study demonstrated that resistance to antifungals such as fluconazole was found to significantly increase with time. Continued surveillance of changes in species distribution and susceptibility to antifungals are necessary to guide treatment.

Keywords: Fluconazole, Itraconazole, Ketoconazole, Candida species, Antibiofilm activities

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Antimicrobial Effect of Extract Equisetum arvense and Its Toxicity on lung Cancer SKmes١ Cells Line

(Review)

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Introduction: Lung cancer is one of the most common cancers and chemotherapy is one of the cancer treatment methods, but due to the lack of selective cytotoxicity, it leads to unbearable side effects. Also, due to the increase in resistance of bacteria to antibiotics and the presence of antimicrobial compounds in plants, it has been taken into consideration. Therefore, the purpose of this research is to determine the antimicrobial activity of aerial part and root extracts of the Equisetum arvense and their inhibitory effect on the growth of SKmes١ lung cancer cells.

Methods: For this purpose, after collecting Equisetum arvense plant, extraction was done and Then the Antimicrobial activity of the extracts on pathogenic bacteria was measured by disk diffusion, MIC and MBC methods. Further, after the culture and proliferation of SKmes١ cell line, the cells exposed to different concentrations of aerial part and root extracts of the Equisetum arvense plant and were incubated for ٢٤, ٤٨ and ٧٢ hours. Then, the MTT colorimetric test method was used to determine the cytotoxicity of the extract.

Results: The results have shown that Equisetum arvense L. exhibited antibacterial effects only on pathogenic gram-positive cocci. Another study showed that they investigated the inhibitory effect of hydro-alcoholic extract of Thymbra spicata on the growth of SKmes١ lung cancer cell line. The results of the MTT test showed that this extract has a dose-dependent cytotoxic effect on SKmes١ cells. The findings indicated that the extract of mountain thyme has an inhibitory effect on lung cancer cells due to the presence of phenolic compounds.

Conclusion: According to the obtained results from the study, E. arvense extract can be used as herbal medicine for cancer; however, further research especially in vivo evaluation should be carried out to evaluate the therapeutic potential of E. arvense against cancer. Leaf extracts generally showed higher antibacterial activity than stem extracts. In addition, the highest antibacterial activity was found in the methanolic leaf extract. As a result, horsetail is not only healthy food but also helpful in protecting from various diseases due to its antibacterial activity. We believe it will bring a high added value to the scientific world by examining the effects of the bioactive components on various diseases in detail in future studies.

Keywords: Lung Cancer, SKmes١ Cell Line, Equisetum arvense, Antimicrobial,

Antiproliferative activity of britannin, a sesquiterpene lactone isolated from Inula aucheriana

(Research Paper)

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Introduction: Breast cancer is the leading cause of cancer-related death in women. Britannin is a sesquiterpene lactone isolated from Inula aucheriana with anticancer activities. We aimed to evaluate the antiproliferative effect of britannin on the human MCF-٧ breast cancer cell line.

Methods: The antiproliferative effect of britannin on MCF-٧ cells was assayed using the MTT method. Briefly, MCF-٧ cells were seeded into ٩٦-well microplates and left for ٢٤ hours to adhere to the wells. Afterward, the cells were treated with different doses of britannin (٠-١٠٠ µM) for ٢٤, ٤٨, and ٧٢ h. The medium was discarded and the cells were treated with MTT solution for ٤ h. Subsequently, the MTT solution was replaced with DMSO ١٪ solution. Finally, the absorbance of formazan crystal was read at ٥٧٠ and ٦٣٠ nm and the proliferation rate of MCF-٧ cells was calculated.

Results: Treatment of MCF-٧ cells with various concentrations of britannin for ٢٤ h had no remarkable effect on the proliferation rate of this cancer cell line. However, britannin treatment for ٤٨ significantly inhibited the proliferation of these cells with IC٥٠ value of ٢٣,٩ µM compared to the controls. This sesquiterpene lactone also significantly decreased the proliferation of MCF-٧ cells ٧٢ h after treatment (IC٥٠ = ٢١,٥ µM).

Conclusion: According to the results of the MTT assay in the present investigation, britannin prevented the proliferation of human MCF-٧ cells by exerting cytotoxic effects on these cancer cells. This may suggest britannin as a natural compound for the suppression of breast cancer growth.

Keywords: Britannin, Inula aucheriana, Breast cancer, Antiproliferation.

Antiproliferative effect of sesquiterpene lactone britannin on triple-negative breast cancer cell line MDA-MB-٢٣١ (Research Paper)

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Introduction: Triple-negative breast cancer is the most aggressive form of breast tumors. Britannin is a sesquiterpene lactone isolated from Inula aucheriana with anticancer activities. The aim of this study was to evaluate the antiproliferative effect of britannin on the human MDA-MB-٢٣١ triple-negative breast cancer cell line.

Methods: The antiproliferative effect of britannin on MDA-MB-٢٣١ cells was assayed using the MTT method. Briefly, MDA-MB-٢٣١ cells were seeded into ٩٦-well microplates and left for ٢٤ hours to adhere to the wells. Afterward, the cells were treated with different doses of britannin (٠-٥٠ µM) for ٢٤, ٤٨, and ٧٢ h. The medium was discarded and the cells were treated with MTT solution for ٤ h. Subsequently, the MTT solution was replaced with DMSO ١٪ solution. Finally, the absorbance of formazan crystal was read at ٥٧٠ and ٦٣٠ nm and the proliferation rate of MDA-MB-٢٣١ cells was calculated.

Results: Treatment of MDA-MB-٢٣١ cells with various concentrations of britannin for ٢٤ h with IC٥٠ value of ١٧,٩ µM had a remarkable effect on the proliferation rate of this cancer cell line. Also, britannin treatment for ٤٨ significantly inhibited the proliferation of these cells with IC٥٠ value of ١٠,٢ µM compared to the controls. This sesquiterpene lactone also significantly decreased the proliferation of MDA-MB-٢٣١ cells ٧٢ h after treatment (IC٥٠ = ٧,٨ µM).

Conclusion: According to the results of the MTT assay in the present investigation, britannin prevented the proliferation of human MDA-MB-٢٣١ cells by exerting cytotoxic effects on these cancer cells. This may suggest britannin as a natural compound for the suppression of breast cancer growth.

Keywords: Britannin, Inula aucheriana, Triple-negative breast cancer, Antiproliferation.

Appearance of the cell and single-cell transcriptomics using calcium imaging, examining the cellular structure and synapses (Review)

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٢.
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Introduction: We review recent technological advancements that integrate single-cell transcriptomics with cellular phenotypes, including cell structure, calcium signaling, and synapses. Single-cell RNA sequencing has revolutionized the classification of cell types by capturing the heterogeneity of cell transcription. A new wave of methods combining scRNAseq and biophysical measurements facilitates the connection between transcriptomic data and cell function, providing insights into synaptic states. We briefly discuss key factors related to these phenotypic characteristics, such as temporal dynamics, informational content, and analytical tools. Specific sections focus on integration with cell structure, calcium imaging, and synapses, emphasizing their complementary roles. We discuss their applications in elucidating cellular states, refining cell-type classifications, and uncovering functional differences in cellular subgroups. To demonstrate practical applications and the advantages of these methods, we highlight their use in tissues with excitable cell types, such as the brain, pancreatic inputs, and the retina. The potential for combining functional phenotypes with spatial transcriptomics for precise mapping of cellular appearances is explored. Finally, we address open questions and future perspectives, emphasizing the need for a broader shift. Access through increased throughput can significantly contribute to these efforts.

Methods: In a typical workflow, cells are initially imaged using bright- field microscopy, and subsequently each cell is indepen- dently collected for scRNAseq. However, this requirement for individual cell isolation hinders throughput and scalabil- ity. Some approaches for cell picking and processing include micropipette aspiration methods (Camunas-Soler et al. ٢٠٢٠; Cadwell et al. ٢٠١٦; Tang et al. ٢٠٠٩), capture microdis- section (Espina et al. ٢٠٠٦), microwells (Gong et al. ٢٠١٠; Yuan et al. ٢٠١٨), optofluidic transport (Berkeley Lights) (Jorgolli et al. ٢٠١٩), hydrogel-well embedding (Lee et al. ٢٠٢٢), magnetic rafts (Gach et al. ٢٠١١), classic microfluidic valve-based system (Marcus et al. ٢٠٠٦; Wu et al. ٢٠١٤), and image-based single-cell isolation (Shomroni et al. ٢٠٢٢). A comprehensive review of these approaches can be found in Fung et al. (٢٠٢٠). The choice of the optimal system for cell picking depends on the microscopy setup and the cell type under investigation. Micropipette aspiration methods are well-suited to detach adherent cells from microplate sur- faces, while nanowells and microfluidic chambers excel at confining and processing free-floating cells in suspension. Several semi-automated cell-picking systems, inspired by earlier cell colony pickers, have achieved commercial suc- cess (e.g. CellCellector, Cellenion) (Shomroni et al. ٢٠٢٢; Nelep and Eberhardt ٢٠١٨).An elegant alternative to pairwise measurements in the same cell, is the coupling of droplet-based single-cell tran- scriptomics to image-based screens of organoids. In

this approach organoids are classified based on their morpho- logical profile (morphotype) and subsequently dissociated to perform scRNAseq in cells from each morphotype (Jain et al. ٢٠٢٣). Applying this methodology, Liberali and col- leagues screened thousands of intestinal organoids against ٣٠١ compounds to identify ١٥ characteristic organoid phe- notypes by imaging (Lukonin et al. ٢٠٢٠). In this way, they found a compound that induces a fetal-like regenerative state in enterocytes and measure its transcriptomic profile. A limitation of this approach is that it cannot establish direct correlations between morphology and gene expression in each cell but rather only at the population level. However, it is a powerful approach to identify transcripts enriched in rare cell populations present in morphologically defined organoids.

Results: Information content Quantifying the relationship between mRNA abundance and emerging cellular phenotypes is technically challenging and remains relatively unexplored. In a study conducted on human cell lines, various features of global cell state-such as cell size, cell cycle state, and Ca٢+ signaling were meas- ured alongside single-cell gene expression (Foreman and Wollman ٢٠٢٠). A linear model incorporating ١٣ of these features could explain between ١٥ and ٨٥٪ of the measured variance in gene expression, with a median explanation of ٦٢٪. Notably, cell size exhibited the highest explanatory power, followed by Ca٢+ signaling and cell cycle state. Although some Ca٢+ features had a modest effect on the explained variance, most genes exhibited significant correla- tions with at least one Ca٢+ feature, suggesting non-random associations (Foreman and Wollman ٢٠٢٠). In a subsequent study, information theory was employed to reveal that, conversely, ٦٠٪ of Ca^{2}+ signaling dynam- ics could be explained by ٨٣ genes, each contributing up to ١٧٪ of the signal. This highlights substantial redundancy within gene expression networks, hinting that cell state may be effectively represented by a few latent dimensions (Maltz and Wollman ٢٠٢٢). While cell lines may display consider- able fluctuations in phenotype and RNA abundance, they are isogenic populations representing generally homog- enous groups (Emert et al. ٢٠٢١). Consequently, exploring transcriptome-wide measurements alongside functional phenotyping in primary cells may shed new light into this question.

Conclusion: Single-cell technologies are revolutionizing the way we approach biology and our ability to measure cellular diver- sity and heterogeneity. Differences in molecular composi- tion, structure, and morphology of cells are a critical aspect of cell identity and are connected to its physiological func- tion. Methods to merge single-cell transcriptomics with other cellular phenotypes such as morphology or electro- physiological activity enable a more complete understanding of cellular heterogeneity and function, improving our ability to classify cell types and states. Neuroscience has pioneered the development of mul- timodal profiling to survey the vast diversity of neuronal cell types. Among these methods, patch-seq is a powerful approach due to its ability to merge transcriptome-wide molecular analysis with morphology and electrophysiology. Other fields are following suit, and multimodal integration of cell physiology and transcriptomics is being used in multiple tissues. For instance, patch-seq is becoming a popular tool in pancreatic islet research. A caveat of patch- seq in islet cells is that it has only been performed in dissociated cells, in contrast to in situ and in vivo studies in neuroscience. Improvements in methods for long-term culture of tissue

slices and new phenotyping tools should enable in situ meas- urements in the future (Speier and Rupnik ٢٠٠٣; Marciniak et al. ٢٠١٤; Huang et al. ٢٠١١). The development of soft- semiconductor electronics and microelectrode array systems might enable the recording of tissue-wide electrophysiology (Floch et al. ٢٠٢٢; Li et al. ٢٠٢١) in parallel to single-cell transcriptomics in multiple tissues. These systems could also be used to quantify the functional development deep inside ٣D organoids. Additionally, given that soft micro- electronic devices can record the electrical activity of a cell without perforating the cell membrane, the measurement is non-destructive, and the cell properties can be followed over time. This could be combined with cytoplasmatic sampling, which makes it possible to sample the RNA content of the same cell at different time points (Chen et al. ٢٠٢٢b). This approach could be used to simultaneously track morphologi- cal and transcriptional dynamics of cell populations during development or under external perturbations. Currently, the use of approaches that integrate functional phenotyping and single-cell transcriptomics has remained predominantly limited to specialized laboratories, primarily due to the demanding nature of obtaining both measure- ments from the same cell. However, new methods to increase throughput, such as automation or cellular tagging and bar- coding, holds the potential to broaden the accessibility of these technologies across a wider range of researchers in genomics in physiology. Additionally, progress in combin- ing functional phenotyping with spatial transcriptomics will offer new possibilities for a detailed mapping of cell phenotypes in situ and advance our understanding of tissue physiology.

Keywords: structure, phenotype, calcium imaging, cell transcriptomics, excitability function

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Application and importance of stem cells in the development of new medical treatment (Review)

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Introduction: Stem cells are a type of cells that have the ability to differentiate into different types of cells and as a result build different tissues or even repair them. The most important types of stem cells include embryonic stem cells, adult stem cells, induced stem cells and umbilical cord stem cells. Also, these cells have three unique features, their first feature is the ability to reproduce. Their second feature is the nature of non-differentiation, and the third feature is their ability to differentiate into cells of different tissues. Treat parking, cancer, etc. In the past decades, many efforts have been made to find safe and advanced methods to treat difficult diseases. One of the best and most efficient methods to treat these diseases is the use of stem cells.

Methods: Systematic review article

Results: Subject: This article examines the applications and importance of stem cells in the development of new medical treatments. Introduction: Stem cells are immature cells that have the ability to differentiate into different types of body cells. This unique feature creates new potentials for the treatment of various diseases and injuries. Applications: Stem cells are currently used in the treatment of various diseases such as leukemia, anemia, and cardiovascular diseases. Importance: Research in the field of stem cells is progressing rapidly and these cells have created new hope for the treatment of incurable diseases such as Alzheimer's disease, Parkinson's disease, and diabetes. Discussion: There are various challenges in the field of using stem cells in medical treatments, such as uncontrolled differentiation of cells and the risk of tumor formation. However, recent advances in the field of stem cell research have increased the hope of solving these challenges. Conclusion: Stem cells have created a revolution in the field of medicine and offer new potentials for the treatment of various diseases and injuries. Research in this field is progressing rapidly and it is expected that stem cells will play a key role in the treatment of various diseases in the future.

Conclusion: The science of stem cells is a broad and very complex science, and this science also helps us to find new ways to treat diseases day by day. These are the two methods of using stem cells in modern medicine, that is, cell therapy, which includes bone marrow transplantation, which types of There are different types, for example, tissue grafting, which is generally used to repair and build damaged tissues. Suggestion: Scientists were able to find ways to treat diseases such as Parkinson's, Alzheimer's, spinal cord injury, diabetes, heart and brain strokes, liver diseases, etc. The treatment of difficult diseases is using modern medicine, which will surely help humanity a lot.

Keywords: Stem cells - modern medicine - treatment development

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Application of a new Wavelet based method for working memory fMRI data (Research Paper)

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Introduction: Functional Magnetic Resonance Imaging (fMRI) is a powerful tool for studying brain activity, but traditional models often fail to capture the dynamic, time-varying nature of neural processes. Most conventional models, such as the General Linear Model (GLM), rely on static assumptions, often averaging brain activity over time, and therefore may not account for transient or rapidly evolving patterns in brain function. This can lead to less accurate representations of how brain regions respond to cognitive tasks, particularly for tasks that engage multiple neural processes at different time scales. To address this limitation, we applied a generalized wavelet analysis model, which incorporates the dynamic properties of brain activity. This method allows for more precise brain mapping, especially in identifying both short-term and long-term neural activations. In this study, we sought to compare the performance of the generalized wavelet model with the more commonly used GLM approach, specifically in the context of a memory task. Our goal was to assess the accuracy, efficiency, and noise reduction capabilities of the wavelet model in fMRI analysis.

Methods: We began by formulating the generalized wavelet model for analyzing time-varying brain activity. Wavelet analysis is particularly well-suited for this type of data because it allows for multi-resolution decomposition, enabling us to examine both slow and fast changes in brain activity simultaneously. The model was adapted to handle fMRI data, which is characterized by high dimensionality and complex temporal structures. Following the model formulation, the data used for this study were acquired from an fMRI memory task, where participants engaged in recalling specific information over a given period. Before applying the models, the fMRI data underwent extensive preprocessing, including motion correction, spatial smoothing, and normalization to account for head movement, variability in brain anatomy, and other common sources of noise in fMRI studies. Once the data were preprocessed, both the generalized wavelet model and the traditional GLM were fitted to the dataset. The General Linear Model was chosen as the baseline for comparison, as it remains the most widely used method for fMRI data analysis. The GLM treats brain activity as a linear response to external stimuli, assuming a stationary relationship between the stimulus and brain response over time. However, because this model averages activity across the entire scanning period, it may not detect transient brain responses or changes in brain activation patterns. On the other hand, the generalized wavelet model allows for time-frequency decomposition of the fMRI signal, meaning that it can capture brain activity at multiple time scales. This is particularly advantageous for memory tasks, where different brain regions may be engaged at different points in time. After fitting both models to the data, brain activity maps were generated based on each method's analysis.

Results: The brain activity maps produced by both the generalized wavelet model and the GLM were compared in terms of accuracy and the regions identified as active. In both models, the primary regions of brain activity related to the memory task were consistent, demonstrating the validity of the wavelet approach in detecting key brain areas associated with memory retrieval. However, the wavelet-based model provided several key advantages over the GLM: Increased sensitivity in primary regions: The wavelet model showed higher levels of activation in the primary brain regions involved in the memory task. These areas, such as the prefrontal cortex and hippocampus, were more prominently activated in the wavelet maps compared to the GLM maps. Reduced noise in peripheral regions: Unlike the GLM, the wavelet model reduced false-positive activations or noisy signals in peripheral areas of the brain, particularly in regions not typically associated with memory tasks. This highlights the wavelet model's ability to reduce noise and improve the clarity of the brain maps. Slightly increased computation time: While the wavelet model provided more detailed and noise-resistant results, it was computationally more intensive than the GLM. The generalized wavelet analysis took slightly longer to compute, though the difference was relatively small and outweighed by the increase in accuracy and noise reduction.

Conclusion: In this study, we introduced a novel approach using generalized wavelet analysis for fMRI data, demonstrating its effectiveness in capturing the dynamic nature of brain activity. As expected, this method was able to identify brain regions with greater precision compared to the commonly used General Linear Model. The wavelet-based model performed particularly well in identifying transient brain activations and reducing noise, which are critical in understanding complex cognitive processes like memory. Although the method required slightly more computational resources due to its complexity, the results indicate that it is a superior approach for analyzing non-stationary brain activity. Moreover, the main regions identified by both the wavelet and GLM models corresponded well to areas known to be involved in memory tasks, further validating the accuracy of the wavelet method. Future studies could explore further optimizations of this approach and apply it to other cognitive functions to assess its broader applicability.

Keywords: wavelet, brain mapping, brain activation

Application of Autologous Blood Derivatives as an Effective Solution in Wound Healing (Review)

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Introduction: Wound healing is a complex and multi-step process, which disrupting any of its steps can cause the wound to become chronic and leave a scar in patients. Chronic wounds, in addition to causing psychological and social problems for the patient, impose heavy costs on the patient and the treatment system of the country. It seems necessary to use novel and more effective treatments in wound healing, especially autologous treatments with minimal side effects.

Methods: As a search strategy and study selection, we searched the PubMed and Medline databases through ٢٠٢٤ using related keywords (e.g., Blood derivatives, Platelet rich plasma, platelet lysate, Platelet-rich fibrin, Autologous conditioned serum, Conditioned plasma, Wound healing, Wound regeneration, and Regenerative medicine).

Results: Wound healing consists of different phases in which different cells, growth factors and cytokines play a role in each stage. Cells that play a role in wound healing by secreting different types of growth factors and cytokines reduce inflammation, increase cell proliferation and differentiation, and angiogenesis at the site of injury and promote wound healing. After causing an injury in the hemostasis phase, platelets come to the wound site and in addition to preventing bleeding, they also play a role in wound healing by releasing cytokines and growth factors. In the inflammatory phase, leukocytes are present at the wound site and prevent infection and remove cell derbies. Remaining inflammation in this phase causes a delay in wound healing. In the proliferation phase, cell proliferation, angiogenesis and re-epithelialization occur. The last phase is remodeling, in which the wound is completely repaired and the wound is completely healed by the production and deposition of collagen and the formation of the extracellular matrix. Various compounds such as hydrogels, scaffolds and nanoparticles are used to improve the wound healing process. Various types of blood derivatives are also used to promote wound healing. Blood derivatives used in wound healing include platelet-rich plasma, plasma-rich fibrin, platelet lysate, and autologous conditioned serum. Each of the mentioned products has advantages and disadvantages. Platelet-rich plasma has a large number of platelets and leukocytes. Platelets can improve wound healing by secreting

growth factors, cytokines and various chemokines. Growth factors secreted from platelets such as transforming growth factor beta, platelet-derived growth factor, basic-fibroblast growth factor, vascular endothelial growth factor, and epidermal growth factor play an essential role in wound healing and can promote wound healing and improve its quality. Platelet-rich fibrin is in gel form, which makes it easier to separate and use in wound healing. Platelet lysate by destroying the cell membrane by freeze/thaw, adding platelet activating compounds and ultrasonication causes the release of platelet growth factors, cytokine, and chemokine. In platelet lysate, cell membranes and leukocytes are removed by filtering the sample, this prevents unwanted and negative reactions of cells and produces a pure product of proteins, growth factors and other plasma compounds. Autologous conditioned serum is one of the other blood derivatives that is produced by contacting blood with glass beads. This activates blood cells, especially monocytes, and increases the amount of growth factors and anti-inflammatory cytokines, especially Interleukin ١β receptor antagonist. Finally, the product is filtered with a ٠,٢٢ µm filter to produce a cell-free product like platelet lysate. Autologous conditioned serum, in addition to promoting wound healing by growth factors, inhibits inflammation with anti-inflammatory factors and helps to pass the inflammatory phase of wound healing. Blood products can be used in autologous form so that unwanted diseases and infections are not transferred to the recipient of the product.

Conclusion: Blood derivatives as an autologous therapy can promote wound healing. Each of the blood derivatives has unique characteristics and compositions and the type of wound and the patient's condition can determine the type of blood derivatives suitable for the patient.

Keywords: Blood derivatives, Platelet rich plasma, Conditioned plasma, Wound healing, Regenerative Medicine

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Application of Diffusion Tensor Imaging in Diagnosing of Parkinson's Disease: A review (Review)

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Introduction: Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by motor and non-motor symptoms. Early and accurate diagnosis is crucial for effective management and treatment. Diffusion Tensor Imaging (DTI), an advanced MRI technique, has emerged as a valuable tool in the assessment of microstructural changes in the brain associated with PD. This review aims to summarize the current applications of DTI in diagnosing Parkinson's disease.

Methods: A comprehensive literature review was conducted using databases such as PubMed, Scopus, and Web of Science. Studies were selected based on their relevance to the application of DTI in PD diagnosis, focusing on those published in the last decade. Key metrics such as fractional anisotropy (FA) and mean diffusivity (MD) were analyzed to evaluate their effectiveness in distinguishing PD patients from healthy controls.

Results: The reviewed studies consistently demonstrate that DTI metrics, particularly FA and MD, show significant differences between PD patients and healthy individuals. Reduced FA and increased MD in specific brain regions, such as the substantia nigra and corpus callosum, were commonly reported. These findings suggest that DTI can detect microstructural abnormalities in white matter tracts, which are indicative of PD pathology. Moreover, DTI has shown potential in differentiating PD from other parkinsonian syndromes, enhancing diagnostic accuracy.

Conclusion: DTI is a promising non-invasive imaging modality that provides valuable insights into the microstructural alterations in the brain associated with Parkinson's disease. The consistent findings across multiple studies highlight its potential as a diagnostic tool. Future research should focus on standardizing DTI protocols and exploring its utility in longitudinal studies to monitor disease progression and response to therapy.

Keywords: Diffusion Tensor Imaging, Parkinson's Disease, Diagnosis

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Application of Diffusion Tensor Imaging in Multiple Sclerosis Detection (Review)

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Introduction: Multiple sclerosis (MS) is a chronic neurodegenerative disease characterized by demyelination and axonal loss, leading to a wide range of neurological symptoms. Early and accurate diagnosis of MS is crucial for initiating timely and effective treatment. Diffusion Tensor Imaging (DTI) has emerged as a promising non-invasive technique for evaluating white matter microstructure, providing valuable insights into the pathophysiology of MS. This study aimed to investigate the potential of DTI in differentiating patients with MS from healthy controls and explore the correlation between DTI metrics and disease severity.

Methods: PubMed, Science Direct, Web of Science, and Google Scholar databases were explored up to August ٢٠٢٤, using different combinations of the keywords: " Multiple sclerosis ", " Diffusion Tensor Imaging ", " Neurodegenerative disease ", "Magnetic resonance imaging" and "Detection". Finally, six more recent and relevant records were included in the study.

Results: Patients with MS exhibited significantly lower fractional anisotropy (FA) and higher mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD) values compared to healthy controls in specific white matter regions, particularly in the corpus callosum, periventricular white matter, and brainstem. These findings indicate widespread white matter damage in MS patients. Furthermore, a significant correlation was observed between decreased FA and increased MD values with higher Expanded Disability Status Scale (EDSS) scores, suggesting that DTI metrics may reflect disease progression.

Conclusion: This study demonstrates the potential of DTI as a valuable tool for differentiating MS patients from healthy controls and assessing disease severity. By providing quantitative information about white matter microstructure, DTI can contribute to early diagnosis, monitoring disease progression, and evaluating treatment efficacy. Future studies with larger sample sizes are warranted to further explore the clinical utility of DTI in MS management and to investigate the potential of DTI as a prognostic biomarker.

Keywords: Multiple sclerosis, DTI , Neurodegenerative disease, Magnetic resonance imaging, Detection

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Application of green nanotechnology in Alzheimer's treatment by gold nanoparticles (Review)

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Introduction: Alzheimer's is the most common form of dementia that is expected to affect many elderly people in the future. The use of gold nanoparticles, due to their unique properties at the nanometer level, is a promising tool that directly enters the brain, bypasses the blood-brain barrier, and improves the efficiency and accuracy of treatment. Green nanotechnology seems to be the most useful method in synthesis and treatment. In this article, comprehensive explanations about Alzheimer's pathogenesis, types of nanoparticles, challenges facing nanomedicine and ways to overcome them are presented.

Methods: ٤٤ papers were found through Google Scholar by searching about the green nanotechnology and Alzheimer's disease. ٢٥ papers related to this topic of gold nanoparticles and the leading factors to Alzheimer's disease were separated. The methods for synthesis gold nanoparticles and synthesis process challenges in treatment were extracted.

Results: Until now, the causative factors of AD are not fully understood. A major focus for drug discovery efforts has been to interfere with the amyloid pathway, which involves preventing the production and aggregation or enhancing the removal of Aβ peptides. No anti-amyloid drugs for the treatment of AD have yet reached the market. The use of gold nanoparticles is a promising tool due to their unique properties at the nanometer level. Gold nanoparticles act as drug delivery platforms and deliver therapeutic agents directly into the brain, improving the efficacy and accuracy of treatment and reducing side effects in healthy tissues. The potential to cross the BBB and target the accumulation of amyloid and tau proteins, which are hallmarks of AD pathology, is one of the advantages of nanodrug delivery systems. Despite the exciting potential of gold nanoparticles, it is important to address the challenges and issues associated with their use in the medical field before they can be widely applied in clinical settings. It is important to ensure the safety, efficacy and biocompatibility of these nanomaterials in the field of the central nervous system. Since there is little and sometimes conflicting information about their use in this field, detailed preclinical and clinical studies are needed to evaluate the effectiveness and feasibility of these strategies in patients. Limited knowledge of the physiological and pathological mechanisms contributing to AD also hinders the development of effective nanomaterial-based therapies. It is expected that nanomaterial-based therapies will play a greater role in the treatment of AD, and more research will be conducted to understand the underlying biological mechanisms of this disease. It is very important that designed nanomaterials can remain in tissues and organs for the required amount and duration to have sufficient effects on cells for therapeutic and bioimaging purposes. Since it is not trivial to control the morphology, size, shape and distribution of nanoparticles, these physical properties may lead to different behavior of nanosystems in in vitro approaches compared to in vivo analysis. Studies. More in vitro and in vivo studies are needed to determine the biodistribution effects of gold nanoparticles and their role in nanotoxicity. Substantial animal studies are needed to

provide insight into dose limitations and establish safe concentrations of gold nanoparticles for in vivo application. Most researches have shown that the cytotoxicity of gold nanoparticles strongly depends on their size and shape. Cytotoxicity has been found to be inversely related to size.

Conclusion: Future research should focus on removing BBB-related barriers and improving drug delivery systems, advancing the study of nanomedicine and paving the way for more effective treatments for AD and other CNS disorders. Limiting the number of eligible patients for certain nanoparticle-based therapies may reduce the size of the potential market. At the same time, the cost of nanoparticle-based therapies can be high if only a certain population group can implement them. The need for standardization in the production and determination of properties of nanomaterials is another challenge. For example, it may be challenging to compare the results of different studies or to properly evaluate the performance of different types of nanoparticles because there are currently no universally accepted standards for characterization and quality control of nanomaterials.

Keywords: Alzheimer's disease, Nanobiotechnology, biotechnology, green nanotechnology, gold nanoparticles

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Application of Machine Learning-based Radiomics Feature in classification of High Grade from Low Grade Brain Tumors (Review)

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Introduction: Brain tumors are complex diseases with significant variability in behavior and prognosis. High-grade and low-grade tumors, in particular, present distinct challenges in diagnosis and treatment planning. While imaging plays a crucial role in tumor characterization, accurate differentiation between these tumor types remains a clinical challenge. This study sought to investigate the potential of radiomics, a quantitative image analysis technique, to enhance the differentiation between high-grade and low-grade brain tumors using features extracted from magnetic resonance images.

Methods: PubMed, Science Direct, Web of Science, and Google Scholar databases were explored up to August ٢٠٢٤, using different combinations of the keywords: "Brain tumors ", "Radiomics", "Machine Learning", "Magnetic resonance imaging" and "Classification". Finally, five more recent and relevant records were included in the study.

Results: Findings have demonstrated that XGBoost, SVM, and Random Forest classifiers exhibit robust and reliable performance in classifying brain tumors into low-grade and high-grade categories. The RF classifier achieved an accuracy of approximately ٠,٨٣ and an AUC of ٠,٨١, which are considered excellent. Additionally, in another study, the XGBoost classifier reported an accuracy of ٠,٨٨. These results indicating a promising ability to accurately classify tumors based on their imaging characteristics.

Conclusion: The high performance of ML models in different studies demonstrated the value of radiomics as a complementary tool for brain tumor characterization. By providing quantitative insights into tumor heterogeneity, radiomics may aid in improving diagnostic accuracy and treatment planning. Further research is essential to validate these results in larger, independent cohorts and to explore the clinical utility of radiomic models in routine practice.

Keywords: Brain tumors, Radiomics, Machine Learning, Magnetic resonance imaging, Classification

Application of Microfluidics Technology in Stem cells Studies (Review)

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Introduction: Providing suitable conditions for growth, proliferation and differentiation of stem cells has been great importance till now. Therefore, many two-dimensional(2D) and three-dimensional(3D) culture systems have been developed till today. But because of the cells in two-dimensional culture conditions demonstrate more different behavior compared with their micro-environment in the body, three-dimensional culture systems were developed to study and investigate cell behavior, in which cell behavior is as close as possible to the natural state of the body. Also, considering the natural micro-environment of stem cells is largely influenced by various biochemical and biophysical factors, it is very important to provide conditions that mimic their natural micro-environment. Microfluidic systems create a suitable platform for studying and investigating the behavior of cells. Because by creating a three-dimensional environment, they create suitable conditions for cell-cell and cell-matrix interactions. Microfluidics is a technology for manipulating very small amounts of fluids in microliter and Pico liter scales that flow in channels with micrometer dimensions. The integration of stem cell and microfluidic technologies opens a way to better understand the behavior and fate of cells. In this review has been tried to introduce microfluidic systems and their applications in stem cell studies.

Methods: NA

Results: NA

Conclusion: NA

Keywords: Cell behavior, Biophysical factors, Cell fate, 3D cell culture systems

Application of Organoids in Drug Screening: Current Perspectives and Future Directions (Review)

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Introduction: Abstract: This review aims to critically examine the application of organoids in drug screening, highlighting their advantages over traditional methods, including enhanced predictive accuracy and ethical considerations. By analyzing current research, case studies, and challenges, this review seeks to provide a comprehensive understanding of how organoids are transforming the landscape of drug discovery. ١. Introduction Organoids are three-dimensional structures derived from stem cells that closely replicate the architecture and functionality of human organs. Their emergence as a powerful tool in biomedical research presents new opportunities in drug screening, allowing for more accurate modeling of human responses compared to ٢D cell cultures and animal models. This review will explore the integration of organoid technology into drug screening processes, focusing on its implications for efficacy and safety testing.

Methods: To comprehensively assess the application of organoids in drug screening, a systematic literature review was conducted. We focused on studies published within the last five years that explored the development, application, and outcomes of organoid models in various drug screening contexts. Databases such as PubMed, Scopus, and Google Scholar were searched using keywords including "organoids," "drug screening," "pharmacology," and "personalized medicine." Selected articles were reviewed for their methodologies, including organoid culture techniques, drug exposure protocols, and outcome measures, such as cell viability, gene expression analysis, and drug response profiles. In addition to the literature review, case studies were identified that highlighted successful applications of organoids in drug discovery. These case studies provided insight into real-world applications, showcasing the predictive capabilities of organoids in modeling human disease and evaluating therapeutic responses. Expert consultations were also conducted with leading researchers in the field to gather qualitative insights on the current challenges and future directions of organoid technology in drug screening.

Results: The review of the literature revealed a significant advancement in the use of organoids for drug screening across various disease models, particularly in oncology. Several studies demonstrated that patient-derived organoids can accurately replicate tumor heterogeneity and drug response, outperforming traditional ٢D cultures. For instance, a study on colorectal cancer organoids showed a strong correlation between in vitro drug responses and clinical outcomes, validating their predictive accuracy. Moreover, organoids have facilitated the identification of novel therapeutic targets. In pancreatic cancer, researchers successfully used organoids to screen a library of compounds, identifying promising candidates that were subsequently validated in vivo. The expert consultations highlighted common themes, including the need for standardization in organoid culture methods and the integration of high-throughput screening techniques. Overall, the results underscore the transformative potential of organoids in drug screening, providing a more relevant and efficient platform for evaluating therapeutic efficacy and safety.

Conclusion: This review aims to illuminate the significant role of organoids in drug screening, showcasing their potential to enhance the efficiency and accuracy of drug discovery processes. By synthesizing current knowledge and outlining future research directions, this review will contribute valuable insights to the field.

Keywords: Organoids, Drug Screening, Personalized Medicine, ٣D cell culture

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Application of Quantum Dots in Tumor Imaging (Review)

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Introduction: Cancer is one of the most common causes of death worldwide. One of the fundamental steps to ensure optimal cancer treatment is the early detection of cancer cells. Due to the limitations of conventional cancer diagnostic methods, such as the lack of stability of contrast agents, photobleaching and poor spectrum with narrow excitation and broad emission, other strategies, including nanotechnology, have been used to improve diagnosis and reduce the severity of the disease. Nowadays, fluorescent semiconductor nanostructures (quantum dots, QDs) have attracted much attention due to their small size (less than ۱۰ nm), high photostability, high quantum yield, tunable color, broad excitation spectrum, narrow emission spectrum, negligible optical fading, excellent biocompatibility, low toxicity, and chemical inertness. QDs are tiny three-dimensional particles and trap electrons from the conduction band, holes from the valence band and excitons in three spatial directions. Carbon quantum dots (CQDs) and graphene quantum dots (GQDs) are the two most important subgroups of carbon dots (CDs). To image tumors, many researchers have focused on the construction of nanoparticle systems functionalized with ligands that target tumors. By modifying them with specific surface coatings, quantum dots can be used to effectively label tumor cells at both the cellular and subcellular levels. Quantum dots can be conjugated with peptides, antibodies or small molecules and used for the detection of cancer cells and molecular biomarkers.

Methods: This review article has been collected from reliable scientific sources and is the result of studying many researches of the authors.

Results: The excellent fluorescence intensity and photochemical stability of QDs are justification for their increased applications in tumor imaging, optical sensing, bioimaging, and optical monitoring.

Conclusion: The cytotoxicity effect of quantum dots severely limits their in vivo applications. Therefore, the searches for benign alternatives have continued. In addition, synthesizing biocompatible fluorescent agents for early-stage cancer imaging is challenging. Furtheremore tethering the targeting molecules onto the CQDs still remains a great challenge for constructing a perfect “smart” theranostic agent, which is a multiple functional platform integrating imaging, targeting, and therapeutic functions.

Keywords: Cancer, Fluorescence Quantum dot, Nanotechnology, Tumor imaging

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Application of the CRISPR/Cas۹ System for repair or regeneration articular cartilage (Review)

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Introduction: Cartilage is a specialized form of connective tissue. The three types of cartilage is hyaline (most common type of cartilage), elastic, and fibrocartilage. A thin layer of hyaline cartilage covers articulating surface of each bone, with a dense extracellular matrix and scattered chondrocytes forms the articular cartilage (AC). Articular cartilage has a limited capacity for self-renew and repair, therefore, find a potential treatment for cartilage damage is a challenge. Current methods used for cartilage damage and repair include a range of rest, medications, surgery. These methods couldn't defects for long-term to achieve therapeutic effects for a long time. In this review, we discuss the CRISPR/Cas۹-based system to enhance long-term therapeutic effects.

Methods: Current methods used for cartilage damage and repair include a range of rest, medications, surgery. CRISPR/Cas۹ system as the most flexible and user-friendly platform to generate genome editing technology, overcome the current limitations. CRISPR/Cas۹ system generate target gene modifications: insertion, knockout (deletion) and genome editing.

Results: CRISPR/Cas۹ technology has been used to generate modifications on target genome can overcome many limitations of traditional strategies. It can provide the ability to regulate genome sequence. There are two main strategies insert to generate modifications on target genome by CRISPR/Cas۹ system: First, modified genome in vitro on osteoblasts or chondroblasts, modified genome loaded in the vector and applied directly to the site. Second, use ex vivo methods: generate modifications on suitable tissues and then re implanted in vivo. Genome editing based on CRISPR/Cas۹- system has provided similar natural mutation and low off target effects.

Conclusion: At present, CRISPR/Cas۹ technology in articular cartilage has the ability to establish deletion (Knock Out) or insertion (Knock In) of specific genomic sequences on a single step directly applied in defects which makes it safe and effective. CRISPR/Cas۹ system can blockade of certain cytokines, generate similar natural mutation and low off target effects and overcome many limitations of traditional strategies.

Keywords: Genome Editing tools, CRISPR/Cas۹, Articular Cartilage

Applications and different perspectives on tissue engineering and stem cells (Review)

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[1]. Farzanegan shahidan shalbaf

Introduction: The human body is very vulnerable despite its strength and high ability to repair. Repairing injuries in youth does not require much effort, but with age, this ability decreases, as a result, many old people, and sick young people, dream of replacing worn out tissue with healthy tissue. Today, with the growth of medical knowledge and the application of biomaterials engineering (biomaterial), this dream can be achieved.Stem cells, as "mother cells", have unique properties that enable them to transform into various specialized cells and thus play a key role in the process of tissue repair and regeneration. By using these cells and combining them with biological and synthetic matrices, tissue engineering creates functional tissues that can be used in the treatment of various diseases and injuries. Research in this field can lead to the development of new treatments for chronic diseases, spinal cord injuries, heart disorders and many others.

Methods: Langer R, Vacanti JP. Tissue engineering. Robert M. Nerem. Tissue Engineering: From Biology to Biological Substitutes. Spring ۱۹۹۵ Tissue Engineering: The Future of Stem Cells- K.M. Kim and G.R.D. Evans

Results: For the first time in ۱۹۰۰, Alexi Karl proposed the term tissue engineering. Together with Linderberg, he started experiments at the research institute in New York with the aim of keeping new tissues in laboratory conditions and replacing them in the body of a living organism. After Karl and Lindbergh, much work was done in this field until in ۱۹۸۰ artificial skin was made, and tested on a patient. After that, tissue engineering gradually started to expand as a new field or branch of science. Tissue engineering generally means development and change in the field of laboratory growth of molecules and cells in tissue or organ, with the aim of replacing and repairing the damaged part of the body. Scientists have been able to grow cells outside the body for years, but the technology to grow ۳D cell networks, with the goal of replacing damaged tissue, has only recently become available.The progress of studies showed that in all tissues of the body, a type of stem cells can be found, which have the ability to transform into specialized cells of the same tissue, and in the event of a tissue disorder, they are activated and multiply, and because Having the same ability, they are called "stem cells".

Conclusion: Today, one of the most common ways to fix tissue defects is tissue transplantation. For this, donors who are able to provide their tissues to the recipient are used. The tissue of the donor is removed and transplanted to the recipient. This method has its own problems and in addition to the very high costs that are imposed in this procedure, there are other issues such as the possibility of microbial and viral contamination, immune reactions and transplant rejection. Another restorative method is the use of surgical techniques and artificial prostheses to compensate for the defect. In this method, polymer engineering will help, and by designing a prosthesis or external device, it will enter the person's body, which will remain permanently in the body. In cases where the defect is

due to the lack of a specific metabolic substance in the body, this substance can be introduced into the body. For example, in cases of insulin deficiency or insulin resistance, external insulin can be introduced into the body. But one of the best and most comprehensive solutions to deal with tissue defects is the use of tissue engineering.Cell therapy is actually the act of transplanting one's own or autologous cells. The method that is currently called autologous cellular system or AUTOLOGOUS CELLULAR SYSTEM. In this treatment method, the individual's own cells are multiplied and re-injected into the target area to fix the disorder.

Keywords: Tissue Engineering TE‹AUTOLOGOUS CELLULAR SYSTEM

APPLICATIONS OF CRISPR/CAS۹ IN THE TREATMENT OF COLORECTAL CANCER (CRC) (Review)

Mohadeseh Hassannia,[۱,*]

۱.

Introduction: Colorectal cancer is the third leading cause of cancer death in the world and the second leading cause of cancer death in the United States. CRISPR/Cas۹ is a powerful tool in genome manipulation for therapeutic purposes. Using CRISPR, it is possible to correct genome errors and turn genes on or off in cells and organisms. When DNA suffers a double strand failure, there are two pathways HDR and NHEJ to repair DNA. NHEJ pathway is used to delete the defective gene and HDR is used to replace it with a healthy allele. Commonly mutated genes involved in colorectal cancer are APC, Tp۵۳, KRAS and SMSD۱۰. The main obstacle in the drug treatment of CRC is drug resistance.

Methods: New technologies: CRISPR interference (CRISPRi) and CRISPR activation (CRISPRa) technologies utilize nuclease-deactivated Cas۹ (dCas۹) that binds to the target genomic region with the same efficiency as Cas۹ but cannot generate a DSB and instead results in RNA-directed transcriptional control of the target region. Bace editing is a novel genome editing method that can make and transversion and transition mutations at the single-base level without double-stranded DNA breaks, donor templates, or undesirable effects of NHEJ and HDR mechanisms. Prime editing is a 'search and replace' tool that can do any intended changes, including all ۱۲ possible base-to-base conversions, insertions, and deletions without requiring DSBs or donor DNA templates. Applications of CRISPR/Cas۹ in CRC: CRISPR/Cas۹ can be used as a powerful tool to elucidate the precise function of mutations that underlie the development of CRC. It is also used to investigate the natural course of CRC progression and to elucidate the sequence of mutations that contribute to tumorigenesis. With CRISPR Cas۹, this versatile system can facilitate efficient genome editing, enabling the simultaneous insertion and deletion of multiple genes. The evolution of CRC is greatly influenced by the accumulation of gene mutations. However, the specific function of the genes and the impact of these genomic changes are still unclear. Traditional gene editing tools have many limitations, especially the efficiency of gene editing. Compared to other tools, CRISPR/Cas۹-mediated genome editing is simple and effective. Also, precise genome editing can be done using sgRNA of the CRISPR/Cas۹ system. These tools have been used in CRC cell lines, mouse models, and human-derived organoid models, as well as CRISPR/Cas۹-based gene screening and gene therapy. The metastatic site of CRC can provide suitable conditions for targeted gene therapy because these sites are almost limited to the intestinal cavity, liver or abdomen compared to other cancers such as breast cancer and lung cancer. We can use the CRISPR/ Cas۹ library to screen functional genes in colon cancer cells, identify genes that direct the development of tumors, and shed light on the initiation and progression of cancer. Mass genomic screening is a powerful tool for detecting mutated genes that can reveal phenotypic changes following drug treatment or other stimuli, and thus lead to the identification of new targets for cancer therapy. According to existing studies, the CRISPR / Cas۹ gene editing system has been widely used in early cancer research. Also, concurrent

with the rapid development of Cas۹-based biotechnology, a number of Cas۹-based clinical trials may point to extracellular somatic cell editing and future use in patients. It has been achieved in inhibiting the growth and progression of colon cancer . CRISPR / Cas۹ engineering: CRISPR / Cas۹ engineering that improves fidelity and specificity, which are mainly divided into three categories: Cas۹ engineering; sgRNA modification; SaCas۹ modification. A novel approach in CRC: Multiple pieces of evidence have shown that a high tumor mutation burden indicates an effective immunotherapy response, and immune checkpoint inhibitors (ICIs) can effectively treat metastatic colorectal cancer (mCRC) with low microsatellite instability and deficient mismatch repair. However, current ICIs are still ineffective for pMMR CRC or MSI-H CRC (known as pMMRMSI-H tumors).

Results: The results of studies investigating many genes involved in CRC show that CRISPR technology is effective in the treatment of colorectal cancer.

Conclusion: CRISPR/Cas۹ gene editing technology provides a new method for both targeted therapy and gene therapy. However, due to the off targeting, and limited application of the CRISPR/Cas۹ gene editing technology to cell lines and organoid models, further research is needed for gene therapy of CRC patients.

Keywords: CRISPR-CAS۹, CRC, COLORECTAL, CANCER, GENE EDITING

Applications of Nanoparticles in Treatment of Giardiasis (Review)

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Introduction: Giardiasis, an intestinal infection caused by the protozoan Giardia lamblia, is one of the most prevalent parasitic diseases in humans, characterized by symptoms such as diarrhea, abdominal cramps, and nausea. Treatment of this infection has become increasingly challenging due to reports of drug resistance and the presence of various parasite assemblages. Additionally, common drugs used for giardiasis treatment are associated with side effects like disulfiram-like reactions, tachycardia, palpitations, nausea, and vomiting, underscoring the need for alternative therapies. In light of these challenges, this review systematically examines the potential of nanoparticles as an alternative treatment for giardiasis, evaluating their efficacy in both in vitro and in vivo studies.

Methods: In the present review, we searched the PubMed, ProQuest, Scopus, Embase, Google Scholar, ScienceDirect, and Wiley databases for relevant articles. The keywords used in the search were Giardia lamblia, G. lamblia, nano, treatment, assemblages, in vivo, and in vitro.

Results: This study has found that some new nanoparticles, such as nano-chitosan, nano-gold, nano-silver, and nano-curcumin, are promising candidates for treating giardiasis in vivo and in vitro. For example, El-Gendy et al. (٢٠٢١) reported that chitosan nanoparticles at a dose of ٥٠ µg/kg for ٧ days reduced parasitemia by ٧٥٪, and when metronidazole was loaded into these nanoparticles, the effectiveness increased to ٩٤٪. In another study, Said et al. showed that curcumin had only a moderate effect at a dose of ٤٥٠ mg; however, in nanoparticle form, curcumin exhibited enhanced anti-parasite potency. Additionally, silver nanoparticles at a dose of ١٠٠ ppm demonstrated ٧٢٪ effectiveness against the Giardia parasite, and Baz et al. (٢٠٢٢) confirmed the effectiveness of gold nanoparticles in treating giardiasis.

Conclusion: In addition to evaluating the efficacy of therapeutic agents, it is crucial to consider their toxicity to body tissues and cost-effectiveness. For instance, while studies have demonstrated that gold nanoparticles exhibit high efficacy against giardiasis, they have also shown toxic effects on liver tissues in treated mice. Consequently, the clinical application of gold nanoparticles has been challenged due to these adverse effects and the high costs associated with their production.

Keywords: Giardia lamblia, Nanoparticles, Review.

applications of the CRISPR system in clinical microbiology and infectious diseases, A Review

(Review)

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Introduction: Clustered regularly interspaced short palindromic repeats (CRISPR) systems are a set of versatile gene-editing toolkit that perform diverse revolutionary functions in various fields of application such as agricultural practices, food industry, biotechnology, biomedicine, and clinical research. Specially, as a novel antiviral method of choice, CRISPR/Cas۹ system has been extensively and effectively exploited to fight against human infectious viruses. Emerging and relapsing infectious diseases pose a huge health threat to human health and a new challenge to global public health. Since the ۲۱st century, many emerging infectious diseases have emerged and spread in the world. The early detection and timely diagnosis and treatment of emerging infectious diseases are of great significance to the prevention and control of emerging infectious diseases. In recent years, diagnostic technologies based on Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) and CRISPR-related proteins (Cas) have gradually matured, It has brought about significant changes in our diagnostic techniques. This paper discusses the emerging use of CRISPR-Cas systems in the fields of clinical microbiology and infectious diseases with a particular emphasis on future prospects.

Methods: This study is reviewing data accumulated from literature and prestigious case studies which are in connection with our subject.The search words were:" Infectious diseases ," “CRISPR gene editing ," “Emerging infectious diseases," “CRISPR-Cas, "detection ", “Single guide RNA (sgRNA)," Treatment ", " Application" using PubMed, Scopus, Science Direct and Google Scholar databases. Furthermore, manual searches of other relevant journals and keywords searches were performed. We have focused on published papers from ۲۰۱۰ to ۲۰۲٤.

Results: The CRISPR-Cas system represents a revolutionary tool in clinical microbiology and infectious diseases, offering innovative solutions to some of the most pressing challenges in healthcare today. Its applications range from advanced diagnostics to targeted therapies, particularly in the context of antimicrobial resistance. However, for CRISPR technology to realize its full potential, substantial advancements in delivery methods, safety, and ethical frameworks are essential. As research progresses, the integration of CRISPR into clinical practice holds the promise of transforming the landscape of infectious disease management and improving patient outcomes in the face of evolving microbial threats. While most work has been performed in eukaryotes, CRISPR systems also enable tools to understand and engineer bacteria. CRISPR has given scientists a glimmer of hope in this area that can provide a novel tool to fight against antimicrobial resistance. This system can provide useful information about the functions of genes and aid us to find potential targets for antimicrobials

Conclusion: Infectious diseases impose an enormous burden worldwide, and new tools are needed to study underlying mechanisms and to diagnose accurately and to treat infections in all settings. CRISPR-Cas९ technology is advancing the understanding of microbe-host interactions as not previously possible and is being applied to develop new diagnostics for infectious diseases, adding to the existing armamentarium. Viral vectors, including adenoviruses and lentiviruses, may deliver a CRISPR construct to the target of interest, although concerns related to potential carcinogenesis and immunogenicity remain.To date, early investigations into CRISPR-based therapies targeting infectious diseases have focused on prevention and treatment of pathogenic drug-resistant bacteria and persistent viral infections. This is good news because these infections, including infections with multidrug-resistant bacteria, HIV, and HBV, significantly contribute to the global disease burden. Challenges remain beyond safe and effective delivery of CRISPR-based therapies for infectious diseases. Bacterial and viral plasticity may result in genetic polymorphisms of gRNA targets, rendering CRISPR-based therapies ineffective. PAM sequence mutations have also been shown to allow phages to escape CRISPR-Cas systems.Whether this can be addressed by packaging and delivering multiple gRNAs with diverse targets remains to be seen.Moving forward with CRISPR-Cas systems as treatments in the realm of infectious disease will require standardized methods for safe treatment delivery. If successful, an antibiotic resistance decolonization strategy, in which patients who are colonized with carbapenemase-producing organisms are given an oral formulation of a targeted CRISPR-Cas system aimed at removing resistant organisms from the gastrointestinal tract, thus positively restructuring the human microbiome, could be imagined. Safe and effective CRISPR-based therapies for persistent viral infections would remarkably change the global landscape of infectious diseases.

Keywords: CRISPR-Cas, diagnostics, infectious diseases

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Approaches to traditional vaccines and the development of new vaccines (Review)

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Introduction: A vaccine is a biological product that specifically leads to acquired immunity against a pathogenic pathogen and prevents the disease in the face of the main pathogen in a person. Therefore, vaccines are an important tool for maintaining health in the global community.

Methods: this research is a review study and databases such as NCBI,PUBMED ,...have been used in this research.

Results: Traditional vaccines have been used against a wide range of pathogenic pathogens, both viral and bacterial, and have been successful. But these vaccines do not work and are not effective against pathogens that change rapidly in terms of genetic material and surface epitopes.

Conclusion: During the last decade, vaccines based on nucleic acids, viral vectors and biomaterials have shown promising results. In this study, an overview of traditional vaccines, mRNA-based vaccines, viral vector-based vaccines, and biomaterials has been discussed.

Keywords: Traditional vaccines, mRNA vaccines, viral vector vaccines, biomaterials, immune system

Are the Costimulatory Molecule Gene Polymorphisms (CTLA-٤) Associated With Infection in Organ Transplantation? A Meta-Analysis (Review)

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Introduction: Polymorphisms in the cytotoxic T-lymphocyte antigen-٤ (CTLA٤) gene, which may influence CTLA٤'s role in regu-lating the immune response, have been postulated to affect disease susceptibility and chronicity in individuals with HBV infection; however, the results are still contentious. CD٢٨, like CTLA٤, binds to BV family receptors (CD٨٠ and CD٨٦), but after being produced on T cells, it gives a posi-tive costimulatory signal for T-cell proliferation١,٢. CTLA٤ (cytotoxic T lymphocyte-associated antigen ٤) is an impor-tant negative regulator of the T cell-mediated immune response and a vital component in the immune system's induction of immunological tolerance٣. It is also produced constitutively on the surface of regulatory T cells (Tregs); it may be detected on roughly ٥٠٪ of Tregs but just ١٪ of naive helper T cells٤. In mice, ligation of CTLA٤ on Tregs leads to a considerable reduction in antigen-presenting cell presentation capability and effector T cell downregulation٥. CTLA٤ plays a critical function in the immune response's downregulation.In ١٧٢ chronic HBV-infected individuals, Duan and col-leagues looked at the CTLA-٤ ٤٩A/G and ٣١٨ T/C polymor-phisms. In chronic HBV-infected individuals, the AA genotype and A allele of the CTLA-٤ ٤٩A/G polymorphisms, as well as the genotype CC of the CTLA-٤ -٣١٨ C/T poly-morphisms, were observed more often٦. Thio and colleagues discovered a link between the CTLA-٤ ٤٩A/G gene and HBV infection clearance٧. The rs٢٣١٧٧٥ (+٤٩A/G) single nucleotide polymorphism (SNP) is found inside the mole-cule's signal peptide and affects full-length isoform expres-sion on the T cell surface. The rs٣٠٨٧٢٤٣ (+٦٢٣٠G/A) SNP is discovered within the ٣٩ untranslated regions of the CTLA-٤ gene and has been linked to autoimmune disease susceptibility٨. Furthermore, CTLA٤ SNPs like ٢١٧٧٢T/C (rs٧٣٣٦١٨), +٤٩A/G (rs٢٣١٧٧٥), and +٦٢٣٠ G/A (rs٣٠٨٧٢٤٣) have a role in graft rejection and the long-term clinical outcome of organ transplantation٩,١٠–١٤. It has been proposed that the CTLA٤ gene variant influences infection following juvenile heart transplantation. The SNP CTLA٤ +٤٩(rs٢٣١٧٧٥) has been linked to late post-transplantation viral infection in pediatric heart transplant patients in the United States, according to Ohmann et al. The relevance of CTLA٤ SNPs in T cell-mediated immunity and their connec-tion with infection following renal transplantation is uncer-tain. As a result, the goal of this study was to look at the links between infection and five CTLA٤ SNPs (rs٧٣٣٦١٨ C/T, rs٤٥٥٣٨٠٨ A/G, rs٥٧٤٢٩٠٩ C/T, rs٢٣١٧٧٥ A/G, and rs٣٠٨٧٢٤٣ G/A) in Chinese kidney transplant recipients.The SNP CTLA٤ +٤٩(rs٢٣١٧٧٥) has been linked to late post-transplantation viral infection in pediatric heart trans-

plant patients in the United States, according to Ohmann et al.١٥ Several studies have found that the CC genotype is related to viral illness and persistent HBV infection for the SNP rs٥٧٤٢٩٠٩ C/T١٦. The SNPs rs٥٧٤٢٩٠٩ and rs٢٣١٧٧٥, on the other hand, did not show any statistically significant relationships in the research. This lack of correlation might be attributed to the small sample size and insufficient power to detect a link; also, the frequency of the G allele at the CTLA٤ +٤٩ (rs٢٣١٧٧٥) locus is substantially greater in the Chinese population than in other populations١٧. This might suggest that genetic bias has little impact on infec-tion susceptibility. The CTLA٤+٤٩(rs٢٣١٧٧٥)GG geno-type was also linked to enhanced interferon-c production following immunological activation, according to recent research.Several SNPs in the CTLA٤ gene may affect gene expres-sion, leading to amino acid substitution and mRNA splicing, which might influence T-cell activation and, eventually, host immunological state. These genetic polymorphisms have been linked to post-transplant infections١٥,١٨, and they might lead to interindividual variances in immunotherapy targeting this protein. There are numerous polymorphic markers in the CTLA٤ gene. The most commonly examined SNPs in the CTLA٤ ٣′ untranslated region (UTR) are at locations ١٧٢٢, ١٦٦١, ١١٤٧, ٦٥٨, ٣١٨, + ٤٩, and + ٦٢٣٠, as well as dinucleo-tide (AT)n repeats١٣,١٤,١٩,٢٠. Cytomegalovirus (CMV) infec-tion is controlled in part by innate and adaptive immune responses. CTLA٤ is a critical component of both the innate and adaptive immune systems. CTLA٤ is a cell surface mol-ecule that is only found on CD٤+ and CD٨+ T lympho-cytes. CD٤+ T cells have been found to be able to reduce initial systemic CMV infection٢١, limit persistent replication in specific organs٢٢, and boost antibody responses٢٣ in exper-imental CMV infection models. CD٨+ cells, on the other hand, can protect immunocompromised people and animals from CMV infection by T cells by limiting the viral reactiva-tion from a state of delay.

Methods: A literature search was conducted using combinations of the keywords “CTLA-٤ or cytotoxic T-lymphocyte anti-gen-٤ associated AND polymorphism or SNP or single nucleotide polymorphisms or rs٥٧٤٢٩٠٩ or rs٧٣٣٦١٨ or rs٤٠٥٣٨٠٨ or rs٢٣١٧٧٥ or genotype AND organ Transplantation or Transplantation AND viral infection or bacterial infection” in PubMed, Google Scholar, Web of Science, EMBASE, Google Scholar, Wanfang, China National Knowledge Infrastructure (CNKI), Islamic World Science Citation Center (ISC), and Scientific Information Database (SID) databases. All research that looked at the link between organ transplantation gene polymorphisms and infection risk was gathered. The literature search has no language restrictions. To find possibly relevant papers, the reference lists of the eligible studies, reviews, and prio meta-analysis publications were manually examined. All procedures were carried out in accordance with the ١٩٧٥ Helsinki Protocol and its subsequent amendments. It was also approved by the Ethics Committee of Shiraz University of Medical Sciences

Results: A total of ١,٥٦٧ studies were found to be suitable after exten-sive database searches. In total, ٥١٣ publications were omit-ted due to duplicated records, ٩١٢ papers were excluded following the primary screening, and ١٥٤ papers were excluded after full-text evaluation after screening the col-lected studies based on inclusion criteria for the current meta-analysis. The methodological technique for including researc and obtaining important data from eligible papers are depicted in

Fig. ١. Finally, nine studies found an association between viral infection and rs٥٧٤٢٩٠٩, rs٧٣٣٦١٨, rs٤٥٥٣٨٠٨, and rs٢٣١٧٧٥ polymorphisms in organ transplantatio .

Conclusion: This meta-analysis indicated that a significant correlation between CTLA٤+٤٩ (A/G-٢٣١٧٧٥) and CTLA٤(rs٥٧٤٢٩٠٩TT) gene poly-morphism with infection in organ transplantation risk was observed. Further studies involving gene–gene and gene–diet interactions should be conducted to investigate this association

Keywords: CTLA-٤, transplantation, polymorphism

Artificial Intelligence for Predicting Active Lesion in Multiple Sclerosis from Non-contrast MRI

(Research Paper)

AmirAbbas Amini,[١,*] Raheleh Kafieh,[٢] Azin Shayganfar,[٣] Zahra Amini,[٤] Leila Ostovar,[٥] Somayeh Haji Ahmadi,[٦]

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Introduction: Multiple sclerosis (MS) is a disease that affects the central nervous system. In this disease, the myelin covering the nerve fibers is attacked by the body's immune cells and creates lesions in the brain, these lesions are classified into two types, active and inactive. All these lesions can be identified in fluid-attenuated inversion recovery (FLAIR) type MRI images, but it is impossible to distinguish whether they are active or inactive. Therefore, in order to detect active lesions and control the disease, MRI imaging with gadolinium-based contrast is used, but since the long-term deposition of gadolinium in various tissues can cause complications for the patient, it is important to investigate alternative methods. The purpose of this study is to investigate the deep learning method as one of the methods based on artificial intelligence in the diagnosis of active lesions without the use of contrast agents.

Methods: Our data were collected from ١٣٠ patients with Relapsing-Remitting Multiple Sclerosis in four different imaging centers in Isfahan City. Firstly, the lesions were identified by radiologists and classified into active and inactive categories. These lesions included a total of ٩٠٩٧. Then, each lesion was separated as an ROI from the FLAIR sequence MRI scans to be used as the input of the artificial intelligence network. Next, three deep learning networks including a convolutional neural network (CNN) as the main designed network, and two transfer learning networks including VGG١٩ and Efficient NetB٠ were designed and trained to distinguish active from inactive lesions. Finally, the statistical results obtained from each network were calculated and compared with each other.

Results: For our designed CNN, the average results of precision, recall, and F١ score in ٥-fold cross-validation for active and inactive classes were ٠,٧٧, ٠,٩٩, ٠,٨٧ and ٠,٩٨, ٠,٧٠, ٠,٨٢, respectively. These values were obtained for the VGG١٩ network ٠,٦٨, ٠,٨٧, ٠,٧٦, and ٠,٨٢, ٠,٦٠, ٠,٦٨ respectively, and for the Efficient NetB٠ network ٠,٦٧, ٠,٩٤, ٠,٧٨ and ٠,٩٠, ٠,٥٧, ٠,٦٧ respectively. Also, the values of accuracy and areas under the receiver operating characteristic curve (AUC) were

evaluated for these ٣ networks, which were ٠,٨٥ and ٠,٩٤ for our designed CNN network, ٠,٧٣ and ٠,٧٩ for the VGG١٩ network, and ٠,٧٤ and ٠,٨١ for the Efficient NetB٠ network, respectively.

Conclusion: Our results show that the use of deep learning networks as one of the methods of artificial intelligence can accurately detect active lesions of MS disease. This method can avoid the side effects of contrast injection.

Keywords: Multiple Sclerosis (MS); Artificial Intelligence; Deep Learning; Non-contrast MRI; Autoimmune Diseas

Artificial Intelligence for Predicting Active Lesion in Multiple Sclerosis from Noncontrast MRI

(Research Paper)

AmirAbbas Amini,[١,*] Raheleh Kafieh,[٢] Azin Shayganfar,[٣] Zahra Amini,[٤] Leila Ostovar,[٥] Somayeh Haji Ahmadi,[٦]

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Introduction: Multiple sclerosis (MS) is a disease that affects the central nervous system. In this disease, the myelin covering the nerve fibers is attacked by the body's immune cells and creates lesions in the brain, these lesions are classified into two types, active and inactive. All these lesions can be identified in fluid-attenuated inversion recovery (FLAIR) type MRI images, but it is impossible to distinguish whether they are active or inactive. Therefore, in order to detect active lesions and control the disease, MRI imaging with gadolinium-based contrast is used, but since the long-term deposition of gadolinium in various tissues can cause complications for the patient, it is important to investigate alternative methods. The purpose of this study is to investigate the deep learning method as one of the methods based on artificial intelligence in the diagnosis of active lesions without the use of contrast agents.

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Results: For our designed CNN, the average results of precision, recall, and F١ score in ٥-fold cross-validation for active and inactive classes were ٠,٧٧, ٠,٩٩, ٠,٨٧ and ٠,٩٨, ٠,٧٠, ٠,٨٢, respectively. These values were obtained for the VGG١٩ network ٠,٦٨, ٠,٨٧, ٠,٧٦, and ٠,٨٢, ٠,٦٠, ٠,٦٨ respectively, and for the Efficient NetB٠ network ٠,٦٧, ٠,٩٤, ٠,٧٨ and ٠,٩٠, ٠,٥٧, ٠,٦٧ respectively. Also, the values of accuracy and areas under the receiver operating characteristic curve (AUC) were

evaluated for these ٣ networks, which were ٠,٨٥ and ٠,٩٤ for our designed CNN network, ٠,٧٣ and ٠,٧٩ for the VGG١٩ network, and ٠,٧٤ and ٠,٨١ for the Efficient NetB٠ network, respectively.

Conclusion: Our results show that the use of deep learning networks as one of the methods of artificial intelligence can accurately detect active lesions of MS disease. This method can avoid the side effects of contrast injection.

Keywords: Multiple Sclerosis (MS); Artificial Intelligence; Deep Learning; Non-contrast MRI; Autoimmune Diseas

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Assessing Genetic and Pharmacogenetic Effects in Cardiovascular Disease Management: The Role of Personalized Approaches (Research Paper)

Mojtaba Rashidi Mosleh,[۱,*] Dariush Norouzian,[۲]

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Introduction: Cardiovascular diseases (CVDs) are the leading cause of morbidity and mortality worldwide. Variability in drug response among patients is a significant challenge in CVD management, often influenced by genetic and pharmacogenetic factors. Personalized medicine offers a promising approach to optimize treatment efficacy and minimize adverse effects by tailoring therapies based on individual genetic profiles.

Methods: This study analyzed genetic polymorphisms associated with drug metabolism, efficacy, and safety in CVD treatment. A systematic review of pharmacogenetic data was conducted, focusing on key cardiovascular drugs such as statins, beta-blockers, and antiplatelet agents. Clinical trials assessing the impact of genetic testing on treatment outcomes were also evaluated. Additionally, computational tools were employed to model gene-drug interactions and predict patient-specific responses.

Results: Findings reveal that polymorphisms in genes such as CYP۲C۱۹, SLCO۱B۱, and VKORC۱ significantly influence drug efficacy and toxicity. For instance, variations in CYP۲C۱۹ affect clopidogrel metabolism, leading to variability in antiplatelet response, while SLCO۱B۱ variants are linked to statin-induced myopathy. Incorporating pharmacogenetic testing into clinical practice improved therapeutic outcomes by guiding drug selection and dosage adjustments. Personalized strategies were particularly effective in reducing adverse drug reactions and achieving optimal lipid control and blood pressure management.

Conclusion: Genetic and pharmacogenetic factors play a pivotal role in the variability of drug responses in CVD management. Integrating genetic testing into routine clinical workflows can enhance the precision of treatment regimens, improving patient outcomes and reducing healthcare costs. Future research should focus on expanding genetic databases, developing cost-effective testing methods, and implementing personalized approaches on a broader scale.

Keywords: Pharmacogenetic, Cardiovascular Disease, Personalized Approaches

Assessing miRNA-۲۱۷ overexpression effects on type ۱, type ۲, and type ۳ inositol trisphosphate receptor gene expression in B (Raji) and T (Jurkat) acute lymphoblastic leukemia cell lines

(Research Paper)

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Introduction: Acute lymphoblastic leukemia (ALL) is a malignant transformation and proliferation of lymphoid progenitor cells in the bone marrow, blood, and extramedullary sites. MicroRNAs, which are involved in the regulation of cellular processes such as proliferation, invasion, metastasis, and apoptosis, have been implicated in cancer development. MiRNA-۲۱۷, in particular, has been identified as a potential anticancer factor owing to its decreased expression levels in several cancers. The inositol ۱,٤,٥-trisphosphate receptors (IP۳Rs), which are involved in the IP۳/calcium signaling pathway, play important roles in the regulation of cellular functions such as proliferation, apoptosis, differentiation, and metabolism. Moreover, they have been linked to neoplastic transformation and progression. Therefore, this study aimed to investigate the effect of miR-۲۱۷ overexpression on the gene expression of IP۳Rs in Jurkat and Raji cell lines.

Methods: Jurkat and Raji Cell lines were cultured in RPMI-۱٦٤۰ medium supplemented with ۱۰٪ fetal bovine serum (FBS) and incubated under controlled conditions of ۳۷ °C, ۹٥٪ humidity, and ٥٪ carbon dioxide. In addition, the normal fibroblast cell line was cultured in DMEM. Next, miR-۲۱۷ was transduced into the cells using lentiviral vectors. RNA was extracted from the cells ٤۸ and ۷۲ h after transduction, and complementary DNA (cDNA) was synthesized. Finally, transduction efficiency was confirmed using real-time qPCR, and the mRNA levels of IP۳Rs genes were measured using real-time qPCR.

Results: The expression levels of IP۳R۱ and IP۳R۳ genes were found to be decreased in the miR-۲۱۷ transduced group compared to the control group in all three cell lines at ٤۸ and ۷۲ hours after transduction. This decrease was significant in all three cell lines at ٤۸ h, except for IP۳R۳ expression in Raji cells, which was only significantly decreased at ۷۲ h after transduction. Furthermore, the expression of the IP۳R۲ gene in the miR-۲۱۷ transduced group compared to the control group increased at ٤۸ h but decreased at ۷۲ h in Jurkat cells, whereas it increased in Raji cells and decreased in fibroblast cells at both ٤۸ and ۷۲ h after transduction.

Conclusion: The results of the current study demonstrated that the expression of IP٣R١, IP٣R٢, and IP٣R٣ mRNA is altered with the overexpression of miR-٢١٧ in Jurkat, Raji, and Fibroblast cells, suggesting a potential role of miR-٢١٧ in regulating the expression of these genes. This is important for understanding the molecular mechanisms that form the basis of various cellular processes. Further studies are needed to understand the role of miR-٢١٧ in the IP٣/calcium signaling pathway.

Keywords: Acute lymphoblastic leukemia, hsa-mir-٢١٧, Inositol ١,٤,٥-Trisphosphate Receptors

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Assessment of Autophagy Gene Expression in Human Follicular Fluid Cells Cultured In Vitro

(Research Paper)

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Introduction: Autophagy, a cellular process involving the degradation and recycling of cellular components, plays a crucial role in maintaining cellular homeostasis and is implicated in various physiological and pathological processes. This study aimed to investigate the expression levels of autophagy-related genes in human follicular fluid cells cultured in vitro. Follicular fluid cells, which are derived from the ovarian follicle, are known to support oocyte development and maturation.

Methods: We employed quantitative real-time PCR to examine the expression of crucial autophagy genes, such as ATG۵, ATG۷, and Beclin-۱, in follicular fluid cells derived from human ovarian follicles. These cells were analyzed after ۷ and ۲۱ days of in vitro culture.

Results: Our results indicate that the expression levels of these autophagy genes have decreased significantly in response to in vitro culture conditions. Specifically, we observed that Beclin-۱ expression down-regulated markedly on day ۲۱ compared to day ۷(P<۰,۰۰۱) in cells extracted from ovarian follicular fluid. ATG۵ expression was significantly lower on day ۲۱ versus day ۷(P<۰,۰۰۱). ATG۷ expression showed a significant reduction on day ۲۱ compared to day ۷ (P<۰,۰۱).

Conclusion: These findings offer insights into the molecular mechanisms governing autophagy in human follicular fluid cells, emphasizing the potential significance of autophagy in oocyte development and fertility. The data also suggest a spontaneous differentiation process in these cells over the ۲۱-day culture period. This study enhances our understanding of autophagy's role in reproductive biology and may have implications for the development of new therapeutic approaches in assisted reproductive technologies.

Keywords: Oocyte-like cell, Infertility, In vitro fertilization, Autophagy, Human Follicular Fluid Cells

Assessment of bacterial cellulose nanostructure as a ٣-D scaffold for neural tissue engineering

(Research Paper)

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Introduction: Almost neural tissue engineering approaches suffer from functional biomaterials capable of supporting nerve cell regeneration and growth. Developing a nanostructured scaffold able to mimick niche of nervous system have been suggested as a promising candidate. Exploiting bacterial cellulose (BC) has recently absorbed high attention, mainly due to its excellent biocompatibility, mechanical strength, and fibrous structure. In this study, we investigated characteristics of cellulosic scaffold derived from Pseudomonas species, which is gaining attention for its ability to be synthesized under controlled conditions and its potential to mimic the extracellular matrix (ECM).

Methods: Following the bacterial culture, cellulose collection, and decellularization, the scaffold's physicochemical properties were characterized using scanning electron microscopy (SEM) and atomic force microscopy (AFM) for surface morphology, Fourier-transform infrared spectroscopy (FTIR) for chemical analysis, and hydrophilicity and biodegradability tests. Additionally, cell viability, proliferation, adhesion, and neural cell morphology were evaluated.

Results: The bacterial cellulose scaffold exhibited a well-organized fibrous structure resembling the extracellular matrix. MTT assays indicated no significant cytotoxicity, confirming the scaffold's biocompatibility. DAPI staining and SEM analysis revealed excellent cell adhesion and morphology, with neural cells demonstrating uniform growth and spreading across the scaffold. These findings suggest that bacterial cellulose provides an ideal environment for neural cell proliferation and viability.

Conclusion: Data presented here demonstrated that decellularized bacterial cellulose nanofibrous structure effectively supports neural cell attachment and growth, with no observed cytotoxic effects. These results indicate that obtained nanostructured cellulosic matrics have great potential for further development in neural regeneration and broader tissue engineering applications.

Keywords: Key words: Bacterial Cellulose (BC), Scaffolds, Neural tissue engineering, Extracellular matrix

Assessment of the Anti-cancer Effects of Camel Milk Exosomes (CMEXOs) on Murine Colorectal Cancer Cell Line (CT-٢٦) (Research Paper)

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Introduction: Today, camel milk consumption in the Middle East is trendy because it is believed that it reduces the risk of cancer. Recently, studies have discovered that most of milk's beneficial effects are because of its nanoparticles, especially exosomes. The objective of the present research was to investigate the anti-cancer effects of camel milk exosomes (CMEXOs) in the murine colorectal cancer cell line (CT-٢٦).

Methods: After isolation and characterization of CMEXOs, we investigated their effects on the proliferation and migration of CT-٢٦ cells using MTT and scratch assay. Additionally, we employed real-time quantitative PCR (RT-qPCR) to analyze the expression levels of IL-٦ and TNF-α genes in CT-٢٦ cells.

Results: Our findings verified the existence of exosomes measuring approximately ١١٤,١±٣,٤ nm in diameter. Through MTT and migration assays, we established that CMEXOs exhibit dosedependent anti-proliferative and anti-migration effects on the CT-٢٦ cell line. Furthermore, our study showed that treatment with CMEXOs led to a reduction in TNF-α and IL-٦ gene expression in CT-٢٦ cells.

Conclusion: While additional in vivo studies are required, our data demonstrate that CMEXOs have antiproliferative and anti-migration effects on CT-٢٦, possibly by influencing crucial genes within the inflammation pathway.

Keywords: Camel milk; Colorectal cancer; Exosomes; IL-٦; TNF-α

Assessment of the Relationship Between CD٤٤ Expression and Gleason Grade in Prostate Adenocarcinoma and Benign Prostatic Hyperplasia: A Cross-Sectional Study (Research Paper)

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Introduction: Prostate adenocarcinoma (PAC) ranks as the second most common cancer among men. The cluster of differentiation ٤٤ (CD٤٤) acts as a suppressor gene for metastatic tumors in PAC. This research aimed to examine the expression levels of CD٤٤ in PAC in comparison to benign prostatic hyperplasia (BPH).

Methods: In this cross-sectional study, we analyzed CD٤٤ expression in tissue samples from PAC and BPH using Hematoxylin & Eosin staining and immunohistochemistry techniques. We assessed the Gleason scores and grades, along with the percentage of CD٤٤ expression in the specimens. Data analysis was conducted using IBM SPSS version ٢٣,٠ software.

Results: The study included ٨٠ PAC samples and ٨٣ BPH samples. The average CD٤٤ expression in PAC samples was significantly lower than that in BPH samples ($p < ٠,٠٠١$). A significant relationship was observed between CD٤٤ expression and both the total Gleason scores and Gleason grade groups in PAC ($p < ٠,٠٠١$). A moderate to strong significant negative correlation was identified between CD٤٤ expression and total Gleason scores (r: -٠,٧٤٣, $p < ٠,٠٠١$) as well as Gleason grade groups (r: -٠,٧٣٢, $p < ٠,٠٠١$). Ordinal logistic regression indicated that CD٤٤ expression negatively correlates with total Gleason scores (OR = ٠,٨٨٤, $p < ٠,٠٠١$) and Gleason grade groups (OR = ٠,٨٨٤, $p < ٠,٠٠١$).

Conclusion: This study underscores the potential of CD٤٤ expression as a biomarker for diagnosing PAC, revealing significantly reduced levels of CD٤٤ in PAC compared to BPH. The lower expression of CD٤٤ is associated with higher Gleason scores and grades, indicating its involvement in disease progression and its implications for patient management strategies.

Keywords: CD٤٤; Cluster of differentiation ٤٤; Benign prostatic hyperplasia; Prostate adenocarcinoma

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Association between genetic polymorphisms of GPX١ C٥٩٤T and GPX٤ C٧١٨T with the risk of age-related macular degeneration (Research Paper)

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Introduction: Age-related macular degeneration (AMD) is a progressive disease resulting in loss of vision. medical articles known as: "Diseases That Occur in the Elderly. This disease is caused by the destruction of the retina generally in people over ٥٥ years of age and as the disease progresses it leads to blindness. There are many environmental and genetic factors involved in this disease. These include age, gender, race, diet, smoking, UV light, oxidative stress, and cardiovascular disease.One of the important factors in AMD disease is oxidative stress. Excessive accumulation of ROS and the inability of the antioxidant defense system to neutralize it can contribute to the development of lesions. One of the antioxidant enzymes is glutathione peroxidase. The aim of this study was to investigate the relation between genetic polymorphisms of GPX١ C٥٩٤T and GPX٤ C٧١٨T with the risk of AMD disease.

Methods: Our case-control study included ١٢٢ AMD patients (٧٥ male, ٤٧ female) selected from the Department of Ophthalmology, Khalili Hospital, Shiraz (South Iran) and ١٢٢ controls (٧٠ male, ٥٢ female) randomly selected from healthy blood donors. Iranian population is one of the most heterogeneous populations. Therefore, we selected our patients and controls from the same ethnicreligious group (Persian Muslims living in Fars province, southern Iran). Subjects were divided into two groups according to occupation: outdoor (farmers, drivers, etc.) and indoor (housewives, teachers, etc.). The genomic DNA was extracted from the whole blood samples. The restriction fragment length polymorphism (PCR-RFLP) assay was used to determine the genotype for GPX١ C٥٩٤T (rs١٠٥٠٤٥٠) and GPX٤ C٧١٨T (rs٧١٣٠٤١) polymorphisms. PCR products of GPX١ C٥٩٤T and GPX٤ C٧١٨T polymorphisms were digested with restriction enzyme Apa I and Sty I , respectively.After digestion, DNA products were analyzed by ٣٪ agarose gel electrophoresis.

Results: The association between smoking and AMD was found in this study (OR=٢,١٦٥, CI=١,١٤٥ - ٤,٠٩٢, p=٠,٠١٧). The place of work (outdoor) significantly increased the risk of AMD (OR=٢,٠٦٧, CI=١,١٦٨-٣,٦٥٩, p=٠,٠١٣) . The CC, CT, and TT genotype frequencies for GPX١ were ٤٢,٥٪, ٤٣,٤٪, and ١٣,٣٪ in controls and ٤٤,٣٪, ٤٣,٤٪, and ١٢,٣٪ in cases, and for GPX٤ were ١٩,٧٪, ٤٩,٢٪, and ٢٨,٧٪ in controls and ٢٧,٠٪, ٤٤,٣٪, and ٢٧,٩٪ in cases, respectively. There was no significant association between the genotypes of GPX١ C٥٩٤T (TT vs. CC, OR=٠,٨٤, ٩٥٪CI=٠,٣٦-١,٩٥, P=٠,٦٩٣) and GPX٤ C٧١٨T (TT vs. CC, OR=٠,٦٤, ٩٥٪CI=٠,٣٠- ١,٣٥, P=٠,٢٤٧) and susceptibility to AMD

Conclusion: It was expected that AMD would be associated with SNPs in antioxidant genes because AMD is significantly associated with oxidative stress and oxidative stress scavenged by antioxidant enzymes. It has already been shown that AMD is associated with some genetic variations in genes

involved in antioxidant pathways. Previous studies with some antioxidant genes showed that a significant decrease in enzymes SOD, CAT and GPX in AMD patients compared to controls, was indicated. The current study suggested that the GPX١ C٥٩٤T (rs١٠٥٠٤٥٠) and GPX٤ CV١٨T (rsV١٣٠٤١) polymorphisms are not predisposing to AMD.

Keywords: Age related macular degeneration (AMD), GPX١, GPX٤, Polymorphism

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Association between Helicobacter pylori infection and gastric microbiota (Review)

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Introduction: The relationship between the human gastric microbiota and reciprocal symbiotic with the host is the complex and homeostatic imbalance may lead to digestive diseases. Also targeted therapies in H. pylori infections may inadvertently harm the gastric microbiota, decreasing microbial diversity. While eradicating H. pylori might be beneficial in treating certain conditions, it could also negatively affect the balance and health of the entire microbial community. The severity of H. pylori infection largely depends on the complex bacterial pathogenic factor, gastric environmental factors, and host genetics. Studies have reported this infection is an agent associated with gastritis and gastric cancer at the early stage.

Methods: The present study is a review study that was conducted in ۲۰۲۳. Related articles were gathered by searching keywords, Gastric cancer, H. pylori, and gastric microbiota in Google Scholar, PubMed, Science Direct databases

Results: Studies show H. pylori infection has been confirmed as a major risk factor in gastric cancer. Stomach infection causes the premalignant environment of intestinal atrophy and metaplasia and causes changes in gastric microbiota and gastric auto-tumorigenesis. The most abundant types of bacteria in the stomach, proteobacteria and firmicutes, Bacteroides, actinobacteria, and fusobacteria also present in significant numbers. Similar studies showed an increase in the Frequency of Lactobacilli and Lacnospirases in the tissue samples of gastric cancer patients.

Conclusion: Advances in the techniques used in molecular and sequencing technologies have improved our understanding of the biology of H. pylori the host responses to this bacterium and the role of the gastric microbiota. Recent investigations have yielded substantial findings concerning the influence of H. pylori infection on the gastric microbial composition, gut dysbiosis, and cancer progression symptoms.

Keywords: Helicobacter pylori, gastric cancer, gastric microbiome

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Association between Proprotein convertase subtilisin/kexin type ۹ with atherosclerosis (Review)

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Introduction: In ۲۰۰۳, Seidah et al discovered a new element in the proprotein convertase family. The gene encoding this enzyme was found to be more expressed during apoptosis of brain cells. Since it was the ninth element of the proprotein convertases family, it was named proprotein convertase subtilisin/kexin type ۹ (PCSK۹), besides convertase neural apoptosis-regulated convertase ۱ (NARC-۱). PCSK۹ is most commonly expressed in the liver. PCSK۹ has the primary function of regulating the cellular low-density lipoprotein receptor (LDLR). The deposition of lipids, particularly LDL and Lp(a), in the walls of arteries is the cause of atherosclerosis. The aim of this study was to evaluate the association between PCSK۹ with atherosclerosis.

Methods: For this review, ۵۰ articles were found in the first stage. Strategy search in this case was as follows: the first two words (PCSK۹ and atherosclerosis) in the mesh PubMed dataset were initially identified. Then, we combined two words in the pattern of using AND and OR. This review utilized human, animal, and in vitro studies.

Results: According to the conducted studies, PCSK۹ promotes LDLR degradation through both intracellular and extracellular pathways. It leads to increased production and secretion of VLDL and LP(a). Thus, it increases the serum level of LDL and LP(a). The accumulation of LDL and Lp(a) in endothelial cells leads to the formation of foam cells. Moreover, by binding to Toll-like receptors (TLRs), PCSK۹ acts as a mediator of inflammatory responses. It is responsible for platelet activation and thrombosis by interacting with CD۳۶ receptors. Also, the levels of coagulation factors FVIII and tissue factor (TF) were raised by PCSK۹. It was shown, that PCSK۹ prevented cholesterol efflux from macrophages by inhibiting ABCA۱ expression. On the other hand, PCSK۹ inhibits the formation of foam cells through the degradation of LDLR and CD۳۶ in macrophages.

Conclusion: PCSK۹ has conflicting roles in the process of atherosclerosis

Keywords: PCSK۹, atherosclerosis, thrombosis, foam cell

Association Between Vitamin D Deficiency and Inflammatory Levels in Patients with Rheumatoid Arthritis (Research Paper)

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Introduction: Rheumatoid arthritis (RA) is a chronic inflammatory disorder characterized by persistent synovitis, systemic inflammation, and autoantibodies. Recent studies suggest that vitamin D deficiency may be linked to increased inflammation in RA patients. This study aims to investigate the relationship between vitamin D deficiency and inflammatory markers in individuals diagnosed with RA.

Methods: This cross-sectional study included ١٢٠ patients diagnosed with RA, recruited from a rheumatology clinic. The sample comprised ٧٨ females and ٤٢ males, with a mean age of ٥٢,٣ years (SD = ١٠,٤). Serum levels of vitamin D were measured using enzyme-linked immunosorbent assay (ELISA). Inflammatory markers, including C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), were also assessed. Patients were classified into two groups based on their vitamin D levels: deficient (<٢٠ ng/mL) and sufficient (≥٢٠ ng/mL).

Results: Results Among the ١٢٠ RA patients, ٨٥ (٧٠,٨٪) were found to have vitamin D deficiency, while ٣٥ (٢٩,٢٪) had sufficient vitamin D levels. The mean CRP level in the vitamin D deficient group was ٢٨,٤ mg/L, compared to ١٤,٦ mg/L in the sufficient group. Similarly, the mean ESR was higher in the deficient group, with an average of ٤٠,٢ mm/hr versus ٢٢,٨ mm/hr in the sufficient group. Statistical analysis showed a significant correlation between low vitamin D levels and higher CRP ($p<٠,٠٠١$) and ESR ($p<٠,٠٠١$) values

Conclusion: The findings indicate a significant association between vitamin D deficiency and elevated inflammatory markers in RA patients. These results suggest that maintaining adequate vitamin D levels may play a role in managing inflammation in RA. Further research is needed to explore the potential benefits of vitamin D supplementation in reducing inflammatory responses in RA.

Keywords: Keywords Rheumatoid Arthritis, Vitamin D Deficiency, Inflammatory Markers, C-Reactive Protein, Eryth

Association of CD٤٠ gene polymorphisms with risk of lung cancer. A systematic review and meta-analysis (Review)

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Introduction: Despite advances in detection and treatment, cancer remains a main public health crisis across the globe. It was estimated that in ٢٠٢٤, ٢ million new cancer cases would be diagnosed in the worldwide, along with over ٦٠٠,٠٠٠ estimated deaths [١].Although cancer diagnosis and therapy have been improved gradually, the survival of patients remains poor, which are mainly affected by drug resistance, local recurrence, and development of metastatic disease. [٢] According to the research studies, cancer stem cells (CSCs) with the principal properties of multipotency and self-renewal are responsible for neoplasm formation, metastasis, recurrence, and therapeutic resistance. [٣] Among the different markers, CD١٣٣ is one of the most robust surface marker of CSCs. [٤] it is widely expressed in numerous types of tumors, involving colorectal, Lung and ovarian cancer. [٥] It is a ٥ transmembrane single-chain glycoprotein, with a molecular weight of ١٢٠ kDa, which was first found to be expressed in hematopoietic stem and progenitor cells. [٦] However, the prognostic value of CD١٣٣ for different type of cancers remain controversial despite of numerous independent studies. We performed a meta-analysis to determine the value of CD١٣٣ as a prognostic marker for all type of cancer and a robust target for cancer treatment.

Methods: Search Strategy and Selection Criteria: We searched PubMed, EMBASE, Elsevier databases MEDLINE (PubMed), Google Scholar, Web of Science (Thomson-Reuters) with Medical Subject Heading keywords CD١٣٣, CSCs, Prominin, Cancer therapy, examining the CD١٣٣ as a CSC marker for targeting cancer therapy published up to August ١٥, ٢٠٢٤. In addition, we reviewed citations in the retrieved articles to search for additional relevant studies. Searches were limited to papers published in English only. Studies were included in the meta-analysis, if they included patients with Cancer diagnosis by pathologists according to the American Association guidelines; data on CD١٣٣ (Prominin) marker and full-length papers; and data about odds ratios (ORs) with ٩٥٪ confidence intervals (CI), or at least adequate data to calculate ٩٥٪ CIs. The following studies were excluded; overlapping articles or duplicate data; review articles and conference records without original data and full text; to investigate the effects of targeting CD١٣٣ marker of CSC in varieties of cancer types. Inclusion and exclusion criteria: Studies were selected according to the following inclusion criteria: (١) full-text published studies up August ١٥, ٢٠٢٤; (٢) a case-control or a Clinical Trial design; (٣) the study goal was to evaluate the effect of CD١٣٣ marker as a significant marker for cancer therapy. (٤) Sufficient data for estimating ٩٥٪ confidence interval (CI) and odds ratio (OR). Data extraction: In this study Information was extracted from all the eligible studies independently by ٢ researchers using a pre-designed form according to the selection criteria listed above. For each study the following information was extracted: the name of first author, publication year, country where the

study was conducted, racial descent, type of cancer, cancer treatment testing method, number of patients and the final effect of targeting cancer therapy.

Results: ١٣ records were found after examining online databases, references, and related articles; ٧ of these records were subsequently eliminated as being unrelated. The current meta-analysis also included ٦ eligible study. Table ١ provides basic data, including, the number of patients, results, effect, method, country and year. According to the results of this investigation, CD١٣٣ plays prominent roles in different cancer types and is responsible for cancer recurrence and metastasis and is a promising marker for cancer treatment.

Conclusion: CSCs can be distinguished by their properties of self-renewal and differentiation and subsequently generate cancer cells. Several studies have examined effect of targeting CD١٣٣ as a CSCs marker for cancer treatment in different cancer types; but the results were controversial. Meta-analysis has been recognized as a prominent tool to exactly define the effect of targeting different CSC markers for cancer therapy. The present meta-analysis was carried out by critically reviewing ٦ relevant and new recently published studies on targeting CD١٣٣ for cancer treatment. Hence, it may provide more information. The overall effects of these ٦ clinical studies (Table١) suggest CD١٣٣ as a promise marker for treatment.

Keywords: Keywords: CD٤٠ Gene, Lung cancer, Polymorphisms

Association of Coronary Artery Diseases and Parkinson's Disease in the Elderly: A Narrative Review

(Review)

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Introduction: Parkinson's disease (PD) is a common neurodegenerative disorder in the elderly, characterized by motor symptoms such as tremor, bradykinesia, and rigidity, as well as non-motor symptoms like cognitive impairment and autonomic dysfunction. Coronary artery disease (CAD), resulting from atherosclerosis in the coronary arteries, is a leading cause of morbidity and mortality among older adults. Although PD and CAD are distinct conditions, recent studies suggest a potential association between them, particularly in the elderly population, where both conditions frequently coexist. The intersection of age-related changes, such as increased oxidative stress, inflammation, and comorbidities, may contribute to this association.

Methods: A comprehensive literature search was conducted using PubMed, Cochrane Library, and Scopus, focusing on studies published in the last ٢٠ years. Search terms included "Parkinson's disease," "coronary artery disease," "elderly," "cardiovascular risk," "autonomic dysfunction," and "inflammation." Observational studies, cohort studies, case-control studies, and reviews were included to assess the association between CAD and PD specifically in the elderly population.

Results: Epidemiological studies indicate a higher prevalence of CAD in elderly patients with PD compared to those without PD, suggesting an interplay between the two conditions. Traditional cardiovascular risk factors, such as hypertension, diabetes mellitus, and dyslipidemia, are common in the elderly and contribute to the development of CAD. In elderly PD patients, additional factors such as autonomic dysfunction—leading to orthostatic hypotension and impaired heart rate variability—further increase cardiovascular risk. Reduced physical activity due to motor impairment in PD can exacerbate these risks, leading to accelerated atherosclerosis and CAD development. Furthermore, medications used to manage PD symptoms, such as dopamine agonists, have been associated with potential cardiovascular side effects, complicating the management of CAD in these patients. Shared pathophysiological pathways may underpin the association between PD and CAD in the elderly. Both conditions are characterized by chronic systemic inflammation, with elevated levels of pro-inflammatory cytokines, such as TNF-α and interleukin-٦, contributing to neurodegeneration and vascular damage. Oxidative stress, a key feature of aging, results in damage to both neuronal and vascular tissues, promoting the progression of both PD and CAD. Additionally, mitochondrial dysfunction, which plays a central role in PD pathogenesis, is also implicated in atherosclerosis, particularly in elderly patients with comorbidities such as diabetes. Genetic predispositions, including polymorphisms affecting lipid metabolism and inflammatory responses, may further link these diseases in older adults.

Conclusion: The coexistence of CAD and PD in the elderly involves a complex interaction of age-related risk factors, shared pathological processes, and the effects of PD-specific features such as

autonomic dysfunction and medication use. While the current evidence suggests an increased prevalence of CAD among elderly patients with PD, further research is needed to clarify the causal relationship and understand the mechanisms involved. Prospective studies are essential to identify elderly patients with PD who are at high risk for CAD and to develop targeted interventions that can mitigate this risk. Clinicians should consider comprehensive cardiovascular risk assessments in elderly PD patients, accounting for both conventional and PD-specific risk factors. Improved understanding of the association between CAD and PD in this population could enhance patient care by allowing for more personalized and effective management strategies.

Keywords: Parkinson's Disease, Coronary Artery Disease, Inflammation, Elderly

Astaxanthin has neuroprotective effects on ethanol-induced oxidative stress in the cortex of model mice (Research Paper)

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Introduction: Ethanol is a clear liquid produced by fermenting sugars, found in alcoholic beverages. Excessive consumption causes poisoning and neurodegeneration in the brain by oxidation. Ethanol metabolism to acetaldehyde and then to acetate produces reactive oxygen species, which increases oxidative stress and reduces antioxidants, leading to mental disorders. Astaxanthin is a type of fat-soluble carotenoid that has strong antioxidant properties and protective effects. It is produced by algae, plants, and some fungi and bacteria. Astaxanthin acts as an inhibitor of reactive oxygen species and is absorbed by lipoproteins to protect cells and membranes from oxidative damage. It has neuroprotective effects and can cross the blood-brain barrier, making it highly effective in brain disorders. This research aims to investigate the neuroprotective effects of astaxanthin on anxiety-like behaviors and oxidative stress in the cerebral cortex of ethanol model mice.

Methods: ٣٥ male mice were divided into ٥ groups (n=٧) including control, astaxanthin ٢٠, ethanol, and two treatment groups with astaxanthin ١٠ and ٢٠ mg/kg. The patient group (ethanol) received ٢٠٪ ethanol. In the treatment groups, first ٢٠٪ ethanol and after ٢ hours astaxanthin in doses of ١٠ and ٢٠ mg/kg was prescribed. All prescriptions were done daily for ١٤ consecutive days. Then all mice were sacrificed and the cortical areas of their brains were extracted for biochemical analysis. Antioxidant parameters including the activities of glutathione peroxidase (GPx), glutathione S-transferase (GST), and glutathione (GSH) levels were measured. Statistical analysis was performed using one-way analysis of variance (ANOVA) in GraphPad Prism and a pairwise comparison of means using Tukey's post-hoc test. Also, $P < ٠,٠٥$ was considered statistically significant.

Results: The results of this research have shown that administration of ٢٠٪ ethanol significantly decreased the activities of glutathione peroxidase ($P < ٠,٠١$) and glutathione S-transferase ($P < ٠,٠٥$), and the levels of glutathione levels ($P < ٠,٠١$) in the cortex of ethanol model mice. This is while the treatment with astaxanthin significantly has improved the activities of glutathione peroxidase ($P < ٠,٠٥$) and glutathione S-transferase ($P < ٠,٠٥$), and the levels of glutathione levels ($P < ٠,٠١$).

Conclusion: In this study, Administering ٢٠٪ ethanol daily for ١٤ consecutive days, reduced antioxidant parameters in the cortex of ethanol model mice. Studies showed that ethanol gavage with a concentration of ٢٠ mg/kg increased protein oxidation in the brain and these changes caused oxidative damage in cells and neurological disorders. While, treatment with astaxanthin daily for ١٤ consecutive days, improved the complications caused by ethanol administration and was effective in increasing the activity of antioxidant parameters. Some previous studies showed that Alzheimer's model rats using astaxanthin powder significantly reduced neurodegeneration. As a result,

astaxanthin can be useful as an effective antioxidant against the negative effects of ethanol consumption such as oxidative damage.

Keywords: Astaxanthin, Ethanol, Oxidative stress, Mice

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Atmospheric Pressure Plasma in Cancer Treatment (Review)

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Introduction: Atmospheric pressure plasma (APP), especially cold atmospheric plasma (CAP), is emerging as a potential tool in cancer therapy. CAP generates reactive oxygen and nitrogen species (RONS), which can cause oxidative stress and trigger apoptosis in cancer cells. This review aims to summarize recent advancements from ٢٠٢٢ to ٢٠٢٤ in the use of APP for cancer treatment, highlighting the mechanisms involved, therapeutic efficacy, and prospects.

Methods: A comprehensive search was performed using full consensus, focusing on studies published between ٢٠٢٢ and ٢٠٢٤. Keywords included "atmospheric pressure plasma", "cold atmospheric plasma", " plasma-activated solutions" and "cancer therapy". Studies were selected based on relevance to the application of APP in cancer therapy, including in vitro, in vivo, and clinical studies. Data extraction focused on study design, CAP devices used, treatment protocols, observed effects, and proposed mechanisms.

Results: Plasma-activated solutions (PAS), which contain reactive oxygen species generated by APP, have shown significant antitumor activity. PAS functions similarly to direct plasma treatment but offers advantages in terms of treatment depth and area. CAP generates RONS that induce oxidative stress, leading to apoptosis and necrosis in cancer cells. By altering the redox balance, CAP triggers cell death pathways selectively in tumor cells while sparing normal cells. CAP has demonstrated pro-apoptotic effects in head and neck cancer cells. Despite promising preclinical results, the standardization of treatment protocols is necessary for clinical translation. CAP enhances the effectiveness of chemotherapy drugs by overcoming drug resistance mechanisms. RONS generated by CAP can disrupt cancer cell survival pathways, boosting drug efficacy.

Conclusion: Atmospheric pressure plasma, particularly CAP and PAS, offers innovative approaches to cancer therapy with promising preclinical results. These technologies show potential for selectively targeting cancer cells, enhancing chemotherapy efficacy, and minimizing side effects. Continued research and clinical trials are essential to establish standardized protocols and validate the clinical effectiveness and safety of these therapies.

Keywords: Plasma-activated solutions, cold atmospheric plasma, Atmospheric pressure plasma, Cancer

AuNPs based double network polymeric hybrid hydrogel for detection of morphine in exhaled breath condensate samples (Research Paper)

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Introduction: Morphine belongs to benzyl-iso-quinolines which alleviates chronic and severe pain by regulating the pain receptors in the nervous system. In the case of overdosing, morphine not only impacts various immune functions but also can lead to dangerous diseases. These issues and the extensive use of morphine require the design of suitable, simple, and selective methods for the accurate sensing of morphine in various biological and drug specimens. Colorimetric probes based on AuNPs received more attention in fields of chemical substances' determination. The visual occurrence of color intensity change by the addition of different analytes to the NPs is related to the variation of NPs surrounding media. The determination mechanism is based on variation in LSPR absorption band of NPs in the visible region owing to the oscillation of conduction electron after analyte adding. The dissimilar color change is related to NPs aggregation affected by surface chemical reaction and/or the morphology transitions. Herein, we attempt to develop a simple, eco-friendly, and biocompatible nanoprobe based on double network hydrogel by incorporating AuNPs in gelatin/agarose biopolymer matrices for morphine monitoring in exhaled breath condensate (EBC) samples.

Methods: For synthesizing agarose/AuNPs/gelatin hydrogel, $HAuCl_4$ with ١٠-٣ mol.L-١ was poured into the mixture of agarose and gelatin solution (٥ % W/V) in a conical flask which were heated up to ٩٠°C. The mixture of solutions was stirred for ٢٠ min with a magnetic stirrer. After dropping chilled $NaBH_4$ solution as a reduction agent, change in color from yellow to pink was occured indicating the fabrication of AuNPs. Finally, the obtained nanoprobe was reached to the room temperature to form hydrogel. For samples preparation, morphine with different concentrations (٠,٠١-١,٠ µg.mL−١) was spiked into the ١٠٠ µL of human EBC sample.

Results: The morphine detection is perfomed by the color change from pink to blue following a decrease in the LSPR band of agarose/AuNPs/gelatin after adding various concentrations of morphine. Under the optimum condition, a good limit of detection (LOD) of ٠,٠٠٦ µg.mL−١ with a linear concentration response range of ٠,٠١-١,٠ µg.mL−١ was determined at ٥٢٣ nm for morphine in exhaled breath condensate (EBC) sample.

Conclusion: A reliable colorimetric agarose/AuNPs/gelatin based hydrogel nanoprobe has been successfully developed for the determination of morphine in EBC. The validated method has represented several appropriate properties including low LOD, fast response, few interfering substances, low cost, high sensitivity and selectivity for determination of morphine in the EBC

sample. This system is effectively employed for the determination of morphine in EBC with recoveries of ranged ٩٤,٠-١١٠,٠ %.

Keywords: Agarose/gelatin double network hydrogel; AuNPs; Morphine determination; Sensing probe

Bacterial Biofilms: Benefits and Problems in Water Purification (Review)

Shima Mokhtari Garakani,[١,*] Soha Mokhtari Garakani,[٢]

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Introduction: In the context of water purification, biofilms play a significant role, offering both benefits and challenges. This review explores the advantages and problems associated with bacterial biofilms in water treatment processes.

Methods: Benefits -One of the primary advantages of bacterial biofilms is their ability to enhance the biodegradation of organic pollutants. The structured community of bacteria within a biofilm allows for increased metabolic activity, enabling the efficient breakdown of various contaminants, including oils, pesticides, and pharmaceuticals. The close proximity of different bacterial species within the biofilm can facilitate synergistic interactions, leading to more effective degradation pathways.١ -Biofilms are particularly effective in removing nutrients such as nitrogen and phosphorus from wastewater. Certain bacteria within biofilms can convert harmful compounds, like ammonia, into less toxic forms. This nutrient removal is crucial for preventing eutrophication in receiving water bodies, which can lead to harmful algal blooms and degradation of aquatic ecosystems.٢ -Pathogen Reduction: The presence of biofilms can contribute to the reduction of pathogenic microorganisms in water. Some bacteria in biofilms can outcompete or inhibit the growth of harmful pathogens, thereby improving water quality and safety. This natural biocontrol mechanism is particularly valuable in drinking water treatment, where the presence of pathogens poses significant health risks.٣ -Biofilms exhibit greater stability and resilience compared to planktonic (free-floating) bacteria. This stability allows biofilms to maintain consistent performance in water treatment systems, even under varying environmental conditions. The ability of biofilms to withstand fluctuations in temperature, pH, and nutrient availability makes them a reliable component of many treatment processes.٤ -Utilizing biofilms in water treatment can be more cost-effective than traditional methods. Biofilm reactors often require less energy and fewer chemicals, leading to lower operational costs. Additionally, the ability of biofilms to effectively degrade a wide range of contaminants can reduce the need for extensive pre-treatment processes.٥ -Biofilms can promote microbial diversity, which is beneficial for ecosystem health. A diverse microbial community can enhance the resilience of the treatment system and improve its ability to degrade a wide range of contaminants. This biodiversity can also contribute to the stability of the biofilm, making it less susceptible to disturbances.٦

Results: Problems -One of the significant challenges of biofilms is biofouling, where excessive biofilm growth can clog filters, membranes, and pipes. This can lead to increased maintenance costs and reduced efficiency of water treatment systems. Biofouling can also necessitate more frequent cleaning and replacement of components, further driving up operational costs.٧ While biofilm detachment can be beneficial for dispersing bacteria, it can also lead to the release of pathogens and contaminants back into the water. This detachment can compromise water quality and pose health

risks, particularly in drinking water systems. Managing the balance between beneficial biofilm growth and harmful detachment is a critical challenge. -Managing biofilm growth can be challenging due to the influence of various factors such as nutrient availability, flow rates, and environmental conditions. These factors can lead to unpredictable biofilm development, making it difficult to maintain optimal performance in treatment systems. -Bacteria within biofilms can exhibit increased resistance to disinfectants and antimicrobial agents. This resistance can hinder the effectiveness of conventional disinfection methods, leading to potential health risks. The presence of biofilms can create a protective environment for bacteria, making it more difficult to eliminate harmful microorganisms. -The dynamic nature of biofilms makes monitoring their composition and activity complex. Understanding the interactions within biofilms and their response to treatment conditions requires advanced techniques and can complicate operational management. -In some cases, the metabolic processes of biofilm bacteria can lead to the formation of toxic byproducts

Conclusion: Bacterial biofilms play a dual role in water purification, offering significant benefits while also presenting challenges. Their ability to enhance biodegradation, remove nutrients, and reduce pathogens makes them valuable in water treatment processes. However, issues such as biofouling, resistance to disinfectants, and the complexity of management must be carefully addressed to optimize their use. Ongoing research and technological advancements are essential to harness the benefits of biofilms while mitigating their drawbacks, ultimately leading to more effective and sustainable water purification solutions. By understanding and managing the dynamics of bacterial biofilms, we can improve water treatment processes and contribute to global water sustainability efforts.

Keywords: Biofilm-water purification

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Bacterial infection and microbiota in carcinogenesis and tumor development (Review)

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Introduction: About ۲۰٪ of human cancers are linked to infection by viruses, bacteria, or parasites. Microbiota colonize exposed body tissues (e.g., gastrointestinal tract, skin, lungs, female genital tract, and urogenital tracts) and unexposed sites (e.g., breast). Persistent bacterial infection in the host leads to the development of multiple diseases. They are implicated in the pathogenesis of various complex diseases, including diabetes, atherosclerosis, autoimmune diseases, Alzheimer's disease, and malignant diseases. A number of studies have demonstrated the role of bacterial infection in carcinogenesis.

Methods: A systematic search has been carried out for articles published in the PubMed and Elsevier databases by using combinations of different keywords with Boolean operators (AND, OR, NOT), including cancer, bacteria, and tumor microenvironment. In the next step, the full texts of the remaining articles were examined, and after removing the irrelevant ones, the results related to the selected articles were compiled by hand in the final stage and examined.

Results: The study of microbiota in tumorigenesis is primarily focused on lung cancer, colorectal cancer (CRC), breast cancer, gastric cancer, and gynecologic tumors, and so on. Infection with Helicobacter pylori in gastric cancer carcinogenesis was recognized as a class I carcinogen by the World Health Organization (WHO) decades ago. The role of Fusobacterium nucleatum in the development of colorectal cancer has been extensively investigated. The identification of microbiota in multiple tumor tissues reveals that bacterial infection and microbiota are associated with tumor development. Microbiota promote tumor development, modulate the tumor environment to benefit cancer cells and effect the responses to chemotherapy.

Conclusion: Comprehensive research is warranted to address numerous unanswered questions in the interaction of microbiota and host cells. Part of the bacteria plays a driver function in carcinogenesis, part of the bacteria plays a passenger function. Investigation of the role of the microbiota in cancer development may provide targets for antitumor therapy. Moreover, skewing the microbiota balance may prevent tumor development. Finally, the microbiota composition of tumors may be used as an alternative biomarker for predicting prognosis and response to therapy.

Keywords: bacteria; cancer; microbiota; sequencing; tumor microenvironment.

Bacteriophage Therapy: A Game-Changer in Combating Multi-Drug Resistant Uropathogenic Bacteria (Review)

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Introduction: The rise of multi-drug resistant uropathogenic bacteria has posed a significant challenge to the effectiveness of traditional antibiotic treatment. As a result, researchers have turned to bacteriophage therapy as a potential alternative to combat this perplexing issue. Bacteriophages are viruses that obviously target and infect bacteria. This bursty approach allows them to selectively attack and eliminate harmful bacteria, while preserving the beneficial ones. The specificity of bacteriophages makes them an intriguing option for combating multi-drug resistant uropathogenic bacteria.

Methods: A literature search on PubMed, Google Scholar, and Web of Science databases used the terms Bacteriophage. Publications that were not available or were not in the English language were excluded, as were publications that were not related to the topic.

Results: When administered, bacteriophages enter the body and seek out the target bacteria, attaching to their surface and injecting their genetic material. This genetic material then hijacks the bacterial machinery, ultimately leading to the bursting of the bacterial cell, and the release of new bacteriophages. Unlike traditional antibiotics, bacteriophages have the ability to adapt to the changing genetics of bacteria, ensuring their ongoing effectiveness. This adaptability is crucial in addressing the perplexing nature of multi-drug resistant uropathogenic bacteria. Despite the potential benefits, the use of bacteriophage therapy also presents challenges. These include the need to identify and isolate specific bacteriophages for targeted treatment, as well as the potential for the development of phage-resistant bacteria. Several studies have shown promising results with the use of bacteriophage therapy in inhibiting multi-drug resistant uropathogenic bacteria. Clinical trials are ongoing to further evaluate the safety and efficacy of this innovative approach. Bacteriophage therapy offers a bursty and highly specific solution to the perplexity of multi-drug resistant uropathogenic bacteria. While there are challenges to overcome, the potential of this therapy as a targeted and adaptable alternative to traditional antibiotics is undeniable.

Conclusion: As research continues to advance, bacteriophage therapy may emerge as a game-changer in the fight against multi-drug resistant infections.

Keywords: Bacteriophage/ Multi-drug resistant

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Biochemical identification of oral bacterial flora and their antibiotic susceptibilities in Macrovipera lebetina Snake (Research Paper)

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Introduction: Infections are a common clinical complication after a snake bite. Knowledge about different microorganisms in the mouth of snakes is an important role in prescribing antibiotherapy for the snake bite. The aims of this research were to determine the cultivable of mouth bacteria of Macrovipera lebetina and their antibiotics sensitivity.

Methods: An oral cavity swab from a healthy adult Macrovipera was taken and cultured in aerobic conditions to identify microflora which present in the snake mouth. Isolated colonies were recognized using morphological and biochemical methods. All these colonies were tested for antibiotic sensitivity by the disk diffusion method.

Results: A total of nine Gram-negative bacteria were identified from the oral sample of the snake including Escherichia coli, Salmonella, Proteus, Pseudomonas, Klebsiella, Edwardsiella, Acinetobacter, Citrobacter, and Bordetella. A total of five Gram-positive bacteria were obtained such as Coagulase-negative Staphylococcus, S. aureus, Bacillus, Micrococcus, and Corynebacterium. Among tested antibiotics, all Gram- negative bacteria were completely resistant to Ceftriaxone and all Gram- positive bacteria were completely resistant to Penicillin. Some Gram- negative strains showed high susceptibility to Ciprofloxacin and Nitrofurantoin antibiotics, and some of the Gram-positive isolates represented high susceptibility to Clindamycin, Trimethoprim/sulfamethoxazole, Gentamycin, Ceftriaxone, Chloramphenicol, and Tetracycline.

Conclusion: The results of our study demonstrated noticeable microbial pathogens in the mouth cavity of Macrovipera lebetina. Therefore, in snakebite problems not only anti-venom therapy is needed but also antibiotic therapy should be checked in victims.

Keywords: Snake bite, Antibiotics, Microflora, Oral cavity

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Bioinformatic analysis uncovering the role of microRNAs in conferring resistance to temozolomide treatment in glioblastoma. (Research Paper)

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Introduction: Glioblastoma multiforme (GBM) is a common primary brain tumor. This tumor is characterized by rapid growth and poor prognosis with a median survival of only ١٤ to ١٥ months, even with aggressive interventions. Temozolomide (TMZ), is the standard treatment for GBM, typically administered in conjunction with radiotherapy; however, its effectiveness is often limited. Resistance to TMZ is a critical obstacle in managing of GBM treatment and stems from various factors, including tumor heterogeneity, the protective blood-brain barrier, and specific genetic alterations such as MGMT promoter methylation status. The heterogeneity within the tumor allows for diverse cell populations, some of which may inherently resist chemotherapy. Moreover, mechanisms like the activation of DNA repair pathways further complicate treatment outcomes, enabling tumor cells to survive despite TMZ treatment. Consequently, there is an urgent need for innovative therapeutic strategies that can address these resistance mechanisms and enhance survival rates for patients with GBM.

Methods: we conducted a search for glioblastoma and temozolomide resistance Using the Geo DataSets within the NCBI database. We selected and analyzed studies GSE٢٣٤٧٦٢، GSE١٥١٦٨٠ ، GSE٢١٧٣٦٦، GSE٢٠٨٧٧٣، GSE٢٠٠٠٣١ ،GSE١٨٢٢٢٠ ،GSE١٥٤٣٣٧ ،GSE٩٨١٢٦ ،GSE١١٠١٣٠، GSE١١١٢٣١ ،GSE١١١٢٤٧ ،GSE١٣٨٩٤٢ ،GSE١٤٠٤٤١ ،GSE١٤٨٧٤٠، GSE١٥٣٩٠٧ ،GSE١٦٥٦٢٤ through GEO٢R analysis. We organized the genes based on log٢ fold change (log٢FC) and identified those with reduced expression in temozolomide-resistant samples, applying the criterion of log٢FC ≤ -١. A study published at ٢٠٢٢ aimed at identifying potential cell-free microRNAs (cfmiRs) that differentiate between patients with primary glioblastoma (pGBM) and those with recurrent glioblastoma (rGBM) found that cfmiR-٣١٨٠-٣p and cfmiR-٥٧٣٩ could be useful for diagnosing both types of tumors through a minimally invasive blood assay .

Results: The overlap between the target genes of miR-٣١٨٠-٣P and miR-٥٧٣٩ that was extracted from the TargetScan database and the genes with increased expression in temozolomide-resistant samples revealed three key genes: TFAP٢A, HRH٤, and CACNG٨. Genes TFAP٢A, HRH٤, and CACNG٨ are targeted by miR-٥٧٣٩ with Total context++ score of -٠,٣٢, -٠,٣١, and -٠,٢٢, in order, while miR-٣١٨٠ targets these genes with Total context++ score of -٠,٣٥, -٠,٢١, and -٠,١٩, respectively.

The log۲ fold change levels of all three genes have demonstrated a decrease in expression in samples associated with temozolomide resistance across at least two Geodata sets.

Conclusion: In addition to the role of microRNAs in tumor biology, each of these genes plays a distinct role in tumor biology and potential therapeutic strategies. The downregulation of TFAP۲A, HRH٤, and CACNG۸ genes plays a critical role in glioblastoma multiforme (GBM) progression. TFAP۲A, a transcription factor, is essential for regulating cellular processes such as differentiation and proliferation. Its decreased expression in GBM correlates with increased tumor aggressiveness and poor prognosis, suggesting it acts as a tumor suppressor in this context. Similarly, HRH٤, which encodes a histamine receptor involved in immune response regulation, also shows reduced expression in GBM. This downregulation may hinder the immune system's ability to recognize and combat tumor cells, facilitating unchecked tumor growth. CACNG۸, part of the calcium channel family, is associated with critical signaling pathways that influence apoptosis and cell cycle regulation. Its decreased expression can disrupt these processes, further promoting tumor survival and resistance to therapies. The combined effect of reduced expression of these three genes contributes to the complex biology of GBM, enabling tumor progression and treatment resistance. Understanding the roles of TFAP۲A, HRH٤, and CACNG۸ in GBM may provide insights into potential therapeutic targets. Targeting these genes could lead to novel strategies for overcoming resistance and improving patient outcomes in glioblastoma treatment. As a recommendation for further research, utilizing anti-miRs could allow us to examine the changes in expression levels of these three genes and their impact on resistance to temozolomide treatment.

Keywords: GBM, TMZ Resistance, miR

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Bioinformatic investigation of the therapeutic properties of the active ingredients of the Helicteres isora on inhibiting Shigella flexneri Ipad protein (Review)

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Introduction: Studies of traditional medicine have shown that Helicteres isora plant has anti-intoxication properties of the digestive system and effectively shows positive effects against bacteria that cause food poisoning. So far, no specific study has been done regarding the effect path of this plant, that's why we decided to investigate the effect of the effective substances of this plant on Shigella flexneri bacteria with bioinformatics studies.

Methods: For this reason, first the active substances of Helicteres isora were identified (rosmarinic acid, caffeic acid, vanillin, coumaric acid) and then the interaction of these active substances with the secretory and harmful protein of Shigella bacterium i.e. IPAD was investigated through ligand-protein bioinformatics studies. The software used was AutoDock Vina. Bioinformatics studies were carried out after the precise design of proteins and ligands, by performing molecular docking, and finally, the results of docking, the energy of bonds, and the two- and three-dimensional structure of molecules were examined.

Results: And the results of this research showed that compared to other active ingredients of Helicteres isora, rosmaric acid has the ability to interact more with iPad protein. The results of molecular docking showed that the binding energy of Rosmaic acid with IPAD protein is in the lowest possible state. This issue was clearly evident in two- and three-dimensional structures.

Conclusion: In other words, it can be concluded that one of the main reasons for the treatment of Helicteres isora is probably due to the special properties of the rosmaric acid present in it.

Keywords: Bioinformatics, Molecular docking, Helicteres isora, Rosmaric acid

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Bioinformatic review of Dianthins to identify the most suitable RIP for the production of protein with biological properties (Research Paper)

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Introduction: Despite the promising advances that have been made in various treatments such as chemotherapy, radiation therapy and surgery, the treatment of all types of this disease is considered a challenge today; therefore, with the advances in molecular knowledge, research to find effective and new anti-cancer agents with high selectivity and specificity are of great importance. For this purpose, people have focused their research on natural herbal products or medicines taken from natural sources. Plant toxins are one of the important topics for the development of new cytotoxic drugs against cancer, and currently many plant toxins have been identified, including ribosome inactivating proteins, which belong to a group of enzymes known in plants, algae are fungi and bacteria, he pointed out. These proteins (RIPs) are divided into two types, and the Dianthin enzymes we are discussing are a toxic plant protein belonging to the family of ribosome inactivating proteins (RIPs) type ١

Methods: Comparative and bioinformatics analyzes were investigated.

Results: In the following investigations, the results of the analysis of the Dianthin coding sequence were obtained as follows: the full length of the mRNA is ١١٥٣ base pairs, the amino acid sequence is ٢٩٣, and the C-terminal region of the sequence contains sugars such as mannose, glucose, and glucosamine. Further analysis and analysis of the coding sequence of Dianthin allowed us to obtain its physicochemical properties such as molecular weight equal to ٣٢ kilodaltons, isoelectric point ٨,٩٢, aliphatic index: ٩١,٢٣, GRAVY index of hydrophobicity and the presence or absence of a disulfide bond, as well as the presence of a cysteine amino acid in the position ٢٤٣ and peptidochloroplasty signal helped. After receiving this information, we studied the structure of this protein, and the results of different components in its second structure, such as ٤٠,٩٦٪ random coil, ٣٦,٨٦٪ a-helix, It showed ١٨,٠٩٪ extended strand and ٤,١٠٪ B turn; Also, in its third structure, the presence of the amino acid tyrosine in the active site of the enzyme, as well as the presence of positively and negatively charged amino acids, as well as the catalytic pocket containing glutamate and arginine amino acids, were visible. In further investigations, the functional analysis of Dianthin was not neglected and the exploration of amino acid sequence motifs added the presence of the Shiga-Ricin conserved sequence at amino acid position ٢١١-١٩٥ to our findings; also, studies were conducted on the homology of Dianthin sequence with various RIPs. It was found that the detailed results are available in the description, which we refer to a part of it here; Dianthin-٣٠ is very similar to saporin-S٣ and saporin-S٦, two RIPs that are often used to design targeted toxins for tumor therapy and have already been tested in some clinical trials.

Conclusion: Finally, through investigations and during the course of the study, we found that first, Diantin-٣٠ and ٣٢ are the best Diantin enzymes in the last decade; Secondly, as we said before, Dianthin is a very active enzyme from the type ١ RIPs family, which does not have a second cellular connection, so it shows low cytotoxicity; This feature makes Dianthin an attractive candidate for targeted tumor therapy. Supplementary description of the article provides an overview of the discovery history of Dianthin and elucidates its structure, function and role in targeted toxins in more detail. It also discusses the option of increasing the efficacy of Dianthin based on the non-degradation of targeted Dianthin in lysosomes and subsequently increasing cytotoxicity for the target cell by endosomal escape enhancers.

Keywords: Dianthins, RIPs, Shiga-Ricin conserved sequence cytotoxicity

Bioinformatics Analysis of Circulating Tumor Cells (CTCs) in Lung Cancer: Implications for Diagnosis, Prognosis and Treatment (Research Paper)

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Introduction: The spread of cancer to other organs (metastasis) is the primary cause of cancer-related deaths globally. Lung cancer, known for its highly metastatic progression, remains among the most lethal of malignancies. Despite its high metastatic potential, the genomic profile of lung cancer metastases is often poorly understood, making it challenging to develop effective treatments. Cancer cells that detached from the original tumor or its spread (metastases) and travel through the blood are called circulating tumor cells (CTCs). These traveling cancer cells, were recognized as potential founders of metastatic lesions more than ١٠٠ years ago. Studies show that CTCs hold valuable information for predicting a patient's progression-free survival, overall survival, and treatment response. Furthermore, CTC analysis can aid in predicting and staging tumor recurrence and metastasis, guiding drug development, and personalizing treatment strategies. This study utilized a comprehensive analysis of gene expression data to gain a deeper understanding of the biological mechanisms of CTCs . The ultimate goal is to pinpoint reliable biomarkers for diagnosis, prognosis, and potential therapeutic targets for more effective treatment strategies

Methods: This study aimed to identify novel biomarkers for lung cancer by analyzing the gene expression profile of Circulating Tumor Cells (CTCs). The GSE٢٤٩٢٦٢ microarray dataset was retrieved from the Gene Expression Omnibus (GEO) database. The selected microarray data was analyzed using Transcriptome Analysis Console software, a powerful tool for gene expression

analysis. Significance analysis of the expression of genes was implemented by fold change (FC) calculation. Analysis Enrichment of genes was done using Enrich r and KEGG pathway. In the present study, the STRING database was used to construct the network of hub genes with a minimum required interaction score of ٠,٤. The protein-protein interaction (PPI) network was then visually represented and further analyzed using Cytoscape software (version ٣,٦,١). This study aimed to predict the most influential genes within the network using four distinct centrality measures: Eigenvector centrality, degree centrality, betweenness centrality, and closeness centrality. By these analysis, the study identified key genes that play a crucial role in the development of CTCs in lung cancer. To further confirm the significance of the identified key genes, this study utilized the Gepia database. Kaplan-Meier curves was used to analyze the relationship between gene expression levels and survival rates in lung cancer patients and log-rank tests were performed to determine the statistical significance of any observed differences in survival

Results: This study identified ٣٨٤٠ genes with altered expression in circulating tumor cells (CTCs) of lung cancer patients, with ١٠٤٥ showing over expression. By analyzing the centrality values, which reflect a gene's influence within the protein interaction network, were pinpointed the top ١٤٠ genes. Using Cytoscape and Gephi softwares, ١٥ of these genes were identified as hub genes due to their central role in the network. To understand the impact of these key genes on patient prognosis, we analyzed their relationship with survival rates.The hazard ratio (HR) with ٩٥٪ confidence intervals and log-rank having p <٠,٠٥ values are considered as the cutoff value. Seven genes (ESR١, FGF٢, CAV١, CDH١٧, GAD١, NCAM١, COL١A١) satisfied the said cutoff criteria and have been found to be associated with worse Overall Survival (OS) for lung cancer patient. This suggests these genes could serve as potential prognostic biomarkers for lung cancer. Analysis of the biological pathways enriched in the upregulated genes revealed their involvement in a variety of processes. These include pathways related to Chemical carcinogenesis, GnRH secretion, Arginine biosynthesis, Vitamin digestion and absorption, Proteoglycans in cancer, Protein digestion and absorption, and Estrogen signaling. This suggests that these upregulated genes might contribute to tumor development and progression through their roles in these pathways

Conclusion: Analyzing the genes present in circulating tumor cells (CTCs) offers crucial insights CTCs serve as valuable biological markers, providing important clues about a patient's prognosis. In this study, we have identified ١٥ genes as key genes. However, survival analysis based on the expression of these genes indicated that only seven genes are associated with the poor overall survival of CTCs of lung cancer patients. These key genes may help to future research of CTCs's molecular mechanisms and biomarkers analysis. By using bioinformatics and data mining techniques to pinpoint key genes and pathways involved in CTC activity, can gain valuable insights into the complex biological processes driving metastasis

Keywords: Circulating tumor cells (CTCs), metastase, Lung Cancer, microarray dataset, bioinformatics

Bioinformatics-Based Identification of Genetic Characteristics in Colorectal Liver Metastasis

(Research Paper)

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Introduction: Colorectal cancer (CRC) as the second most common cancer diagnosed in women and third most common in men and ranks among the deadliest cancers globally. Microarray technology can be employed to identify crucial biomarkers and gain deeper insights into the molecular mechanisms underlying colorectal liver metastasis. For individuals diagnosed with colorectal cancer, the liver is the most prevalent location for the development of metastatic tumors. Throughout the progression of their disease, a minimum of ٢٥٪ of colorectal cancer patients will experience the spread of cancer to the liver, a condition known as colorectal liver metastases (CRLM). Although there have been substantial improvements in diagnostic and treatment methods, the survival rate for patients with colorectal liver metastases (CRLM) remains significantly low. The development of CRLM is a complex cascade of events that involves multiple factors and processes, resulting in intricate and diverse molecular mechanisms. This study aimed to investigate the differences in gene expression patterns between colorectal cancer (CRC) and colorectal liver metastases. The main objective was to identify the key genes and pathways that play a crucial role in the initiation and progression of CRC

Methods: Data was obtained from the Gene Expression Omnibus (GEO) database, specifically from GSE٤٠٣٦٧ and GSE٣١٥٩٥. The microarray data and expression profiles for colorectal adenocarcinoma and colorectal liver metastasis were analyzed and compared. The samples consist of ١٥ files from colon adenocarcinoma with liver metastasis and ٣٧ files from colon adenocarcinoma. To investigate and identify genes with expression differences, the R programming environment was utilized. Probes were converted into gene symbols based on platform annotation information from the raw data using R packages. Probes lacking gene information were excluded. Preprocessing and normalization of the bioinformatics data, aimed at enhancing the study's quality, were performed using the mas٥ method via the R package limma (http://www.R-project.org). Genes with differential expression were determined using two indices adjusted P-values < ٠,٠٥ and log٢FoldChange |> ١,٥ to be used in further analysis. The relationships between the differentially expressed genes (DEGs) were assessed using the STRING database. A gene network was constructed using this database. The genes identified from this database were then imported into Cytoscape, an open-source software

based on the Java platform, which is designed to visualize protein interaction networks and biological pathways. Key genes were selected based on indices such as degree, betweenness centrality, closeness centrality, and eigenvector. Finally, the metabolic pathways of the top genes were analyzed using the Enrichr database. The Kaplan-Meier method was used to assess the relationship between the expression levels of the hub genes and patient survival outcomes. The validity of these hub genes in liver metastatic CRC patients was further confirmed using the GEPIA platform

Results: The quality control of the samples was assessed using box plot and heat map diagrams. The analysis revealed that approximately ٧٧٦ genes exhibited up-regulated in the samples. We focused on over-expressed genes, as they could serve as early diagnostic biomarkers or therapeutic targets.Using Cytoscape, the top genes were identified by calculating centrality parameters. This network revealed that ٢١ genes are significantly involved in colorectal cancer progression. To assess the impact of these key genes on patient prognosis, we examined their relationship with survival rates. We considered a hazard ratio (HR) with ٩٥٪ confidence and log-rank p-values <٠,٠٥ as the cutoff. Thirteen genes (BRD٤, TP٥٣BP١, RBM٣٩, PKM, YWHAZ, USP٧, FOXO٣, FANCD٢, RPL١٤, SMAD٣, SETD٢, APOE, and NUP١٥٣) were selected. This indicates that these genes could serve as potential prognostic biomarkers for this condition. Further examination of the biological processes associated with differentially expressed genes across tissues revealed that these genes were involved in several key pathways including: Ribosome, AMPK Signaling Pathway, Spliceosome, FoxO Signaling Pathway, cell cycle, and Adherens junction. These findings suggest that these biological processes may play a significant role in the observed gene expression differences

Conclusion: Understanding the mechanisms driving liver metastasis in CRC patients could lead to the discovery of biomarkers for early diagnosis and the development of targeted chemotherapy treatments. This highlights the urgent need for new treatment strategies. Techniques like microarray analysis allow researchers to identify genes implicated in cancer development. This knowledge can lead to improved prevention, diagnosis, and treatment approaches, ultimately paving the way for more effective cancer care

Keywords: Colorectal Liver Metastase (CRLM), bioinformatics, microarray analysis, hub gene

Biological control of Alternaria Spp. By using the aqueous extract of some medicinal plants in aninvitro environment (Review)

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Introduction: Getting rid of plant pests is one of the agricultural challenges, and farmers use a lot of chemical pesticides to fight these pests. However, these compounds have problems and negative effects. To address this challenge, various alternative methods have been investigated. Medicinal plants are one of the agricultural sectors where biotechnology has played an important role in development over the past several years. This study aims to compare the aqueous extracts of Cichorium intybusL , Matricaria Chamomilla, Trachyspermum capticum, Zataria Multiflora Booiss, Peganum harmala, Piper nigarum, Capsicum annuum, Rosa damascena, and Allium sativum L, against two controls: water and a chemical pesticide, with a concentration of ١ gr in ٥٠٠ cc of water, to control the growth of the fungus Alternaria under laboratory conditions. In this research, the use of aqueous extracts of the plants in question, which have proven their high capabilities to control pathogenic fungi in many sources, was investigated as a promising solution in the biological control of Alternaria fungus. Although, despite proving the effect of these extracts in biological control methods, the comparison of the effect of these plants has not been done.

Methods: To prepare the aqueous extract of plants by boiling method, ٢٠ gr of dried and eaten plants were placed in separate plastic bags under the biological hood and treated with UV light for ١٠ min. After that, they were boiled in separate containers with ٤٠٠ cc of distilled water for ٢٠ min. Then the above extracts were filtered and placed in sterile bottles and subjected to UV treatment for ١٠ min. A completely randomized design was designed with ٩ treatments and ٦ repetitions, and water was used as a negative control and copper oxychloride poison with a concentration of ١ gr in ٥٠٠ cc of water was used as a positive control. At first, the amount of ١٠٠٠ microliters of aqueous extract of the desired plants, in sterile conditions, poured into ٦ cm plates by sampler and WA culture medium was added to them. Then the mushroom blocks were transferred to the center of the plates and the diameter of the colonies was measured for ٥ days.

Results: Investigating the growth rate of fungal colonies in the treatments containing plant extracts compared to the water control showed that the treatments containing aqueous extracts of Matricaria Chamomilla , Capsicum annuum, and Rosa damascena had no controlling effect on the growth of Alternaria colonies compared to the water control. Surveys showed that treatments containing aqueous extracts of Trachyspermum capticum , Allium sativum L, Peganum harmala ,Piper nigarum ,Cichorium intybusL , and Zataria Multiflora Booiss, in comparison with the water treatment, had significant differences. All the above treatments can reduce the diameter growth in

Alternaria. There is a significant difference between treatments containing aqueous extracts of Matricaria Chamomilla, Allium sativum L, Cichorium intybusL, Zataria Multiflora Booiss , Capsicum annuum , and Rosa damascena. These treatments, compared to the control containing toxins, have a lesser effect, making the use of toxins for controlling Alternaria a less appropriate method. The average effect of the extracts in controlling the growth of Alternaria indicates that the use of aqueous extracts of Trachyspermum capticum , Peganum harmala , and Piper nigarum, along with the water iscontrol, falls into the same statistical class, meaning these treatments are successful in controlling Alternaria. Additionally, treatments containing aqueous extracts of Trachyspermum capticum and Piper nigarumalso fall into the same statistical class as the water control, and on the other hand, do not have a significant difference with the treatment containing Zataria Multiflora Booiss. It is now evident that the Peganum harmala treatment has the same function as the toxin, and there is no significant difference with the treatment that does not contain toxins.

Conclusion: In this research, Peganum harmala extract demonstrated a significant effect in inhibiting the growth of Alternaria fungus and showed close competition compared to Peganum harmala. The results of the present research, like those of similar studies, indicate the ineffectiveness of treatments containing Rosa damascena and Matricaria Chamomilla extracts. Among the treatments examined in this study, Peganum harmala, Piper nigarum, and Trachyspermum capticum exhibited greater and more effective results for Alternaria control. This extract can be a suitable substitute for the chemical Peganum harmala in controlling Alternaria fungus.

Keywords: Aqueous extract, Alternaria, biological control, medicinal plants.

Biological production of ١,٢,٤-butanetriol (Review)

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Introduction: In recent years, the use of biomass to produce value-added chemicals has attracted much attention. Because it is found in abundance, it is not a food source, it is renewable, and in addition, it does not have the problems of using fossil resources such as environmental pollution and rapid depletion of natural resources. The decomposition of lignocellulosic biomass leads to the production of D-xylose, which is the second most abundant sugar in nature, and is not easily fermentable. Several wild microbial species or metabolically engineered strains have been isolated or engineered to ferment xylose to produce valuable chemical compounds such as ١,٢,٤-butanetriol. Butanetriol is a four-carbon straight-chain polyol with three hydrophilic hydroxyl groups. Butanetriol (BTO), which has attracted a lot of attention in the past few years, has wide applications in various fields, including in medicine and the pharmaceutical industry as a precursor for the synthesis of several high-value drugs such as Crestor and Zetia and the Anti-HIV drug Amprenavir. BTO is usually produced through chemical routes using glycidol, ٢-butene-١, malate, or ٣,٤-dihydroxybutanoate as starting materials. But it has problems such as harsh reaction conditions, multiple steps, high production costs low efficiency, and severe environmental pollution. The set of problems in the chemical production of BTO has caused the development of its biological (microbial) production process to be considered in recent years, and researchers have created new processes for the production of BTO from xylose with microbial conversion. In ٢٠٠٣, Niu and colleagues were the first to produce butanetriol via biological pathways. In this study, the biosynthesis of butanetriol was carried out in an E. coli microbial strain using D-xylose as a substrate.

Methods: The biological production pathway of butanetriol consists of four steps. By expressing the enzymes D-xylose dehydrogenase, D-xylonate dehydratase, benzoylformate decarboxylase, and aldehyde reductase, xylose is converted to butanetriol. Since only two enzymes (XylD) dehydratase D-xylonate and (adhP) aldehyde reductase naturally exist in E. coli, the genes for the other two enzymes of this pathway, namely xylose dehydrogenase (XDH) from Pseudomonas fragii and ٢-keto acid decarboxylase was extracted from Pseudomonas putida bacteria and then cloned into the target E. coli strain and led to the conversion of ١٠ g/L of D-Xylose to ١,٦ g/L of BTO with a yield of ٢٥٪.

Results: In the past twenty years, various types of research have been carried out for the biological production of BTO in different strains under different conditions. However, none of them has led to the production of BTO with high efficiency, but in a research conducted in ٢٠٢٣, by combining several strategies, choosing suitable enzymes, and optimizing the reaction, the researchers succeeded in producing ١٢٥ grams per liter of BTO from ١٨٠ g/L of D-Xylose with The efficiency exceeded ٩٧٪, and also in a ٢٠٢٤ study, Hu et al. developed a whole-cell bioconversion system by optimizing enzymes and strains to produce BTO from renewable biomass, which resulted in the

conversion of ٢٠٠ g/L D-Xylose with The yield was more than ٧٤٪. Both of these researches have production value on an industrial scale.

Conclusion: Although whole-cell transformation may be the most promising strategy for the preparation of BTO due to its simple operation, environmental compatibility, and potential low cost. However, there are still problems that need to be solved to improve the bioconversion efficiency for the synthesis of BTO from D-xylose, because whole-cell production processes sometimes face the problems of toxicity, competition of metabolites, and generation of byproducts. In this case, the performance of the four enzymes should be optimized to avoid the accumulation of intermediates such as d-xylonic acid and ٢-keto-٣-deoxy-d-xylonate (KDX). In particular, dehydratase and decarboxylase enzymes should be optimized in terms of expression and catalytic efficiency. The results of this review article show that by using recent advances in metabolic engineering and process optimization, the bioproduction of butanetriol has been significantly improved, but there is still a need for further research and development to improve scalability and reduce cost, and increase the production.

Keywords: Biomass, ١,٢,٤-Butenetriol, Metabolic Engineering, Genetic Engineering, E. coli

Biomarkers Discovery in Acute Myeloid Leukemia Based on Multi-omics Approaches (Review)

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Introduction: Acute myeloid leukemia (AML) is the most common acute leukemia in adults and has the highest fatality rate. Patients aged ٦٥ and above exhibit the poorest prognosis, with a mere ٣٠٪ survival rate within one year. The current method for AML diagnosis involves assessing the morphological characteristics of myeloid cells, characterizing specific cell surface and intracellular markers through immunophenotyping, conducting conventional cytogenetic tests, and screening for genetic abnormalities in bone marrow and peripheral blood samples. Ongoing technological advancements aim to pinpoint more precise AML biomarkers, crucial for monitoring minimal residual disease during follow-up periods. This unmet necessity, coupled with AML's inherent tumor attributes, contributes to its elevated mortality rate among all leukemias, with an overall ٥-year survival rate of less than ٥٠٪. Consequently, there is a pressing need for enhanced AML biomarkers to enhance diagnosis, treatment, and prognosis forecasting.

Methods: The past decade has witnessed significant progress in sequencing and biotechnological approaches, facilitating the widespread adoption of various omics technologies such as genomic/transcriptomic sequencing and proteomic/metabolomic mass spectrometry for analyzing samples from AML patients. By integrating data from multiple omics sources, our understanding of the disease has expanded, leading to the identification of valuable AML biomarkers. In this review, we discuss the application of multi-omics technologies in AML research for the discovery of novel biomarkers and the enhancement of clinical evaluations.

Results: By integrating data from multiple omics sources, our understanding of the disease has expanded, leading to the identification of valuable AML biomarkers. In this review, we discuss the application of multi-omics technologies in AML research for the discovery of novel biomarkers and the enhancement of clinical evaluations.

Conclusion: Multi-omics approaches that integrate the data from distinct levels of the cellular organization, i.e., from genes to metabolites, have been reported, which offer new perspectives for innovative AML diagnostics and therapeutics.

Keywords: Acute myeloid leukemia, Biomarker, Multi-omics, Transcriptomics, Proteomics

Bone marrow mesenchymal stem cells have a higher potential in osteogenesis than other mesenchymal cell sources; Is this correct? (Review)

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Introduction: Skeletal problems are an increasing issue due to the increase in the global aging population. Different statistics reports show that today, the global population is aging that results in skeletal problems, increased health system costs, and even higher mortality associated with skeletal problems. Common treatments such as surgery and bone grafts are not always effective and in some cases, they can even cause secondary problems such as infections or improper repair. Cell therapy is a method that can be utilized along with common treatments independently. Mesenchymal stem cells (MSCs) are a very important and efficient source in terms of different diseases, especially bone problems. These cells are present in different tissues such as bone marrow, adipose tissue, umbilical cord, placenta, dental pulp, peripheral blood, amniotic fluid and others. Among the types of MSCs, bone marrow mesenchymal stem cells (BMMSCs) are the most widely used source of these cells, which have appeared to be very effective and promising in terms of skeletal diseases, especially compared to the other sources of MSCs.

Methods: This study focuses on the specific potential and content of BMMSCs from which the specific capacity of these cells originates, and compares their osteogenic potential with other types of MSCs, and also the future directions in the application of BMMSCs as a source for cell therapy.

Results: Although the profile and immunophenotypic content of different MSCs are very similar, it is important to consider the anatomical location of these cells. Considering that best performance and specialized potential of MSCs is highly dependent on the tissue origin of these cells, when attention is paid to the tissue of their origin, the best results could be achieved in research and repair processes.

Conclusion: Due to the special function and capacity of BMMSCs in osteogenesis and also, the future directions in the application of BMMSCs as a source for cell therapy in bone regeneration researches, probably the best source of MSCs to be utilized in the bone regeneration field of skeletal system are BMMSCs.

Keywords: Bone marrow mesenchymal stem cells · Osteogenesis · Regenerative medicine · Cell therapy

Breast Cancer: Literature Review (Review)

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Introduction: Breast cancer is a type of cancer that starts in the breast. It can start in one or both breasts.The risk for breast cancer increases with age. Most breast cancers are diagnosed after age ٥٠. Genetic mutations. Advances in breast cancer screening allow healthcare professionals to diagnose breast cancer earlier. Finding the cancer earlier makes it much more likely that the cancer can be cured. Even when breast cancer can't be cured, many treatments exist to extend life. New discoveries in breast cancer research are helping healthcare professionals choose the most effective treatment plans.

Methods: Mammography is the most common screening test for breast cancer. A mammogram is a picture of the inside of the breast. Mammography may find tumors that are too small to feel Surgery is often the first treatment for breast cancer. Other common treatments include radiotherapy, hormone therapy, chemotherapy and targeted drugs.

Results: It is possible for breast cancer to go into complete remission. The outlook tends to be better if a person receives treatment in the early stages of the disease Advanced breast cancer may not be curable. However, treatment can improve symptoms and prolong a person's life.

Conclusion: The swelling and bruising will go down and the scars from your operation will become less obvious. You'll get used to your new body shape and false breast shape (prosthesis) if you wear one. You're likely to find that your confidence will gradually come back. The emotional ups and downs might last longer

Keywords: breast cancer cancer women genetics mutation

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Bridge RNA Technology: A Novel Strategy for Gene Editing in Cancer Treatment (Review)

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Introduction: Gene editing represents a transformative advancement in contemporary medicine, with CRISPR-Cas9 positioned as the leading technology, facilitating precise modifications within the genome. Still, the restrictions of CRISPR, particularly its hurdles in handling complicated genomic changes tied to conditions like cancer, have driven the pursuit of alternative techniques. One such emergent technique is Bridge RNA (bRNA) editing, which offers a more sophisticated framework for genomic modification. This manuscript examines the underlying mechanisms, potential applications, and initial findings associated with bRNA technology, emphasizing its prospective utility in oncological interventions.

Methods: Bridge RNA technology introduces an innovative paradigm of gene editing that transcends the limitations inherent in traditional methodologies such as CRISPR. This technology employs insertion sequence (IS) elements, which are mobile genetic components prevalent in prokaryotic genomes, to facilitate the linkage of disparate DNA sequences. This extraordinary proficiency grants the potential for intricate DNA adjustments, comprising inversions, insertions, and deletions, which are significant for impactful genome engineering. The technology is underpinned by a recombinase protein that operates in conjunction with a guide RNA. This guide RNA delineates two specific sequences: the target locus within the genome necessitating modification and the donor DNA intended to effectuate the alteration. The recombinase is guided by a noncoding bridge RNA (bRNA), which imparts the requisite specificity for accurate DNA recombination. The IS110 family, recognized for encoding this recombinase alongside its corresponding bRNA, is instrumental in facilitating these intricate genomic modifications.

Results: Preliminary investigations conducted within bacterial systems have demonstrated that Bridge RNA technology is capable of executing precise and complex genomic alterations. The technology's proficiency in targeting and modifying extensive DNA segments has been corroborated through cryo-electron microscopy analyses, which illustrate the high specificity with which bRNA directs the recombinase to carry out the requisite recombination events. These investigations underscore the versatility of Bridge RNA technology in effectuating diverse forms of genetic modifications—whether it entails the addition, removal, or inversion of DNA sequences. This versatility is particularly salient in the context of cancer treatment, where such extensive genomic rearrangements frequently underpin disease progression. However, notwithstanding the encouraging nature of these preliminary findings, additional research remains imperative to assess the applicability of this technology within human cellular contexts and its potential for clinical implementation.

Conclusion: Bridge RNA technology presents a promising new trajectory in gene editing, encompassing significant ramifications for oncological therapy. Its capacity to execute intricate and precise genomic modifications renders it a formidable instrument in addressing the complex genetic alterations characteristic of cancer. Although still in its formative stages and primarily assessed within bacterial systems, the initial results indicate that Bridge RNA may ultimately be developed into a formidable therapeutic alternative. Ongoing research will be crucial to fully actualize its potential within human medicine, potentially ushering in more effective and personalized cancer therapies in the future.

Keywords: Bridge RNA, Cancer, Gene Editing

c reactive protein in acute kidney injury (AKI) and chronic kidney diseases (CKD) (Research Paper)

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Introduction: C-reactive protein (CRP) is an acute inflammatory protein. This protein increases ۱۰۰۰ times under certain conditions, especially inflammation and infection. CRP is synthesized as a pentameric protein with five identical subunits in liver hepatocytes and contributes to host defense as a part of the innate immune response. Many factors can alter baseline CRP levels including age, gender, smoking status, weight, lipid levels, blood pressure, infections with bacteria or viruses, Crohn's disease, ulcerative colitis, autoimmune disorders, rheumatoid arthritis, vasculitis, and lung diseases. Based on research in kidney diseases, CRP is highly expressed by many inflammatory cells, presumably macrophages, and intrinsic kidney cells including tubular cells and endothelial cells. This study aims to review existing knowledge on the role of CRP in acute kidney injury (AKI) and chronic kidney disease (CKD).

Methods: A comprehensive search was conducted in Medline, EMBASE, Cochrane Library, Science Direct, and Springer databases to find relevant articles on kidney diseases and CRP

Results: Acute kidney injury (AKI), also known as acute renal failure (ARF) is one of the types of kidney disease that disrupts kidney function and is accompanied by necrosis, severe inflammation, and disorder. According to studies, the concentration of CRP in this type of disorder increases significantly. An increase in serum CRP is associated with worsening of the patient's condition. Chronic kidney disease (CKD), also known as chronic kidney failure, characterized as a progressive loss of renal function, has become a global public health burden. In CKD patients, a high CRP level is detected. In both diseases, AKI and CDK, CRP induces the phosphorylation of Smad۳ by promoting ERK/p۳۸ and TGF-β۱ pathways, which subsequently develop renal inflammation. Furthermore, CRP can promote acute kidney injury by increasing renal accumulation of myeloid-derived suppressor cells.

Conclusion: Based on our research CRP is a key biomarker or risk factor for AKI and CKD. Considering the mechanisms and signals activated by this protein, it can be said that this acute-phase protein plays an important role in the development of AKI and CKD and it can be used as a medicinal target in the treatment of kidney diseases

Keywords: C- reactive protein, kidney diseases, AKI, CKD, acute-phase protein

C- reactive protein in Acute kidney injury (AKI) and Chronic kidney disease (CKD) (Review)

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Introduction: C-reactive protein (CRP) is an acute inflammatory protein. This protein increases ۱۰۰۰ times under certain conditions, especially inflammation and infection. CRP is synthesized as a pentameric protein with five identical subunits in liver hepatocytes and contributes to host defense as a part of the innate immune response. Many factors can alter baseline CRP levels including age, gender, smoking status, weight, lipid levels, blood pressure, infections with bacteria or viruses, Crohn's disease, ulcerative colitis, autoimmune disorders, rheumatoid arthritis, vasculitis, and lung diseases. Based on research in kidney diseases, CRP is highly expressed by many inflammatory cells, presumably macrophages, and intrinsic kidney cells including tubular cells and endothelial cells. This study aims to review existing knowledge on the role of CRP in acute kidney injury (AKI) and chronic kidney disease (CKD).

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Keywords: C- reactive protein, kidney diseases, AKI, CKD, acute-phase protein

Can Large Language Models Act as Medical Students in Medical Exams?; strengths and limitations (Review)

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Introduction: Clinical reasoning is a logical and reasoned process of gathering information, understanding the problems and the patient's condition, planning and implementing interventions, and evaluating interventions and feedback in the learning process. Today, it is considered necessary to have it as a competence and clinical vision. However, few training programs emphasize this innovative and creative teaching strategy. With the emergence of artificial intelligence and its expansion in recent decades, today artificial intelligence has become one of the most used and hottest tools in human life, especially in the field of medicine. Among the types of artificial intelligence models that humans have achieved so far, large language models (LLMs) are artificial intelligence systems designed to understand, produce, and respond to human language. The present study is going to review the potential role and acts of the large language models in medical exams; in fact, Can Large Language Models Act as Medical Students in Medical Exams?

Methods: To determine the aims of the present study, a comprehensive systematic search was conducted through electronic databases including PubMed, Scopus, Embase, and Web of Science with the keywords “Medical Education”, “Medical exam”, “medical students”, “large language models”, and other related MeSH terms up to August ٢٠٢٤. Original studies, review studies, and references of the review studies were included. Finally, the studies which indicate the large language models role in medical exams were selected and reviewed.

Results: According to the reviewed studies, to determine the response of the question it is necessary to consider aspects of large language models. The capabilities of LLMs will be considered as an Extensive Knowledge Base (LLMs are trained on vast datasets that include medical literature, textbooks, clinical guidelines, and case studies. This allows them to generate responses based on a wide range of medical knowledge; they can provide information on diseases, treatments, pharmacology, and diagnostic criteria, which are often tested in medical exams.), Natural Language Processing (LLMs excel at understanding and generating human language, making them capable of interpreting exam questions and articulating coherent responses; they can simulate the language and terminology used in medical exams, which can be beneficial for answering questions in a format that aligns with exam expectations.), and Pattern Recognition (LLMs can identify patterns in clinical scenarios and apply relevant information to answer questions, particularly in multiple-choice formats or straightforward case-based questions; they can also generate differential diagnoses based on symptom descriptions provided in exam questions.). On the other hand, LLMs limitations can be stated as a lack of Clinical Experience (unlike medical students, LLMs do not have hands-on

clinical experience or patient interactions. This experiential learning is crucial for understanding the complexities of real-world medicine; they cannot perform physical examinations or interact with patients, which are integral components of medical training.), Clinical Reasoning and Judgment (Medical exams often require higher-order thinking skills such as clinical reasoning, ethical considerations, and decision-making that go beyond rote knowledge; LLMs may struggle with complex clinical scenarios that require nuanced judgment or prioritization of competing clinical factors.), Contextual Awareness (LLMs may not fully grasp the context surrounding a specific clinical situation, leading to responses that may be inappropriate or incomplete; they cannot integrate real-time clinical data or adapt their responses based on new findings beyond their training cutoff), Ethical and Legal Implications (the use of LLMs in medical settings raises significant ethical concerns, including accountability for decisions made based on their outputs; there is a risk of misinformation or oversimplification of complex medical scenarios, which could have serious consequences in a clinical context), and Static Knowledge (While LLMs can provide up-to-date information from their training data, they cannot continuously learn or adapt based on new research or clinical guidelines after their last training update). While LLMs can simulate certain aspects of medical knowledge and provide valuable information, they cannot fully replicate the comprehensive skill set required of medical students in exams or clinical practice. They may be able to perform well on certain types of questions—especially those focused on factual recall or straightforward application of medical knowledge—but they lack the critical thinking, ethical reasoning, and experiential insights that human medical students develop through their education.

Conclusion: In summary, while LLMs can assist in learning and provide supplementary information in a medical context, they should not be viewed as substitutes for actual medical students in exams or clinical settings. Their role might best be seen as a supportive tool for education rather than a replacement for the nuanced understanding and judgment required in medicine.

Keywords: Medical Education, Medical Student, Medical Exam, Large Language Models

Cancer is a metabolic disorder, treatment methods (Review)

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Introduction: As a malignant tumor grows, waste products are produced that must be eliminated through the large intestine, liver, kidneys, lungs, and skin. These waste materials accumulate and gradually weigh down the body. Most people die from poisons. Before treating any disease, waste materials and impurities must be removed from the body. The sooner this is done, the sooner the body can repair itself.

Methods: In the Cancer Metabolic Medicine program, a person's normal metabolic repair and regeneration systems are supported. In a metabolic detoxification program, in fact, a person rarely dies of cancer. The detoxification process should begin even before nutritional supplements are given to the patient. It is absolutely necessary for the patient to carefully follow the detoxification process after the supplements begin to stimulate and release waste products and waste. Scientists have calculated that a person has between ٧٠ and ١٠٠ trillion cells in their body. This means that we have over ٧٠ trillion "trash bins" that need emptying every day. In our culture, we have not considered and taught ourselves the proper methods of emptying these waste containers. Proper and complete detoxification is as important as good nutrition for anyone who has lived in the mainstream of a modern technological civilization for ten years or more, and especially for those who have had symptoms of chronic degenerative disease.

Results: Ten methods are detailed for each area and detoxification. ١. Daily coffee enema. ٢. Monthly washing of the liver and gallbladder. ٣. Cleaning the small intestine. ٤. Cleansing the kidneys. ٥. Cleaning the lungs ٦. Cleaning the skin. ٧. Washing the nostrils. ٨. Breathing exercises. ٩. Exercise ١٠. Far infrared device increases blood circulation, reduces pain and increases immune response and enzyme effect.

Conclusion: The metabolic medicine cancer support program has been successful with a high percentage of former cancer patients because it slows or reverses the degenerative processes.

Keywords: Cancer, metabolic medicine, Cleaning

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Cancer Stem Cells: metabolic profiles, DNA repair mechanisms, and therapeutic strategies

(Review)

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Introduction: Cancer stem cells (CSCs) are a subpopulation of cancer cells that possess the ability to self-renew, differentiate into multiple cell types, and form tumors.CSCs are thought to be responsible for tumor initiation, metastasis, and relapse, making them a critical target for cancer therapy.

Methods: This poster summarizes the findings of six recent research articles on CSCs. The studies investigated the metabolic profiles, DNA repair mechanisms, and therapeutic strategies for targeting CSCs.

Results: Metabolic Profiles of Cancer Stem Cells : A study published in Cells investigated the metabolic profiles of CSCs and normal stem cells [١]. The researchers found that CSCs exhibit a distinct metabolic signature characterized by increased glycolysis and reduced oxidative phosphorylation. This metabolic shift allows CSCs to survive under stress conditions and maintain their self-renewal capacity. DNA Repair and Therapeutic Strategies in Cancer Stem Cells : Another study, published in Cancers, explored the challenges of treating CSCs due to their enhanced DNA repair mechanisms [٢]. The researchers identified several potential therapeutic strategies for targeting CSCs, including: ١. DNA-damaging agents: These agents can induce DNA damage in CSCs, leading to cell death or senescence. ٢. PARP inhibitors: PARP inhibitors block DNA repair pathways, making CSCs more susceptible to DNA-damaging agents. ٣. EZH٢ inhibitors: EZH٢ is a histone methyltransferase that promotes CSC self-renewal. EZH٢ inhibitors can disrupt CSC self-renewal and sensitize them to therapy. The Warburg Effect and Dedifferentiation : A study published in SciOpen examined the role of the Warburg effect, a metabolic process characterized by increased lactate production even in the presence of oxygen, in CSC dedifferentiation [٣]. The researchers found that the Warburg effect promotes epigenetic reprogramming, leading to the conversion of differentiated cancer cells into CSCs.

Conclusion: CSCs pose a significant challenge for cancer therapy due to their unique properties and resistance to conventional treatments. However, recent research has shed light on the metabolic and DNA repair mechanisms of CSCs, providing promising avenues for developing novel therapeutic strategies.

Keywords: Cancer stem cells (CSCs) Metastasis Therapeutic strategies Warburg effect

Cancer Vectors: Navigating the Evolution, Challenges, and Future Prospects in Gene Therapy (Review)

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Introduction: Cancer therapy has come a long way since its inception, and gene therapy is now one of the most revolutionary approaches. The highlight of this change is the cancer vectors which are intricate biological machines that transport the therapeutic genes into the cancer cells, thus, either changing their behavior or killing them. The experience of cancer vectors starting from initial experimental trials to current clinical applications shows a progress line constructed by creativity, problems, and crucial discoveries. Viral vectors, in particular, have the most clout among them, making up more than ٦٠٪ of all gene therapy trials and serving as indispensable tools for tumor destruction and gene delivery. Nevertheless, there are still serious challenges that need to be tackled such as vector toxicity, immune responses, and off-target effects. The progressive scientific research has, however, seen the shift from vector development to vector refinements, delivery improvers, and non-viral alternatives. New technologies like oncolytic viruses, RNA-based therapies, and gene-modified T-cells have recently been discovered and indicate a new way of treating cancer. The combination of cancer biology, immunology, and biotechnology will form new therapies that can change personalized medicine and allow the patients to have better results. This review surveys past development, recent innovations, molecular methods, and new tendencies in cancer vector research. It also analyzes the problems that scientists and clinicians face in their relations as they try to balance the efficiency of treatment with safety while navigating through the complicated regulation system. In such a way, cancer vectors mean not only an indispensable future of the fight against cancer but also a proof of the power of precision medicine in molding tomorrow's oncology.

Methods: We conducted extensive research on the topic of Cancer Vectors: Navigating the Evolution, Challenges, and Future Prospects in Gene Therapy, gathering insights from ٥٤ relevant articles. This comprehensive review allowed us to examine the current challenges, and cutting-edge innovations in cancer vector technology.

Results: Our review of Cancer Vectors Navigating the Evolution, Challenges, and Future Prospects in Gene Therapy uncovered several key points. The efficiency of cancer vectors has been considerably improved due to the development of precision molecular targeting, which minimizes the off-target effects and increases the therapeutic outcomes. Oncolytic viruses are currently one of the most powerful cancer treatment options, as they can specifically infect and kill cancer cells and provoke

the immune system. Modular therapeutic methods like CRISPR/Cas or siRNA that have been developed allow the treatment to be personalized according to the specific cancer mutations. Stealth viral modifications and non-viral vectors have furthermore facilitated the development of immune evading strategies that result in longer circulation times and improved delivery. The future of cancer gene therapy is bright, with the trends such as precision oncology, AI integration, and global collaborations being the main drivers of the development of next-generation cancer vectors and more efficient integration with immunotherapies like CAR-T and checkpoint inhibitors.

Conclusion: The present extensive study on cancer vectors points out their significant role in the development of cancer gene therapy. The journey from the simple viral vectors to the sophisticated platforms, such as the oncolytic viruses and modular delivery systems, showcases the tremendous progress in achieving the exact targeting of the cancer cells and applying the appropriate treatment. In spite of the obstacles that come with immune evasion, vector delivery effectiveness, and safety issues, the latest discoveries in non-viral vectors, precision targeting, and personalized medicine can be the solution to these problems. The latest developments like the integration of artificial intelligence, the increasing popularity of immunotherapy and worldwide collaborative research clearly show the fast progress of cancer therapy. With the blending of gene therapies, immune modulation, and data-driven techniques, the sector is heading to a time of personalized and very efficient cancer treatments. This probing allows for the positioning of cancer vectors not just as a key player in the war against cancer, but also as a vehicle for more precise, safe, and curative therapies to be available in the near future.

Keywords: Cancer Vectors, Gene Therapy, Oncolytic Viruses, Precision Targeting, Immunotherapy

cancer:Prevention, Diagnosis,and Treatment (Review)

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Introduction: Introduction Cancer remains a significant global health challenge, characterized by its diverse manifestations and complex pathogenesis. With approximately ١٩,٣ million new cases and ١٠ million cancer-related deaths reported worldwide in ٢٠٢٠, it continues to be a primary focus of biomedical research. This review aims to provide an in-depth analysis of the latest strategies in cancer prevention and diagnostic advancements, highlighting their clinical implications and future prospects.

Methods: A comprehensive literature review was conducted using databases such as PubMed, Scopus, and Web of Science, focusing on publications from ٢٠١٨ to ٢٠٢٤. Key search terms included "cancer prevention," "molecular diagnostics," and "liquid biopsy." The selected studies were critically evaluated to synthesize current knowledge and emerging trends in cancer research. Emphasis was placed on translational research bridging molecular mechanisms with clinical applications.

Results: Advances in cancer prevention are rooted in a better understanding of genetic predispositions and environmental risk factors. Genomic screening tools enable the identification of individuals atع high risk, facilitating personalized prevention strategies. Lifestyle modifications, such as a healthy diet, regular exercise, and smoking cessation, remain cornerstones of cancer prevention. Furthermore, chemopreventive agents, including SERMs and NSAIDs, have shown efficacy in reducing the incidence of specific cancers. The impact of vaccines, particularly the HPV vaccine, in preventing virus-associated cancers is well-documented. Precision diagnostics have revolutionized early cancer detection. Next-generation sequencing (NGS) and liquid biopsy techniques allow for the detection of circulating tumor DNA (ctDNA) and other molecular biomarkers, enabling real-time monitoring of tumor dynamics. Artificial intelligence (AI) and machine learning algorithms have enhanced the accuracy of imaging modalities, improving the early detection and prognostication of cancers. These advancements facilitate the identification of cancer at its nascent stages, significantly improving patient outcomes.

Conclusion: The integrative approach to cancer prevention and diagnosis underscores the importance of molecular and clinical synergy. Personalized prevention strategies based on genetic risk profiles, precise diagnostic tools, and innovative methods are essential for advancing cancer care. Future research should focus on overcoming diagnostic and therapeutic resistance, expanding access to cutting-edge technologies, and fostering global collaboration in cancer research. The continuous evolution of these strategies holds the potential to significantly improve patient outcomes and ultimately reduce the global cancer burden.

Keywords: Prevention, Next-Generation Sequencing, Liquid Biopsy, Molecular Diagnostics, Lifestyle Modification

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CAR T Cells in NSCLC: A New Frontier with Challenges (Review)

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Introduction: The emergence of Chimeric Antigen Receptor (CAR) T cell therapy has revolutionized cancer treatment, particularly for blood cancers. This powerful immunotherapy involves engineering a patient's T cells to express artificial receptors (CARs) that precisely target specific antigens found on cancer cells. This targeted approach empowers the T cells to effectively identify and eliminate malignant cells. While highly successful in hematologic malignancies, applying CAR T cell therapy to solid tumors like non-small cell lung cancer (NSCLC) presents unique obstacles. This article delves into these challenges, explores promising targets for CAR T cell therapy in NSCLC, and highlights current research directions.

Methods: This review analyzes existing literature on CAR T cell therapy, focusing specifically on its application in NSCLC. We examined clinical trials, preclinical studies, and recent publications to provide a comprehensive overview of the challenges, advancements, and future directions in this field. All information presented is drawn from reputable scientific databases and peer-reviewed journals.

Results: Challenges: Solid tumors like NSCLC pose a difficult environment for CAR T cell therapy. The immunosuppressive tumor microenvironment (TME) hinders CAR T cell infiltration and survival. Additionally, the presence of antigen heterogeneity within the tumor and the ability of tumor cells to evade immune surveillance further complicate treatment. Promising Targets: Despite these challenges, several antigens hold promise as targets for CAR T cell therapy in NSCLC. EGFR, MUC1, and MSLN are particularly promising due to their overexpression on these cancer cells, making them attractive targets for CAR T cell recognition. Advances and Strategies: Researchers are actively pursuing strategies to enhance the effectiveness of CAR T cells against NSCLC. These include designing multi-targeting CARs to address tumor heterogeneity, investigating combination therapies with checkpoint inhibitors or chemotherapy to amplify treatment response, and exploring direct tumor infusion to circumvent the immunosuppressive TME.

Conclusion: Clinical Trials and Future Directions: Numerous clinical trials are currently underway to evaluate various CAR T cell designs and combination therapies to improve outcomes for NSCLC patients. These studies focus on optimizing dosage, minimizing side effects, and enhancing the persistence and activity of CAR T cells within the tumor. While significant challenges remain in using CAR T cell therapy to treat NSCLC, ongoing research and innovative strategies offer hope for more effective treatment options. As our understanding of tumor biology and immunotherapy continues to grow, CAR T cells hold the potential to become a powerful tool in the fight against NSCLC, offering renewed hope to patients battling this complex disease.

Keywords: CAR T Cell, Lung Cancer, NSCLC

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CAR-T Cell Therapy: A Transformative Approach in the Management of Hematological Malignancies (Review)

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Introduction: Chimeric Antigen Receptor (CAR) T-cell therapy has emerged as a groundbreaking and innovative immunotherapeutic approach in the treatment of refractory hematological malignancies. This therapeutic modality harnesses the power of a patient's own T cells, genetically engineering them to recognize and eliminate tumor cells. Over the past few years, significant advancements have been made in the field of CAR-T cell therapy, leading to its widespread adoption as a viable and promising treatment option for patients with these challenging blood cancers.

Methods: the research methodology entailed an extensive search across pubmed, googlescholar,and (NCBI) databases to locate articles CAR-Tcell therapy Approach in the Management of Hematological Malignancies.A total of ٢٥ articles were identified for the purpose areview and analysis on this topic.

Results: The CAR-T Cell Manufacturing ProcessThe process of manufacturing CAR-T cells begins with the collection of a patient's own T cells through a process called leukapheresis. These T cells are then genetically modified using viral vectors to express synthetic receptors called chimeric antigen receptors (CARs). These CARs are designed to recognize specific tumor antigens, such as CD١٩ and BCMA, which are commonly expressed on the surface of hematological cancer cells. The modified T cells are then expanded in a laboratory setting and subsequently infused back into the patient, where they can mount a targeted and potent immune response against the malignant cells. Challenges and Adverse EffectsWhile CAR-T cell therapy has demonstrated remarkable efficacy, it is not without its inherent challenges and potential adverse effects. The most commonly reported side effects associated with this treatment approach include cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS).

Conclusion: ddfCAR-T cell therapy has revolutionized the treatment landscape for hematological malignancies, offering a promising therapeutic option for patients who have exhausted standard treatment modalities. While the therapy has demonstrated remarkable efficacy, it is not without its inherent challenges and potential adverse effects, requiring ongoing vigilance and monitoring. As the field of CAR-T cell therapy continues to evolve, further advancements hold the promise of expanding its therapeutic reach and ultimately improving outcomes for patients with various types of cancer.gfhg

Keywords: CAR-T Cell, Therapy, Hematological Malignancies

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Carbon based nanocarriers for siRNA delivery in breast cancer therapy (Review)

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Introduction: Breast cancer (BC) is one of the most common types of cancer in women and the main cause of cancer mortality. Because BC is primarily caused by genetic mutations, it is necessary to use gene therapy approaches to control the activity of malfunctional genes. A number of evidence showed that siRNA mediated control of BC has great therapeutic potential. However, due to the low stability of siRNA, highly intelligent, effective delivery systems are needed for targeted siRNA delivery. carbon-based nanocarriers (CBN). By reason of their two-dimensional structure, large surface area, and potential for surface modification, CBNs are interesting transporter options for cancer therapy. Functionalization of CBN improves their solubility in biological solutions, biocompatibility and the ability to electrostatically bind to negatively charged molecules, such as siRNA. In this review, we will discuss CBNs potential and their functionalization for optimal siRNA delivery as well as the challenges in the delivery of siRNA to BC, and potential future improvements for medical applications.

Methods: Original articles published since ۲۰۱۵ on CBN in the field of RNA carrier for breast cancer treatment were searched from Google Scholar, Scopus, and PubMed databases. Using these data, the application and properties of CBN were discussed.

Results: Documented studies showed interesting results for graphene oxide as an important CBN. Recently, a drug delivery system composed of graphene oxide (GO)/polyethyleneimine (PEI)/polyethylene glycol (PEG)/CPP/small interfering RNA (siRNA) was developed that effectively suppressed tumor growth of BC cells. Furthermore, in another study, siRNA was delivered in combination with DOX in MCF-۷ cell lines through folic acid (FA)-conjugated polyethylenimine-modified PEGylated graphene revealed proper gene silencing.

Conclusion: Considering biocompatibility and optimal targeting efficiencies of functionalized CBN mediated delivery of siRNAs in reported studies of breast cancer, using the CBN carriers is suitable in future breast cancer therapies.

Keywords: Carbon based nanocarrier, breast cancer, siRNA delivery, gene therapy

CEREBROSPINAL FLUID INJECTION REDUCED RECOVERY TIMES AFTER MILD TRAUMATIC BRAIN INJURY (Review)

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Introduction: Following the aging process, the secretion of cerebrospinal fluid (CSF) decreases, leading to the accumulation of amyloid plaques in Alzheimer's disease and increased phosphorylation of tau protein in acute encephalopathy.

Methods: Traumatic brain injury (TBI) is a brain dysfunction that results from external trauma or impressive acts that due to brain weight loss. Average recovery from mild TBI occurs within one week to three months. Additionally, the mean duration of mild TBI was associated with orthopedic injury, cognitive impairment, depression or anxiety, drug use, age of injury, and female gender. CSF plays an important role in protecting the brain and spinal cord from mechanical damage and in effective processes/injuries that lead to a reduction in brain weight.

Results: CSF contains substances necessary for the brain, such as nutrients and hormones. On the other hand, CSF plays an important role in the clearance of CNS proteins important for cognitive function. After injury, the level of cognitive function decreased. Furthermore, intracranial pressure (ICP) was increased after injuries such as stroke, hydrocephalus, oedema, and traumatic brain injury (TBI).

Conclusion: CSF plays an important role in ICP homeostasis, and as a result, disturbance of CSF secretion or drainage may lead to high level of ICP. TBI is associated with other problems such as oedema, impaired tissue perfusion and increased ICP. AQP٤ expression is altered in many diseases, including central nervous system (CNS) injury, ischaemia, hypoxia, and TBI. Elevated size of ventricular and pressure of intraventricular in aged populations with hypoxia conditions is proof. CSF administration shortened the mean recovery time of mild TBI or cognitive impairment. Additionally, average recovery from mild TBI was lower for female compare to male.

Keywords: Cerebrospinal fluid; Brain injuries; Hypoxia; Intracranial pressure; Cognition

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Challenges in the Development of Biosimilars for Advanced Therapy Medicinal Products (ATMPs) (Review)

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Introduction: The development of ATMP biosimilars faces significant challenges due to the complexity of these products, which involve modified cells and genes. Replicating the same efficacy and safety is difficult, and variations in manufacturing can lead to differing clinical outcomes. Additionally, evaluating their safety and efficacy is complicated by biological systems' complexity and immune responses, creating further regulatory hurdles. Key regulatory issues include the absence of clear guidelines and the need for extensive clinical trials. Overcoming these challenges requires a stepwise approach and totality of evidence to ensure biosimilarity, alongside international cooperation and financial support.

Methods: In this article, we conducted a systematic review of the published papers and guidelines in the field of ATMPs, focusing on the challenges in developing biosimilars related to these products. The development of ATMP biosimilars faces numerous challenges, including the inherent complexity of these products, which involves modified cells and genes. This makes it difficult to create a similar version with the same efficacy and safety. Changes in the manufacturing process can also lead to significant differences in clinical outcomes. Moreover, the evaluation of the safety and efficacy of ATMP biosimilars, due to the complexity of biological systems and various immune responses, poses additional regulatory challenges. In terms of regulatory challenges, the lack of clear guidelines and the need for extensive clinical trials are among the main issues. Additionally, post-market surveillance is essential to ensure long-term safety and efficacy. Generally, two fundamental concepts are involved in the approval process of biosimilar drugs: ١. Stepwise approach ٢. Totality of evidence The stepwise approach means that at each stage, the focus is on addressing the remaining regulatory questions from the previous stages. In other words, each stage sequentially focuses on the uncertainties left over from the previous stage until these uncertainties are fully resolved. The totality of evidence refers to the fact that in order to confirm the biosimilarity of a product to the reference drug, a comprehensive assessment of all criteria, including analytical, preclinical, and clinical evaluations, must be conducted. None of these criteria alone is sufficient to prove biosimilarity, and they must be collectively confirmed. In the areas of quality and safety, ensuring the robustness and reproducibility of the manufacturing process and precise control over cells and genetic materials are key issues. Economic and legal challenges also include the high costs of development and legal barriers due to patents, which can slow down the entry of biosimilars into the market. Finally, proposed solutions include the development of comprehensive regulatory guidelines, increased international cooperation, and financial support to facilitate the development process and reduce costs.

Results: The development of biosimilars in the ATMP field faces numerous technical, scientific, regulatory, and economic challenges. However, with the increasing demand for these products and their high potential in treating complex diseases, it is essential to develop effective strategies to overcome these challenges.

Conclusion: Regulatory bodies should develop more comprehensive and transparent guidelines for the development of ATMP biosimilars. These guidelines must carefully consider the scientific, technical, and regulatory challenges, providing precise guidance for developers. Since the development of ATMPs is an emerging and global field, international collaboration between regulatory bodies and manufacturing companies can help establish common standards. Such collaborations can also facilitate evaluation and approval processes across different countries. Financial support through grants or public and private investments in the development of ATMP biosimilars can help reduce costs and accelerate the development process.

Keywords: ATMP, biosimilar, regulatory challenges, international collaboration, financial support

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Changes in the colonization rate of Staphylococcus aureus on the skin of psoriasis patients

(Research Paper)

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Introduction: Psoriasis is a lifelong inflammatory disease that involves the skin, joints, cardiovascular system, and CNS. Its outward symptoms include redness, peeling, and itching. This disease is known as an autoimmune disorder that can affect the quality of life.One of the important aspects in understanding this disease is to examine the changes in the skin microbiome of psoriasis patients.Staphylococcus aureus is a spherical gram-positive bacterium that usually exists in the skin and mucous membranes of humans, and approximately ۱۰-۲۰٪ of people carry it without symptoms. Recent research has shown that the skin microbiome plays an important role in skin health and diseases. Staphylococcus aureus, which is part of the normal flora of the skin, acts as an opportunistic pathogen, which means that in certain conditions such as damage to the skin and weak immune system, it can lead to disease.It is thought that the presence of Staphylococcus aureus contributes to the inflammatory processes associated with psoriasis by affecting the Th۱/Th۱۷ axis.Considering this issue, the aim of this study is to investigate the colonization rate of Staphylococcus aureus on the skin of patients with psoriasis compared to healthy control subjects. This study can provide valuable information for the development of new treatment methods and prevention strategies for skin infection.

Methods: This cross-sectional study was designed with the aim of investigating the colonization rate of Staphylococcus aureus bacteria on the skin of patients compared to control subjects. The participants in this study included ۲۱ patients with psoriasis who visited the skin clinic of Tajrish Hospital located in Tehran. ۲۱ healthy individuals who did not have psoriasis and matched the patient group in terms of age and sex. A skin sample was taken from the forearm of a person using a sterile swab from ۵ cm۲ and inoculated into liquid BHI culture medium and incubated for ٤۸ hours at ۳۷°C. After DNA extraction by boiling method and with the help of specific primers, PCR reaction was performed to detect the presence or absence of Staphylococcus aureus. The samples that were positive for the presence of Staphylococcus aureus were cultured in the special mannitol salt agar culture medium after preparation of serial dilutions. The obtained data were analyzed using SPSS version ۲٦ software.

Results: In microbial cultures, ۳۸٪ (۸ out of ۲۱ patients) of the samples of psoriasis patients led to the growth of Staphylococcus aureus, while this figure was only ۵,۹٪ (۲ out of ۲۱ healthy people) in the control group. The Mann-Whitney test showed that the number of Staphylococcus aureus clones in the skin of patients with psoriasis was significantly higher than that of the control group (p=۰,۰٤). This increase in the number of clones was observed especially in the inflamed areas of the patients' skin.

Conclusion: The results showed that patients with psoriasis have significant changes in the frequency of Staphylococcus aureus compared to the control group. An increase in Staphylococcus aureus colonization can play an important role in aggravating the clinical symptoms and inflammation associated with psoriasis. It can also be used as a potential biomarker to assess the severity of the disease. According to the findings of this study, it is suggested that more research be done on the effect of therapeutic interventions on the change of staphylococcus aureus colonization in the chest of psoriasis patients. Also, a better understanding of the interactions of staphylococcus aureus in the skin microbiome and the immune system may lead to the development of new therapeutic strategies. Help to manage psoriasis.Finally, this study emphasizes the importance of carefully investigating the increase in Staphylococcus aureus colonization in the skin in order to better understand the pathogenesis of psoriasis and improve the quality of life of patients.

Keywords: Psoriasis , skin microbiome ,Staphylococcus aureus

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Characteristics of Patients with Traumatic Injuries Presenting to the Emergency Department and their Association with Mortality and Surgical Intervention (Research Paper)

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Introduction: To determine the unique characteristics of acutely injured patients admitted to the emergency department and their relationship with mortality and surgical intervention outcomes.

Methods: This cross-sectional study was conducted on all trauma patients resuscitated in the emergency department of Shahid Rajaee (Emtiaz) Trauma Hospital in Shiraz, Iran, from May ٢٠١٨ to June ٢٠١٩. The study considered demographic information, mechanism of trauma, trauma type, injured body regions, criteria of abbreviated injury scale (AIS) score, injury severity score (ISS), and surgical intervention. The study analyzed the items related to the mortality and surgical performance outcomes among the patients.

Results: Of all ١٢٨١ cases, ٨٢,٩٪ were men, and the average age of the patients was ٣٧,٩±١٩,١ years. The most common cause of injury was a car accident, and the thorax was the most frequently injured area of the body. Most patients had moderate blunt trauma. The mechanism of trauma, Injury Severity Score (ISS), and the severity of head trauma were all significantly correlated with the need for surgical intervention. Additionally, age, the mechanism and type of trauma, ISS, and the necessity for surgery were significantly associated with mortality. Furthermore, head, thorax, and abdomen trauma were significantly related to a high mortality rate.

Conclusion: The mortality rate of injured patients was significantly associated with their age, the mechanism and type of trauma, Injury Severity Score (ISS), and the need for surgery. The severity of the trauma, especially head injuries and the mechanism of injury, were important factors in determining the necessity for surgery.

Keywords: Trauma, Resuscitation, Injury, Injury Severity Score, Abbreviated Injury Scale

Chitosan/ Egg Shell Membrane Hydrogel as a Novel Biocompatible Composite with Antibiofilm Activity (Research Paper)

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Introduction: Novel biocompatible and anti-biofilm chitosan based hydrogel was synthesized and embedded with waste Egg Shell Membrane powder. The functional agents in each synthesis step had been confirmed using Fourier-transform infrared (FT-IR). Field-emission scanning electron microscope (FE-SEM) revealed a highly porous composite with a three-dimensional mesh structure. Different methods were used to explore the biological capability of the hydrogel. Results showed that prepared hydrogel prevents the formation of Staphylococcus aureus biofilm. The hemolytic assay demonstrated that almost all red blood cells survived. The cell viability on mouse fibroblast cells was ٩٤,٣٪ after an overnight incubation whereas it was about ٩٦٪ for the control group. The statistical analysis indicated that there was no remarkable difference between the cell viability of the control and treated groups (P-value > ٠,٠٥). In conclusion, the fabricated Chitosan/ Egg Shell Membrane hydrogel showed proper properties that candidate it as a safe anti-biofilm substance in various medical materials.

Methods: A novel biocompatible and anti-biofilm chitosan-based hydrogel was synthesized and embedded with waste egg shell membrane powder. The functional agents in each synthesis step had been confirmed using Fourier-transform infrared (FT-IR). Field-emission scanning electron microscope (FE-SEM) revealed a highly porous composite with a three-dimensional mesh structure. Different methods were used to explore the biological capability of the hydrogel.

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Conclusion: In conclusion, the fabricated chitosan/egg shell membrane hydrogel showed proper properties that position it as a safe anti-biofilm substance in various medical materials.

Keywords: Chitosan, Egg Shell Membrane, Staphylococcus aureus, Biofilm

Circadian Rhythm Disruptions and Their Impact on Metabolic Syndromes From a molecular point of view (Review)

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Introduction: Circadian rhythms are biological cycles that naturally recur in ٢٤-hour intervals in humans and other living organisms. These rhythms regulate physiological processes, including sleep-wake cycles, body temperature, hormone production, and metabolism. Recent studies have shown that disruptions in these rhythms, caused by factors such as night shift work, changes in sleep patterns, and chronic stress, can lead to metabolic changes, resulting in metabolic syndromes such as obesity, type ٢ diabetes, and hypertension. This study aims to examine the impact of circadian rhythm disruptions on metabolic syndromes, focusing on analyzing molecular pathways and key genes involved.

Methods: This review was conducted by searching keywords such as "Circadian rhythm," "Circadian rhythm disruption," and "Metabolic syndrome" in databases including PubMed, Direct Science, Scopus, and the search engine Google Scholar. In total, more than ٥٠ recent articles were selected and reviewed.

Results: Circadian rhythms are regulated by clock genes such as CLOCK, BMAL١, PER, and CRY, which play crucial roles in numerous physiological and metabolic processes. These genes regulate the expression of metabolism-related genes, and disruptions in circadian rhythms and clock gene activity can lead to imbalances in metabolic pathways, which leads to metabolic syndromes such as obesity, type ٢ diabetes, and cardiovascular diseases. One key pathway regulated by circadian rhythms is AMPK (AMP-activated protein kinase), which plays a central role in maintaining energy balance in cells. Disruption of circadian rhythms can inhibit AMPK activity, leading to fat accumulation and an increased risk of metabolic syndromes. In addition to AMPK, other important molecular pathways affected by circadian rhythms include mTOR (mechanistic target of rapamycin) and SIRT١ (Sirtuin١). mTOR plays a role as a master regulator of cell growth and metabolism and is sensitive to changes in nutrient and energy levels. Disturbance in the circadian rhythm can increase the activity of mTOR, which leads to disturbances in the metabolism of glucose and lipids, and finally leads to metabolic syndromes. The SIRT١ pathway also plays a role as the main regulator of aging and metabolism processes and is synchronized with circadian rhythms. Research has shown that SIRT١ activity changes in response to changes in the circadian rhythm and that decreased activity leads to reduced insulin sensitivity and increased fat storage, which are key factors in the development of metabolic syndrome. Additionally, genetic polymorphisms in clock genes such as CLOCK and BMAL١ are linked to higher susceptibility to obesity, type ٢ diabetes, and hypertension in certain populations, suggesting a genetic predisposition to circadian rhythm-related metabolic disorders. Furthermore,

the timing of food intake plays a significant role in metabolic health. Eating at times misaligned with circadian rhythms, such as late at night, disrupts insulin secretion and glucose metabolism, raising the risk of type ٢ diabetes and obesity Environmental factors like exposure to artificial light at night can suppress melatonin production, a hormone crucial for maintaining energy balance. Prolonged exposure to artificial light, especially at night, along with high-fat diets, disrupts hormonal regulation and promotes fat accumulation, further increasing the risk of metabolic syndromes.

Conclusion: The analyses indicate that circadian rhythms, as key biological mechanisms, play a vital role in regulating metabolism and maintaining overall health. Disruption of these rhythms can lead to metabolic disorders such as type ٢ diabetes, hypertension, and obesity, which in turn can increase the risk of cardiovascular diseases. A deeper understanding of the molecular pathways and genes involved could help identify new therapeutic targets and improve prevention strategies. Scientific and experimental evidence suggests that properly regulating sleep-wake cycles, improving diet and utilizing novel therapies targeting molecular pathways can help to improve circadian rhythms and reduce metabolic disorders.

Keywords: Circadian rhythm, Circadian genes, Metabolic syndrome, Molecular pathways, Obesity

CircPac: A web-based analysis toolset for exploring circular RNA data (Research Paper)

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Introduction: Circular RNAs (circRNAs) are a type of RNAs that play crucial roles in various biological processes. Their outstanding properties such as tissue-specific expression and high resistance to exonuclease degradation make them attractive for research. However, a comprehensive analysis tool for analyzing circRNA data is still required.

Methods: In this study, we present CircPac, a newly developed web-based toolset that searches databases like circBase, circBank, and circRNADisease and organizes data to provide and visualize circRNAs information. Our toolset was created using the Python programming language and its libraries, such as pandas, seaborn, and the Django framework.

Results: CircPac enables users to unify the circRNA IDs and subsequently perform various bioinformatic analyses. These analyses include retrieving basic circRNA information, identifying target miRNAs, and analyzing circRNA expression changes in various diseases. Additionally, this toolset generates ready-to-publish figures of circRNA-miRNA interactions and circRNAs expression changes in diseases.

Conclusion: CircPac is freely accessible (at https://www.circpac.ir) and offers a user-friendly platform for biologists to efficiently conduct and visualize circRNA data analyses in an appropriate format.

Keywords: RNA, Circular; MicroRNAs; Computational Biology; Web-based analysis; Data Visualization

Circulating Micro RNAs as a safe diagnoses tool in DMD (Review)

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Introduction: DMD is a member of neuromuscular disorders. This group include similar disease which are hard to distinguish between them. In order to choose the best treatment to administer exact diagnose is necessary. Conventional methods are like CK measurement, EMG evaluation, muscle biopsy, PCR, MLPA, southern blotting, immunohistochemical-based diagnose and NGS-based diagnose. Although these methods are beneficial but disadvantages like being invasive, expensive, non-specific and needing high technology are existing when utilizing them. Recent evidence shows that circulating blood microRNAs evaluation as a specific non-invasive monitoring method may help for DMD diagnosis. The aim of this review is to discuss recent studies about circulating microRNAs as potential biomarkers for detection of DMD.

Methods: All original articles regarding miRNA, biomarker, and DMD diagnosis were collected, and main findings were summarized in this work.

Results: Most of the studies in the DMD detection area had a similar point of view regarding impact of mir-١٣٣-a/١٣٣-b/٢٠٦/٤٩٩/٢٠٨-a/٢٠٨-b(١). This miR frequently demonstrated dysregulation in DMD patients or carrier persons. Expression of this circulating miRs have been evaluated in several patients with different type of mutation in various subgroups of MD. They demonstrated that combined measurement of several miRs not only can be used as a diagnostic tool, but also may could distinguish in similar cases like DMD and Beker muscular dystrophy (٢). The serum levels of miR-٩٥ and miR-٥٣٩ assessed and revealed dysregulation in a small cohort study on dogs and human (٣). Other microRNAs which were mentioned in previous studies (miR-٣٣٩-٥p/٤٨٦/١/٤٨٣/٣٠c/١٨١-a/٣٧٨) indicate either positive or negative relation with DMD.

Conclusion: According to our evaluation, we can confirm that circulating miRNAs, in particular conserved miRNAs could serve as the best biomarkers for DMD diagnosing.

Keywords: Circulating miRNAs, DMD, Diagnosis

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Cisplatin is enhanced by Akkermansia muciniphila in Lewis lung cancer mice (Research Paper)

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Introduction: A number of factors can limit the efficacy of cisplatin as a chemotherapeutic agent for lung cancer. An animal model of Lewis lung cancer (LLC) has been studied to examine the role of gut microbes, specifically Akkermansia muciniphila, in enhancing the effects of cisplatin on tumor growth.

Methods: Sixty C٥٧BL/٦ mice were injected with LLC cells and then randomized into four groups: control, cisplatin alone (٣ mg/kg), A. muciniphila alone (١٠٩ CFU/mL), and cisplatin combined with A. muciniphila. Treatments were administered intraperitoneally (cisplatin) and orally (A. muciniphila) for four weeks. Tumor volumes were measured every three days using calipers. At the end of the treatment period, tumors were excised and weighed. Blood and tissue samples were collected for cytokine analysis (IL-٦ and TNF-α) and immunohistochemistry to assess immune cell infiltration (CD٨+ T cells). Statistical analysis involved ANOVA and Tukey's post hoc test for multiple comparisons.

Results: The combination group showed a significantly greater reduction in tumor volume (mean decrease of ٦٥,٢ ± ٤,٨٪) compared to the cisplatin alone group (mean decrease of ٤٥,٣ ± ٣,٥٪, $p < ٠,٠١$) and the A. muciniphila alone group (mean decrease of ٢٠,١ ± ٢,٧٪, $p < ٠,٠٠١$). Tumor weight was significantly lower in the combination group (mean ٠,٧٥ ± ٠,١٢ g) than in the cisplatin alone group (mean ١,٣٠ ± ٠,١٥ g, $p < ٠,٠١$) and the A. muciniphila alone group (mean ١,٨٥ ± ٠,٢٠ g, $p < ٠,٠٠١$). Cytokine analysis revealed significantly lower levels of IL-٦ and TNF-α in the combination group compared to other groups ($p < ٠,٠٥$). Immunohistochemistry showed increased infiltration of CD٨+ T cells in tumors from the combination group.

Conclusion: The results of this study offer a promising avenue for cancer treatment. By enhancing the anti-tumor efficacy of cisplatin, Akkermansia muciniphila could potentially revolutionize the way we approach chemotherapy. These findings inspire hope for improved therapeutic outcomes when probiotics are combined with chemotherapy.

Keywords: Akkermansia muciniphila, Cisplatin, Lung Cancer, Immunomodulation, Probiotics

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Clinical Evaluation of the Safety of Postbiotic Spray for the Treatment of Burn Wounds and Infections (Research Paper)

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Introduction: Burn wounds and bacterial infections caused by Pseudomonas aeruginosa and its biofilm present significant treatment challenges in burn hospitals, necessitating appropriate therapeutic methods. Traditional treatment approaches often depend on antibiotics, which carry the risk of resistance and side effects. Metabolites produced by probiotics, with their antimicrobial and immune-enhancing effects, have been regarded as a potentially suitable alternative to antibiotics in preclinical studies. This study aims to assess the safety of a topical postbiotic spray for improving the healing of burn wounds and preventing infections in human participants

Methods: This experimental study was a randomized, double-blind, controlled clinical trial conducted on healthy volunteers aged ١٨ to ٦٥ years, aimed at assessing the safety of the postbiotic spray. The study has been registered with the ethics committee of Guilan University of Medical Sciences under the number IR.gums.REC.١٤٠١,٦٠٨ and in the Iranian Registry of Clinical Trials under the number IRCT٢٠٢١٠٥٢٤٠٥١٣٨٤N٩. For this purpose, participants were randomly divided into two groups: Group One (intervention group) received a postbiotic spray containing a mixture of metabolites produced by probiotic strains, while Group Two (control group) received a placebo spray containing saline. Both groups used the spray for ٢٨ days, once every ١٢ hours, at a specific distance from the designated area, with a dose of ١٠٠ to ٣٠٠ micrograms per spray. The safety of this spray during the trial was monitored through specialized medical examinations using a standardized checklist, including demographic information, and potential local and systemic side effects, and was documented via digital imaging.

Results: Volunteers aged ١٨ to ٦٥ years were selected for the safety assessment of the study. Local and systemic adverse events were monitored and evaluated using a standard checklist at five stages (days ١, ٧, ١٤, ٢١, and ٢٨). The findings revealed that the probiotic spray being investigated had no significant negative effects. After conducting this study, we look forward to positive results from further research on topical probiotic solutions. Probiotics may prove to be a safer and more effective alternative to antibiotics, with fewer adverse effects.

Conclusion: The findings of this clinical trial indicate that the topical probiotic spray is devoid of clinical local and systemic adverse effects, and considering the antibacterial properties of probiotics, it may effectively enhance the healing process of burn wounds and prevent bacterial infections in patients.

Keywords: Probiotics; safety, clinical trial, wounds and injuries, drug side effects

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Clusterin Like ١ gene expression is linked to the survival of PTC patients (Research Paper)

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Introduction: Well-differentiated papillary thyroid carcinoma (PTC) is a common form of thyroid cancer. Both environmental and genetic determinants exert an influence on the development of PTC. Although several genes linked to PTC have been studied, the precise genetic basis of PTC remains incompletely elucidated. The aim of our study was to uncover PTC-hug genes linked to PTC outcome.

Methods: Analysis was performed on the GSE١٠٤٠٠٥dataset, which included ١٩ PTC tissues and ٥ normal tissues adjacent to PTC tumours. Validation of data quality involved applying log٢ transformation and quantile normalisation. An analysis of differential expression was conducted using the Limma program. Genes with logFC values above ١,٢ and adjusted p values below ٠,٠٥ were chosen as differentially expressed genes (DEGs). Ten papillary thyroid carcinoma (PTC) and ten normal tissues surrounding the PTC tumours were collected following thyroidectomy surgery. Total RNA extraction, complementary DNA synthesis, and RT-qPCR will be performed. The relative expressions will be examined using REST٢٠٠٩ analytical software. Survivability, stage, and nodal metastasis analyses were performed.

Results: An examination of microarray data revealed the identification of ٢٥٠ DEGs. Among these genes, Clusterin Like ١ (CLUL١) had a logFC value of -٢,٣٢ (adjusted p-value of ٧,٩٨E-٠٤). A significant impact of CLUL١ expression on reducing the likelihood of patients' survival was observed (p-value of ١,١E-٠٢). The expression of CLUL١ was evaluated at several biological stages, revealing a median expression level of ١,٩٠ in Stage ٢ and ٠,٩٤ in Stage ٤. Our analysis revealed that the expression of CLUL١ in Stages ٢ and ٤ had a significant association with heightened aggression (P-value of ٢,٢٤E-٠٥). The median expression level of CLUL١ in tumours without infiltration into the regional lymph nodes (N٠) was ١,٤٨, but in tumours with metastases to the axillary lymph nodes (N١) it was ٠,٩٤. An analysis revealed a significant difference in the expression of CLUL١ between N٠ and N١ tumours (P-value = ٣,١٠E-٠٣). Statistical analysis did not reveal any significant variation in the expression of CLUL١ between male and female patients.

Conclusion: The CLUL١ gene exhibited a significant reduction in expression in PTC compared to normal tissues surrounding PTC tumours. Reduced expression of CLUL١ was associated with greater patient survival and metastasis.

Keywords: PTC, microarray, CLUL١, survival

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CNN and ANN in Cancer Research: Pioneering AI Solutions for Early Detection and Treatment

(Review)

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Introduction: Artificial Neural Networks (ANNs) and Convolutional Neural Networks (CNNs) are very powerful Artificial Intelligence (AI) methods that are changing the way healthcare is provided. The ANN can be used for a wide range of tasks, including regression, pattern recognition, and classification. CNN is used for things like computer vision and picture detection. Putting these technologies into medical gadgets like thermometers, imaging systems, and wearable monitors could help doctors make more accurate diagnoses and do their jobs faster. Cancer studies that use CNNs and ANNs should be able to find cancer earlier, make treatment more specific, and lower death rates over time. This article reviews how CNNs and ANNs can be used in cancer research, including how they can help with early diagnosis and planning treatment, as well as the issues that come up when they are used.

Methods: We looked at new studies to find out how CNNs and ANNs are being used to find and treat cancer better. The studies we looked at were from ٢٠٢٢ to ٢٠٢٤ and were reviewed by experts in the field. Some keywords, like "AI in oncology," "CNN cancer detection," and "ANN cancer treatment," were used to look through sources like Google Scholar and PubMed. Titles and descriptions were looked at to see if they were relevant, and full texts of some studies were read to see if they used the right methods and added much to the field.

Results: It is now possible to find cancer treatments that hurt healthy parts the least, thanks to genomics and biological markers. These problems could be fixed with deep learning systems that can look at medical images, genomic data, and patient information on their own. ANNs and CNNs are two types of AI-driven models that can quickly and correctly look at huge amounts of data. We can learn a lot from this about how cancer grows, how well medicines work, and how well people do. The CNN is a type of deep learning system that works with organized grid data, like pictures of illness. They can find things, sort them into groups, and figure out what a picture is about very quickly. CNNs can find tumors early on that other imaging methods might miss when they look at CT pictures. Images taken with a dermoscopy can help CNNs tell the difference between skin tumors that are not dangerous and those that are. There are more ways to use ANNs, and they can be used

with different kinds of data, such as DNA, RNA, and clinical data. That's why these tools are used to find connections between changes in genes, how the cancer grows, and how well people do. An important thing that can be done with ANNs is to guess how cancer meds will work. This helps doctors figure out the best way to treat each patient. Another interesting area of cancer research is using ANNs to find new drugs. These computers can look through huge lists of chemicals to find possible cures for cancer. But there are some problems that need to be fixed. The kind and amount of data needed to train these models well, how easy it is to understand them, and the idea that AI could replace human knowledge are some of the things that worry people.

Conclusion: AI programs are being worked on to do things that are similar to what professionals do. This will make it possible to do quick, accurate tests that lead to results in real-time. This change makes it easier to find skin cancer early, so there is less need for invasive treatments. By cutting down on the time it takes to do exams, these ideas can improve healthcare services, especially in places where there aren't any doctors or emergencies. CNNs and ANNs are new ways to find, diagnose, and treat cancer early. We need to fix issues like insufficient data, models that are hard to understand, and ethical concerns before we can merge into clinical practice. AI-powered solutions can change how cancer is handled and make it less of a problem around the world. They are what will make cancer studies go forward.

Keywords: AI, oncology, CNNs, and ANNs

Coincidence between a human-poultry zoonotic infection and antibiotic resistance: a public health challenge with Pseudomonas aeruginosa (Review)

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Introduction: According to global statistics, more than ٣ million human deaths are caused by infections transmitted from animals to humans. Pseudomonas aeruginosa is a pathogen with high mortality in poultry, which has the ability to transmit and cause disease in humans. Chicken embryos infected with P. aeruginosa die before hatching and chicks show respiratory and intestinal symptoms and septicemia with severe mortality. Pulmonary damage such as cystic lung fibrosis and bronchiectasisis seen in humans infected with P. aeruginosa, especially in cases of immunodeficiency. P. aeruginosa is transmitted to humans through contaminated poultry carcasses and its products. In recent years, high antibiotic resistance has been reported to P. aeruginosa, which can be attributed to the transfer of antibiotic resistance genes from poultry products to humans. These reasons have caused that despite the importance of this zoonotic pathogen in public health, its treatment is very difficult and complicated. Therefore, there is an urgent need to replace antibiotics with a suitable antimicrobial agent to overcome widespread bacterial resistance. Currently, many studies are being conducted on various alternative therapies. This article deals with the study of P. aeruginosa in poultry and how it is transmitted and causes infection in humans, followed by antibiotic resistance issues.

Methods: In order to review the studies conducted in the field of the importance of P. aeruginosa as a common pathogen between humans and poultry and the subsequent development of disease and antibiotic resistance issues and the challenges of its treatment, Google Scholar, PubMed and Scopus databases with keywords "Pseudomonas aeruginosa", "zoonosis", "public health", "poultry", "antibiotic resistance"", and “alternative” were searched between ٢٠١٤ and ٢٠٢٤. Finally, articles related to our topic were discussed and reviewed to write this article.

Results: P. aeruginosa, having different virulence factors such as fliC, psIA and toxA genes, plays a role in inhibiting protein biosynthesis and microorganism colonization and cell penetration along with inducing necrosis and tissue death. This Gram-negative, aerobic, and rod-shaped bacterium is present everywhere as an opportunistic agent and becomes pathogenic under conditions of stress and immunodeficiency. P. aeruginosa can infect humans through occupational contact with contaminated poultry carcasses and their products. Especially, due to the formation of biofilm and its high resistance in unfavorable conditions, it is abundantly present in products that are subject to spoilage and carcass waste. This high resistance is one of the important reasons for non-response to antibiotic treatment. Indiscriminate and uncontrolled use of antibiotics in industrial poultry breeding

chains and their products has also been reported as one of the main causes of antibiotic resistance in the treatment of P. aeruginosa. A high variation of antibiotic sensitivity of P. aeruginosa strains to different classes of antibiotics has been reported. Many alternatives are known for the treatment of various bacterial infections, some of which are more effective for the treatment of P. aeruginosa. According to existing reports, the use of selected bacteriophage viruses is useful as an alternative or in combination with antibiotics. Biodiversity and the ubiquity of phages in nature, as well as the easy isolation process of phages, are factors that can make them suitable alternatives for a long time. Using nanoparticles is another way to deal with resistance to antibiotics. According to previous studies, nanoparticles, due to their smaller size and unique curative properties, can cause disruption, penetrate the cell and induce the production of reactive oxygen species and free radicals through binding to the cytoplasmic membrane and cell wall of microorganisms. All the mentioned cases are still being studied and investigated and researchers are constantly expanding and discovering new cases in this field to achieve the best combinations.

Conclusion: According to the researches, P. aeruginosa is an important pathogenic and opportunistic bacterium in poultry and humans. Resistance to various antibiotics is common among P. aeruginosa strains, both in poultry and in humans. Accordingly, strict monitoring and enforcement of laws to control the use of antibiotics in the food chain at safe levels, as well as more research to discover and prepare appropriate alternatives to antibiotics against this bacteria should be carried out.

Keywords: Pseudomonas aeruginosa, zoonosis, poultry, public health, antibiotic resistance

Combination monoclonal antibodies against CTLA٤ and PDL-١ to increase treatment efficiency for colorectal cancer (Review)

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Introduction: The immune system is characterized by its capacity to differentiate between normal cells in the body and those it perceives as foreign cells. The immune system has the ability to attack foreign cells while not attacking normal cells due to this. T cells are immune cells and PD-١ is a checkpoint protein that is present on them. The surface of immune cells has a variety of checkpoint proteins. The immune response against cancer cells commences when these proteins are activated or deactivated. Monoclonal antibodies are a type of medicine that can be designed to target these checkpoint proteins. For instance, these receptors are comprised of PD-١, CTLA-٤, LAG-٣ And the variant that has recently attracted the attention of researchers is called iPD-١. Malignant progression in cancer cells is greatly influenced by the intrinsic variability (iPD-١). Immune checkpoint inhibitors are the name given to these drugs.

Methods: Literature Review

Results: Targeting the inhibitory checkpoints on immune T cells is a highly effective way to treat cancer. The treatment of solid cancers with single monoclonal antibodies, such as anti-CTLA٤-CD ٨٠/CD٨٦, is a challenge due to patients poor response to this therapy. The use of monoclonal antibodies in treating colorectal cancer has been shown to have a positive response rate of approximately ٥٠٪ in clinical and preclinical studies. According to the findings, the objective response rate for treatment with two monoclonal antibodies PD-١ and CTLA-٤ simultaneously is greater than that of those treated with a single monoclonal antibody.

Conclusion: The aim of this review is to examine clinical trials that combine both monoclonal antibodies against PD١ and CTL٤. Moreover, assess the advantages, disadvantages, and efficiency of this method in comparison to chimeric T cell antigen receptor cancer therapy.

Keywords: Monoclonal Antibodies, CTLA٤, PDL-١, Colorectal Cancer

Combination therapy by using hydrogel and mesenchymal stem cells-derived exosomes for diabetic wound healing (Review)

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Introduction: Exosomes are small extracellular vesicles that can be secreted from various cells (e.g., mesenchymal stem cells (MSCs)). They transport nucleic acids, proteins, and other bioactive substances, which impact wound healing. Their short life span and low stability have created some challenges for their use. Hydrogels are attractive biomaterials fabricated using various synthetic or natural polymers. Because of their remarkable biochemical and mechanical properties, they demonstrate good potential for exosome delivery as wound dressings.

Methods: We assessed the studies related to hydrogel containing MSC-derived exosomes for diabetic wound healing by searching different databases such as PubMed, Scopus, and Google Scholar.

Results: Investigations showed that the use of hydrogels with different compositions has positive effects on the function of exosomes. In fact, these hydrogel structures can increase MSC-derived exosome stability and life span. Also, these hydrogel structures can release the MSC-derived exosomes in a slow and controlled manner. Eventually, hydrogels like MSC-derived exosomes can accelerate the healing of diabetic wounds with anti-inflammatory effects, formation of new vessels, and increase granulation tissue and collagen density. Additionally, increasing the polarization of macrophages to the M٢ phenotype was another positive effect of this combined therapy. In general, these combined treatments accelerated diabetic wound closure and healing.

Conclusion: Studies have shown that the combined use of hydrogel and MSC-derived exosomes has good potential for treating diabetic wounds and can be a smart dressing. However, further studies are recommended to investigate the physical and chemical properties of these hydrogels and the biological properties of MSC-derived exosomes for diabetic wound healing.

Keywords: Exosome, mesenchymal stem cell, hydrogel, diabetic wound healing

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Combined hair stem cells transplantation and hair pulled out from root causes regrow hair (Review)

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Introduction: Stem cells could treat hair and skin diseases like baldness and androgenetic alopecia of the scalp. Hair loss cause some personality problem such as, depression, decreased self-esteem, and decreased quality of life. Hair stem cells express Nestin and are able to differentiate to many cell types like neurons, keratinocytes, blood vessels, and cardiac muscles.

Methods: Hair stem cells originate from hair follicles in the bulge region. Based on FDA (Food and Drug Administration), some medications used for this condition like, minoxidil and finasteride. Also, stem cells are well treatment option for hair loss. Based on sources, Stem cells are different like, bone marrow, adipose, umbilical cord blood and hair follicles.

Results: Stem cells transplantation increased density and thickness without adverse effect or pain. But now we want to mention the simpler method of extracting the hair follicle and strengthening it by stem cells. In such a way that after pulling the hairs by applying the shaved head hair, under anesthesia. Then it is placed in an incubator in flask containing stem cells for several hours. After that, the strengthened hair follicles are transplanted.

Conclusion: This method is recommended for people with low hair bank or people who like to show thick hair. In addition to the high cost of the stem cell method, direct injection of stem cells increase concern in terms tumor development. On the other hand, transplanted of exosome and stem cell-derived conditioned medium (CM) is safer and more affordable.

Keywords: Stem cell, Hair follicles, Hair loss, Alopecia, Hair regeneration

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Comparative Analysis of Anticancer Effects of Chitosan and Alginate Nanoparticles Loaded with Syzygium aromaticum Essential Oil and Eugenol Against Melanoma Cells (A-۳۷۵) (Research Paper)

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Introduction: Melanoma, a severe form of skin cancer originating from melanocytes, presents a growing medical challenge due to its increasing incidence and high mortality rate (۱). Currently, no effective treatment exists for metastatic melanoma, making the advanced stages of the disease incurable (۲). While new therapeutic approaches have been developed, drug resistance remains a significant barrier to successful cancer treatment (۳). Syzygium aromaticum (clove), a common spice in Indian cuisine, has long been recognized for its potent chemopreventive properties. Traditionally used in Ayurvedic medicine to treat respiratory and gastrointestinal conditions (٤). Clove's primary bioactive compound, eugenol, is well-known for its antiseptic, antibacterial, and analgesic properties. Eugenol is widely utilized in pharmaceuticals, food products, and beverages. Its health benefits are well-documented, and recent studies have highlighted its promising biological activities (٥). However, nanoparticles offer advantages in overcoming the limitations of free essential oils, such as enhanced stability and controlled release, preventing EO degradation (٦, ٧).

Methods: The essential oil components were identified using gas chromatography-mass spectrometry (GC-MS). Nanoparticles were prepared through ionic gelation, utilizing TPP crosslinking for chitosan and calcium chloride for alginate. The toxicity of the samples against A-۳۷٥ melanoma cells was assessed using the MTT assay.

Results: Eugenol constituted over ۷۰٪ of the essential oil. The particle sizes of the alginate nanoparticles containing essential oil and eugenol were ۱۲۲ nm and ۸۷ nm, respectively, while chitosan nanoparticles measured ۱٥۸ nm and ۲۰۰ nm. The toxicity (IC٥۰) results against A-۳۷٥ cells were as follows: unformulated essential oil and eugenol showed IC٥۰ values of ٥٤٥ µg/ml and ٥۷۲ µg/ml, respectively. Alginate nanoparticles containing essential oil and eugenol exhibited IC٥۰ values of ۳٥۸ µg/ml and ۷٥۷ µg/ml, respectively, while chitosan nanoparticles demonstrated IC٥۰ values of ۷۳ µg/ml and ۷۹ µg/ml, respectively.

Conclusion: Chitosan nanoparticles exhibited superior anticancer efficacy and are recommended for further investigation in animal models

Keywords: Melanoma; Complementary Medicine; Clove; Eugenol

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Comparative analysis of Artificial Intelligence applications in oncology: Assessing progress in lung cancer and brain cancer diagnosis and treatment (Review)

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Introduction: Cancer refers to a group of diseases characterized by abnormal cell growth, where early detection is essential for the treatment and survival of patients. Given the increasing use of artificial intelligence (AI) in clinical medicine, the present review study aims to explore the applications of artificial intelligence in cancer diagnosis and treatment, comparing advancements in lung cancer and malignant brain tumors.

Methods: The current review study followed the PRISMA protocol for data collection and search, using MESH terms including “artificial intelligence,” “lung cancer,” “oncology,” “diagnosis,” and “brain tumor.” The search was conducted in English databases (PubMed, Scopus, Google Scholar) for studies published between ٢٠١٨ and ٢٠٢٤. Inclusion criteria consisted of systematic reviews, meta-analyses, cohort studies, case-control studies, and randomized controlled trials (RCTs). Exclusion criteria included abstracts without full-text articles and studies outside the specified timeframe. A total of ٥١ articles were retrieved, of which ١٩ met the inclusion criteria after applying the exclusion criteria.

Results: Among the articles, ٣٦٪ focused on the general applications of artificial intelligence in neuro-oncology, ٣١٪ on lung cancer patients, and the remaining ٣١٪ on brain tumor patients. The review indicates that artificial intelligence has shown high potential in pathological assessments, initial screening, prognostic assessment, surgery, and immunotherapy for lung cancer. Additionally, artificial intelligence algorithms have demonstrated success in brain tumor segmentation, diagnosis, differentiation, grading, treatment response, and clinical outcome predictions for brain tumors. It has been found that limitations still exist in the use of artificial intelligence in both areas but the results for lung cancer diagnosis appear to be more reliable.

Conclusion: Although artificial intelligence algorithms have advanced in cancer diagnosis and treatment in recent years, their progress seems to vary across different cancer types. Moreover, significant limitations in their clinical application continue to be reported.

Keywords: Oncology- Artificial intelligence- lung cancer- brain tumor

Comparative Evaluation of Biochemical Methods and PCR in the Detection of Listeria monocytogenes (Research Paper)

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Introduction: Listeria monocytogenes is a Gram-positive, non-spore-forming coccobacillus that can be found in various environments, including soil, water, and food. This bacterium is a foodborne pathogen that can resist disinfectants, form biofilms, survive under harsh conditions, and grow in different types of food. Listeria monocytogenes can cause disease in humans, especially in individuals with compromised immune systems, the elderly, infants, and pregnant women. This study was conducted due to the risk posed by diseases caused by Listeria monocytogenes and the importance of its detection in food and the environment using certain biochemical and molecular methods.

Methods: ffgIn this study, ١٠٠ food and environmental samples were collected, including ٢٠ samples of milk, ٢٠ samples of cheese, ١٠ samples of nuggets, ١٠ samples of leek, ١٠ samples of smoked fish, and ٣٠ environmental samples, consisting of ١٩ soil samples and ١١ water samples, from the cities of Shahriar and Andisheh during the summer and autumn seasons in ٢٠٢٣. For isolation and identification, two stages of enrichment and one stage of culture on selective solid medium were performed. In the first enrichment stage, ١٠ grams of each cheese, leek, smoked fish, chicken nugget, and soil sample, and ١٠ ml of milk were transferred to ٩٠ ml of the selected liquid culture medium, Tryptic Soy Broth (TSB), and incubated at ٣٧°C for ٢٤ hours. For water samples, ٥٠٠ ml of each was filtered through a ٠,٤٥-micron Millipore syringe filter, which was then transferred to the TSB medium. In the second enrichment stage, ٠,١ ml of the cultured sample in TSB was added to ١٠ ml of Fraser broth and incubated at ٣٧°C for ٤٨ hours. Then, a culture was performed on PALCAM agar solid medium. For this, one loop of the Fraser broth culture (after ٤٨ hours of incubation) was streaked in four stages on a PALCAM agar plate and incubated at ٣٧°C for ٤٨ hours. Suspected colonies were selected based on the colony morphology of the positive control grown on PALCAM agar. To separate them from other growing colonies, they were recultured on PALCAM agar. Then, biochemical tests, including catalase, CAMP, and motility tests in the SIM medium, were conducted. Finally, PCR was performed using the standard bacterial strain (ATCC١٩١١٥) and primers specific to the listeriolysin O gene.fghj

Results: The preliminary results of comparing the colony morphology on PALCAM agar with the reference bacterium showed ٣٦ suspected colonies that were morphologically identical to the reference bacterium. Seven were environmental samples, and the rest were food samples (١١ milk,

١١ cheese, ١ nugget, ٢ smoked fish, ٣ leeks, ٤ water, and ٤ soil). However, the results from biochemical tests varied: out of the ٣٦ colonies analyzed, two were positive for motility, three were positive for the CAMP test, and one was positive for catalase, which in total, identified three of the ٣٦ colonies as positive. Two colonies were both motility and CAMP positive, and one colony was both catalase and CAMP positive; all three were from food samples (two cheeses and one nugget). However, the PCR results indicated the formation of a ٤٤٦-base-pair fragment, showing Listeria monocytogenes contamination in ٢٢ of the analyzed samples, three of which were environmental samples (٦ milk, ١٠ cheese, ١ nugget, ١ smoked fish, ١ leek, ٢ water, and ١ soil).

Conclusion: The findings of this research revealed a significant discrepancy between the results obtained from biochemical and molecular tests. According to the molecular results, a considerable percentage of the samples were contaminated with Listeria monocytogenes, whereas the biochemical methods indicated a much lower percentage. This notable difference could serve as a valuable topic for future studies. Future researchers can not only repeat the experiment to investigate the reasons for the inconsistency between the two methods, but also examine clinical samples in addition to food and environmental samples.

Keywords: Listeria monocytogenes, food, environment, biochemical methods, PCR

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Comparative Study of the Efficacy and Side Effects of Liposomal Platinum-Based Nanodrugs Versus Conventional Chemotherapy in the Treatment of Advanced Colon Cancer (Research Paper)

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Introduction: The treatment of advanced colon cancer has historically relied on conventional chemotherapy, which, despite its efficacy, often results in significant side effects that impact patients' quality of life. In recent years, advancements in nanotechnology have introduced liposomal platinum-based nanodrugs as a promising alternative. These nanodrugs are designed to enhance the delivery of chemotherapeutic agents directly to cancer cells, potentially increasing efficacy and reducing systemic toxicity. This study aims to compare the efficacy and side effects of liposomal platinum-based nanodrugs with those of traditional chemotherapy in patients with advanced colon cancer.

Methods: This comparative study was conducted on a sample size of ٢٠٠ patients diagnosed with advanced colon cancer. The sample included ١٢٠ males and ٨٠ females, with a mean age of ٥٥ years. The participants were randomly divided into two groups: the experimental group (Group A), which received liposomal platinum-based nanodrugs, and the control group (Group B), which received conventional chemotherapy. Each group consisted of ١٠٠ patients. The treatment regimen for Group A involved the administration of liposomal platinum-based nanodrugs at a dose determined by body surface area, while Group B received standard doses of conventional chemotherapeutic agents. The primary endpoints were overall survival (OS), progression-free survival (PFS), and incidence of side effects, which were monitored over a ١٢-month period. Secondary endpoints included quality of life assessments and response rates, measured through imaging and biomarker analysis.

Results: The study revealed that the overall survival rate at ١٢ months was significantly higher in Group A (٧٠ patients) compared to Group B (٥٥ patients). Progression-free survival was also notably improved in Group A, with ٦٥ patients showing no disease progression at the end of the study period, compared to ٥٠ patients in Group B. The incidence of severe side effects, such as grade ٣ and ٤ neutropenia, was lower in Group A (٢٠ patients) compared to Group B (٣٥ patients). Additionally, gastrointestinal toxicity, including nausea and vomiting, was reported in ٣٠ patients in Group A and ٤٥ patients in Group B. Quality of life assessments indicated that patients in Group A had better overall scores, with ٦٠ patients reporting significant improvements, compared to ٤٠ patients in Group B. Response rates, determined through imaging, showed that ٥٠ patients in Group A had partial or complete tumor reduction, whereas only ٣٥ patients in Group B demonstrated similar outcomes.

Conclusion: The findings of this study suggest that liposomal platinum-based nanodrugs offer a superior alternative to conventional chemotherapy in the treatment of advanced colon cancer. The enhanced efficacy, evidenced by higher overall survival and progression-free survival rates, coupled with a lower incidence of severe side effects, highlights the potential of nanodrug therapy to improve patient outcomes. These results support further research and development of liposomal nanodrugs as a viable option in oncological treatment protocols

Keywords: Advanced colon cancer, liposomal platinum-based nanodrugs, conventional chemotherapy, overall surviv

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Comparison of bioactive compounds of honey and royal jelly in controlling infectious diseases

(Review)

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Introduction: Bee products such as honey, propolis, and royal jelly, in addition to their nutritional value, have many therapeutic properties, including antimicrobial properties, accelerating wound healing, treating digestive disorders, and protective effects on reproductive health. Honey is a natural sweetener. The composition and quality of honey depend on various factors and has many therapeutic properties such as antibacterial, antiviral and antifungal. Biological activities of honey depend on phenolic compounds, such as phenolic acids and flavonoids. Different types of honey such as Manuka, thymol, pine and chestnut have strong healing and antioxidant properties (١). Royal jelly (RJ), as a bee product, has received attention for its medicinal properties, including antimicrobial, antioxidant, and anticancer activity. RJ has multiple biological properties such as anti-tumor, anti-allergic, anti-inflammatory and immune system regulation (٢).

Methods: Honey is a solution rich in fructose and glucose, which, in addition to sugar, contains various nutrients such as vitamins (C, B٦, thiamin, riboflavin, niacin, pantothenic acid), minerals (calcium, copper, magnesium, iron, manganese, potassium, phosphorus, sodium, zinc) and bioactive compounds such as polyphenols (phenolic acids and flavonoids). The exact composition of phenolics in honey varies depending on the type of plant from which the bees collected the nectar. Royal jelly is a viscous gelatinous substance composed mainly of water, protein and carbohydrates. . This substance is rich in minerals, vitamins, enzymes and bioactive compounds such as royalactin, ١٠-hydroxy-٢-decenoic acid and polyphenols. Polyphenol compounds in royal jelly include phenolic acids and flavonoids, which have many medicinal properties. Honey inhibits the growth of bacteria with its low acidity, high osmotic pressure and antioxidant compounds (٣).

Results: Honey is a natural product rich in nutrients that has various healing properties. This substance is effective against microbial infections, prevents the proliferation of malignant cells, reduces blood sugar levels in diabetic patients, and protects the nervous, respiratory, and digestive systems (٤). Due to its antimicrobial, antioxidant, antitumor, immune system modulating, estrogenic, anti-inflammatory, liver protection and nerve protection properties, royal jelly is used in food, cosmetic, health and medical fields. RJ fights against a wide range of pathogenic bacteria such as P. aeruginosa, E. coli and S. aureus. RJ shows promise as an alternative treatment for life-threatening health conditions. Because of their antimicrobial properties,honey and royal jelly have a high potential to replace antibiotic drugs (٥).

Conclusion: With the increase of antimicrobial resistance, bee products have been proposed as a natural and promising source to deal with bacteria, fungi and microorganisms. These products have a strong antimicrobial activity that depends on their chemical composition. Bee products, such as royal jelly, propolis and honey, are rich sources of bioactive compounds with diverse biological properties. The composition of these products is significantly different due to the diversity in the diet of bees. Studies have shown that bee products have an effective role, especially in wound healing. The antimicrobial, antioxidant, immune-modulating and anti-inflammatory properties of these products accelerate the wound healing process (1).

Keywords: Honey, Royal jelly, Antimicrobial, Antioxidant

Comparison of food intake and anthropometric indices in hirsutism women and healthy women of reproductive age referring to women's clinics of Shahid Rahimi Hospital in Khorramabad city in the summer of ۱٤۰۲ (Research Paper)

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Introduction: Hirsutism is an increase in end-to-end and androgen-dependent hair in women that can occur due to idiopathic causes, ovarian problems, adrenal glands, pituitary gland and taking medications. The aim of this study was to determine the prevalence of hirsutism and its relationship with factors such as Body Mass Index (BMI), menstrual pattern, acne, history of PCOS, skin and hair color, and family history. The present study was designed to investigate and compare the history of dietary intake and anthropometric indices in women with hirsutism and healthy women. Also ،considering that if anthropometric indices and dietary intake on hirsutism can be prevented by relatively simple measures ،this study was designed to help eliminate or reduce the occurrence of hirsutism in women.

Methods: This study is a case and control study. In this study, the group of patients includes all women with hirsutism who referred to obstetrics and gynecology clinic in Shahid Rahimi Hospital in the summer of ۱٤۰۲. The comparison group included healthy women of reproductive age who were the same number as the case group, who had been referred to the obstetrics and gynecology clinic at the same time considering the inclusion criteria.

Results: It was observed that there was a significant difference between the two groups except for occupation, smoking and the presence of underlying disease (P>۰,۰٥) in other variables of child, education and family history (P<۰,۰٥). Based on the table ۱-٤, it can be seen that in the control group, only ۹,۳ percent of people had a family history of hirsutism, compared with ٤۹,٥ percent of those with hirsutism. The mean BMI of hirsutism group was significantly higher than healthy group (P<۰,۰۰۱).

Conclusion: It was found that dietary patterns and obesity play an important role in the development of hirsutism. Reducing the consumption of medium and high-fat dairy products, having a healthy lifestyle and maintaining normal weight in the range of normal have an effective role in preventing hirsutism.

Keywords: food intake ; anthropometric indices ; hirsutism

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Comparison of the effect of eight weeks of aerobic exercises in water with the addition of honey and cinnamon on hormonal parameters in infertile women (Research Paper)

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Introduction: ۳. Introduction: Studies have shown that there is a strong connection between inactivity and infertility. Sports activities improve the secretion of sex hormones in women due to the improvement of blood circulation and secretions of endocrine glands. On the other hand, both honey and cinnamon are very effective foods in increasing the secretion of hormones involved in fertility. Cinnamon is a spice with antioxidant and anti-diabetic properties. It is a very good source of minerals such as potassium, iron, the factor that supplies blood to the glands, and calcium. The purpose of this study is to compare the effect of aerobic exercise alone and with supplements. effects of honey and cinnamon on hormonal parameters in infertile women aged ۲۰ to ۲۵ years.

Methods: In this research, ٦۰ infertile women (this group of women who had less than half an hour of physical activity and movement per day) with an average age of ۲۰ to ۲۵ and a similar BMI were randomly selected. The subjects were divided into two groups: exercise in water alone and exercise with honey and cinnamon supplements. The training protocol of water exercise is eight weeks, three days each week, and two hours of aerobic exercise every day (starting with ۵۰٪ of the maximum heart rate in the first and second weeks, and in the seventh and eighth weeks, the training intensity reached ۷۵٪ of the maximum heart rate. which were controlled with smart watches and polar heart rate monitors) in water at a depth of one meter and daily consumption of ۱۵۰ mg of cinnamon and ۱٦ grams of pure honey was given half an hour before the start of training. Then, the measurement of thyroid hormones (TSH, T٤, T۳) and sex hormones LH, FSH, Estrogen, Progesterone in the obtained sera was done by ELISA method. Finally, SPSS software and Independent-samples T-Test were used.

Results: The level of thyroid hormone in the statistical test did not show a significant difference in the secretion of basic thyroid hormones ($p>۰,۰۵$). However, the levels of LH-FSH-PROGESTRONE-ESTROGEN hormones showed a significant difference in the training and dietary supplement groups ($p\leq۰,۰۵$).

Conclusion: Water sports and hydrotherapy have an effect on the function of endocrine glands, especially sex hormones. But the lack of change in thyroid hormones may have been caused by the type and duration of training. And in this case, it is better to control and review the type and intensity of exercise.

Keywords: Aerobic exercises, honey, cinnamon, infertile women

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Complete inhibition of phosphatase and tensin homolog promotes the normal and oxygen-glucose deprivation/reperfusion-injured PC۱۲ cells to cell death (Research Paper)

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Introduction: PTEN antagonizes PI۳K/AKT cell survival pathway. The effect of PTEN inhibitors has been rarely examined on cell survival following reperfusion injury. We investigated the neuroprotective effect of SF۱٦۷۰, as a new PTEN inhibitor, on an in vitro stroke-like model.

Methods: PC۱۲ cells were exposed to OGD/R. The cells were treated in five conditions as follows: NO/NG; ٦۰ minutes OGD; ٦۰ minutes OGD and ٦ h reperfusion; OGD/R treated with ۱۰ µM SF۱٦۷۰, and NO/NG treated with ۱۰ µM SF۱٦۷۰. Phosphorylation levels of AKT, P۳۸ in PC۱۲ cells were measured by immunoblotting. The cell viability was also determined by colorimetric assay.

Results: The results of the current study showed that SF۱٦۷۰ increased p-AKT, and decreased p-P۳۸, p-JNK, and cell viability in the PC۱۲ cells exposed to OGD/R insult. This paper demonstrated that complete inhibition of phosphatase activity of PTEN promoted cells toward death, possibly through attenuation P۳۸ signaling pathways in OGD/R PC۱۲ cells.

Conclusion: Overall, our results demonstrated that complete inhibition of phosphatase activity of PTEN not only did not exhibit neuroprotective effect but also promoted PC۱۲-deprived cells to death.

Keywords: OGD, Reperfusion Injury, AKT, P۳۸, MAPK, PC۱۲ Cells

complications of hpv viruses (Review)

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Introduction: hpv virus or human papilloma virus belong to papilloma virid family . more than ۲۰۰ types being discovered some of them only lead to beneign and harmless lesions like warts and some lead to dangerous diseases like skin and mucosal cancers .

Methods: this research has been collected by reliable sites such as elsevior , popmed , etc

Results: human papilloma viruses are small , non enveloped virus consist of ۸۰۰۰ base pairs that infect mucosal and cutaneous epithelia in a vertebra . genom of hpv consist of the early regeons e۱to e۷ necessory for replication and and the late regeon proteins l۱ and l۲ that are required for virion assembly and the largely non coding part or lcr which contains cis elements that are necessary for the replication and transcription of viral dna . some types are beneign not cancerous and some causes cancer after infecting . like cervix , oral , nasopharyngeal, rectal and penil

Conclusion: hpv infection is kind of viral infection and in most cases , contamination is done through the skin and mucous membranes. depending on the type that causes the infection , it leads to different results from warts to cancers .

Keywords: warts, cancer , virus , contamination, replication

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Computational drug repurposing based on the RNA sequencing data analysis for colorectal cancer

(Research Paper)

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Introduction: Colorectal cancer (CRC) is the third most common diagnosis malignancy and the second leading cause of mortality worldwide. Given the prevalence of CRC, its high heterogeneity, and the limitations of its treatments, exploring novel therapeutic options is a pressing issue that needs to be addressed. Drug repurposing offers an affordable solution by identifying new indications of approved or investigational drugs to develop new treatments for a different disease. RNA sequencing (RNA-seq) is one effective approach that helps discover new functional genes. Besides, RNA-Seq has an immense application in cancer research and development of cancer therapeutics. Therefore, this study aimed to reveal the drug-repurposing candidates for CRC by applied a computational drug repurposing pipeline using the RNA-seq data.

Methods: The RNA sequencing of ٢٠ colorectal tumor samples with matched adjacent normal colorectal tissue under the accession code GSE١٤٢٢٧٩ were obtained from the GEO database (https://www.ncbi.nlm.nih.gov/geo/). The differentially expressed genes (DEGs) between CRC and normal tissues were obtained by using GEO٢R. Next, the Library of Integrated Network-based Signatures (LINCS) database was used to identify potential candidate drugs which can reversed the expression of DEGs. Then, through considerable literature review and drugbank (https://go.drugbank.com) studies, the top-ranked drugs with the highest p-value were selected. Besides, all DEGs were subjected to GO and KEGG pathway enrichment analysis on the Enrichr online platform (https://maayanlab.cloud/Enrichr/). GO analysis categorizes genes function into three parts: biological processes, cellular components, and molecular functions.

Results: This study identified ٤٧١٣ genes with |log٢FC|>١ and P-value <٠,٠١ as DEGs: ٢٥٢٦ upregulated and ٢١٨٧ downregulated genes. In drug list, we selected cancer and non-cancer drugs, among which Pentobarbital and Canertinib can be mentioned. Pentobarbital is used to induce sleep, cause sedation, and control certain types of seizures. Canertinib is a pan-erbB tyrosine kinase inhibitor which work against esophageal squamous carcinoma. GO ontology analysis demonstrated that for biological processes analysis, DEGs were mainly enriched in extracellular structure organization, cellular component were significantly enriched in collagen-containing extracellular matrix, and molecular function was enriched in frizzled binding. The results of KEGG pathway enrichment indicated that the DEGs were mainly enriched in cell adhesion molecules and Wnt signaling pathway.

Conclusion: This study proposed Pentobarbital and Canertinib drugs as promosing repurposable candidate for the treatment of CRC progression that it's probably can used to different stages of disease progression.

Keywords: Colorectal cancer; Drug repurposing; RNA sequencing

Computational Investigation of DNA Aptamer-OmpA Protein Interactions for Enhanced Biosensor Development in Klebsiella pneumoniae Detection (Research Paper)

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Introduction: Klebsiella pneumoniae is an opportunistic bacterium and a frequent cause of infections, such as urinary tract infections, bacteremia, or respiratory tract infections that mainly affect immunocompromised patients [١]. Timely and accurate detection of this bacterium is crucial for correct medical intervention [١]. Short strands of DNA or RNA, named aptamers, are currently attracting increasing interest as alternatives to antibodies for their use in biosensing [٢]. The higher binding affinity of these molecules towards selected targets may allow detection strategies for pathogens [٢]. This article employs computational approaches to explore the recognition process between a DNA aptamer and outer membrane protein A (OmpA), a critical surface protein in Klebsiella pneumoniae, which has been identified as a potential target in previous studies [٣]. This interaction was explored to potentially provide key insights into the design of more effective biosensors for bacterial detection.

Methods: The DNA aptamer sequence used in this study was previously obtained through the SELEX methodology, specifically for the detection of Klebsiella pneumoniae [١]. The OmpA protein structure was retrieved from Protein Data Bank PDB ID: ٧RJJ [٤]. To prepare the protein structure for docking, we minimized it with the YASARA web server[٥]. Using AlphaFold٣ [٦], the ٣D structure of the DNA aptamer was predicted and the secondary structures of the DNA aptamer were analyzed using NUPACK [٧], providing crucial insights into its folding characteristics. HADDOCK٢,٤ web server [٨] was used for docking the aptamer and the protein. The top-rated docking output clusters were chosen according to Haddock score, cluster size, and interaction energy values. Finally, we used PyMOL[٩] to examine the polar interactions between aptamer and OmpA protein at a ٥Å distance.

Results: Docking led to the identification of Cluster ٩ as the highest-scored complex, with a Haddock score: ٢١,٩ ±٢٦,٤ The calculated for van der Waals and electrostatics energies were –١٢٥,٨ ± ١٠,٥ and -٢٦٤,٤ ± ٧٩,٦ respectively. Calculation of the interaction between aptamer and protein showed a buried surface area of ٢٩٦٠,٢ ± ١٧٥,٧ Å² for this complex. Suggesting a large contact region formed by these two molecules. Extensive mapping of the polar interactions identified multiple interaction sites between aptamer and OmpA protein. Including ARG-٥٣٥, ARG-٤٥٣ and LYS-٤٥٢. These interactions indicate that the aptamer is a good candidate for targeting OmpA, making it feasible for advancing novel biosensing designs.

Conclusion: This study demonstrates the value of integrating in silico tools along with experimental SELEX for optimizing DNA aptamer-protein interactions, which is crucial for developing efficient biosensors. By leveraging computational methods before or after SELEX, we can rapidly identify and

refine aptamer candidates, thereby accelerating the development of diagnostic approaches for Klebsiella pneumoniae. These findings highlight the importance of incorporating in silico approaches early in the biosensor design process, offering a cost-effective and swift solution for enhancing pathogen detection.

Keywords: Klebsiella pneumoniae, DNA aptamer, in silico analysis, biosensor, OmpA protein

Computational prediction of multidrug-resistant Acinetobacter baumannii Epitopes: A bioinformatic approach to Acinetobacter vaccine development (Research Paper)

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Introduction: Acinetobacter baumannii, a Gram-negative bacterium, has become a prominent nosocomial pathogen, especially in intensive care units. Its capacity to develop resistance to multiple antibiotics, including polymyxins, has resulted in the emergence of multidrug-resistant (MDR) strains. This alarming trend underscores the urgent need for innovative therapeutic strategies, with vaccine development being a particularly promising approach. The advent of computer-aided vaccine design presents a viable pathway for developing effective vaccines. Research indicates that several proteins are overexpressed in MDR A. baumannii, such as B Barrel Outer Membrane Protein (BAM), Porin, and Lipoproteins. These proteins play a key role in cell membrane formation, maintaining outer membrane integrity, and contributing to the bacterium's drug resistance mechanisms. Consequently, they represent potential candidates for vaccine development. In this study, epitopes were devised for these proteins using specific bioinformatics tools.

Methods: Protein sequences retrieval The FASTA-formatted amino acid sequences of outer membrane proteins: BamD (A۰A۰۰۹Q۲E۵), Putative lipoprotein (B۰VSC٦), Porin subfamily protein (A۰A۰٦۲IZ۲۵), and Peptidoglycan-associated lipoproteins (A۰A۰۰۹TK٤١ and A۰A٤۰٤ASL۳) were obtained from UniProt (https://www. uniprot.org/) database. And saved for subsequent analysis. Epitope Prediction In this step, we aimed to predict linear B cell, Cytotoxic T lymphocyte (CTL), and Helper T lymphocyte (HTL) epitopes. To achieve this, different bioinformatics servers capable of identifying these specific types of epitopes were employed. Prediction of B-Cell Epitopes The prediction of linear B cell epitopes was conducted using the IEDB database (http://tools.iedb.org/bcell/). The Bepipred Linear Epitope Prediction ۲,۰ method was employed for this purpose. Prediction of MHC class I binding epitopes we utilized the IEDB web server to predict ۹-mer epitopes with potential binding affinity to MHC-I molecules, employing the IEDB recommended method ۲۰۲۰,۰۹ (NetMHCpan EL ٤,۱). A cut-off value of percentile rank<۱ was set to identify high-affinity epitopes, and the reference human HLA allele set was used for prediction. Prediction of MHC class II binding epitopes For MHC class II binding epitopes, we used the IEDB web server to identify ۱۵-mer epitopes with potential binding affinity to MHC-II molecules, employing the NetMHCIIpan ٤,۱ EL prediction method. The human HLA-DR allele set was used as the MHC source species, and high-affinity epitopes were screened by adjusting the percentile rank<۱ as the cut-off value. The antigenicity and allergenicity assessment The antigenicity of selected epitopes was predicted using VaxiJen v۲,۰ server (by set of ۰,٤ threshold). And, their allergenicity was checked by the employment of Allertop server.

Results: The top-scoring HTL and CTL alleles were predicted from MDR A. baumannii proteins using the IEDB database. Specific peptides and their corresponding length, Antigenicity score, and allergenicity nature are presented.

Conclusion: Epitope prediction is the foundational step in the design of multi-epitope vaccines. This study focused on predicting potential B-cell, CTL, and HTL epitopes using various bioinformatics servers and criteria to identify peptides with high binding affinity to human HLAs. The selected epitopes were both immunogenic and non-allergenic.

Keywords: Acinetobacter, Bioinformatics, Vaccine, Epitope-prediction

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Computational studies on inhibitory effects of Steppogenin against collagenase as an Anti-aging agent (Research Paper)

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Introduction: Collagenase is a type of matrix metalloproteinase in three forms that digests triple-helical collagen, an essential structural protein in human skin. This collagen degradation is crucial in various activities like breaking down old tissue, building new tissue, and involving specific cells. After biological aging, there is a marked increase in collagenase activity, leading to modifications in collagen configuration within the extracellular matrix, which subsequently results in skin changes such as wrinkles. Flavonoids are polyphonic compounds that are primarily found in fruit and food plants. Flavonoids have significant antioxidant features that help protect the skin from oxidative damage. Steppogenin is classified as a flavonoid and is commonly found in Moraceo plants. This compound's inhibitory features, such as its role in inhibiting tyrosinase, are proven. However, its inhibitory effect on collagenase has not been thoroughly studied. This study aims to investigate the inhibitory effect of steppogenin on collagenase enzymes using computational studies.

Methods: We started the study, by extracting steppogenin from the PubChem site and converting it into a PDB format suitable for the docking process. The collagenase enzyme was obtained from the RCSB PDB site using the ٢D١N code, and unnecessary parts of the protein, such as water molecules, were eliminated to get a clearer view of the interactions later in docking. Molecular docking was carried out to investigate the interaction between Steppogenin and collagenase using AutoDock Vina.

Results: Steppogenin and collagenase enzyme (code: ٢D١N) formed a ligand-protein complex through hydrogen bonding with an affinity of -٨,٤٤٨ kcal/mol. Two chains A and B are connected to the ligand. ARG١٥٥ created the first hydrogen bond in the B chain, where the NH٢ group of the protein interacted with the oxygen atom of the ligand. ILE١٢٢ formed the second hydrogen bond in the A chain, where the protein's oxygen atom interacted with the ligand's hydrogen atom.

Conclusion: Based on the results of bioinformatic interactions, it is recommended that the inhibitory property of steppogenin be investigated in laboratory conditions.

Keywords: Steppogenin, Collagenase, Anti-aging, Bioinformatic, Inhibitory effects

Correlation Between Reduction of E-cadherin Expression and Triple-Negative Breast Cancer

(Review)

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Introduction: Triple-negative breast cancer (TNBC), an aggressive subtype of breast cancer, is characterized by deficiency of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor-۲ (HER۲). Identification of novel prognostic markers would allow a better characterization of this subgroup of breast cancers and aid in therapeutic decisions. Recently, a new panel of biomarkers was identified in order to provide both prognostic and predictive information in TNBC. Among them, some of the most promising markers are the Androgen receptor, E-Cadherin, and Ki-٦٧ expression. E-cadherin is a transmembrane glycoprotein that mediates calcium-dependent cell-to-cell adhesion, fundamentally important to the generation of a polarized epithelial phenotype.

Methods: In the current study, keywords including E-cadherin, Triple-Negative Breast Cancer, and Progression were reviewed from the list of Mesh and other credible websites including PubMed, Science Direct, and Google Scholar, and the data was organized. The searches comprised all published papers from ۲۰۱۳ to ۲۰۲۳. All of the full text was considered, and the papers manifested as only abstract were excluded. The full papers selected focused on the reduction of E-cadherin expression in triple-negative breast cancer only. A total of ٥٠ papers were selected and studied in this review.

Results: Evidence suggests that collective invasion plays a major role in tumor progression. Numerous studies showed that E-Cadherin is involved in collective cell behavior that leads to invasion and metastasis. Moreover, experimental evidence indicates that the loss of E-cadherin expression is crucial for the acquisition of the invasive and metastatic capacities of epithelial tumors. Also, Downregulation of E-cadherin expression represents an epithelial-to-mesenchymal transition hallmark and is associated with chemoresistance in TNBC. Articles showed the loss of E-cadherin expression has been found to be significantly associated with a lack of estrogen receptor expression, the expression of cytokeratins ٥/٦ and/or epidermal growth factor receptor, and a basal-like phenotype in breast cancer. Unfavorable prognosis significance of the loss of E-cadherin expression has been demonstrated in different studies. Thus, its absence is frequently associated with a large tumor size, metastatic lymph node status, local or regional tumoral recurrence, low grade of differentiation, advanced tumoral stage, and triple-negative subtypes.

Conclusion: The role of E-Cadherin in cancer progression is established and well-documented, represented by repression of E-Cadherin expression at the primary tumor site. E-Cadherin has been

classified as a tumor suppressor and diminished E-Cadherin expression in epithelial cancer cells has been related to the process of epithelial-to-mesenchymal transition in multiple carcinomas, including breast cancer and to the acquisition of chemoresistance.

Keywords: E-cadherin, Triple-Negative Breast Cancer, Progression

Crimean- Congo hemorrhagic fever (Review)

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Introduction: Crimean-Congo hemorrhagic fever (CCHF) is a disease transmitted by ticks that can cause symptoms ranging from mild to severe, and it has been reported in over ۳۰ countries. Prompt identification and isolation of individuals with suspected or confirmed CCHF, along with the implementation of suitable prevention and control measures, are crucial for preventing the spread of the disease from person to person. Crimean-Congo hemorrhagic fever (CCHF) is the result of a virus carried by ticks, specifically a member of the Nairovirus genus in the Bunyaviridae family. Initially, the disease was noted in soldiers from the former Soviet Union stationed in Crimea during World War II, which is why it was named Crimea hemorrhagic fever.. Subsequently, scientists determined that the virus identified in Crimea was identical to the Congo virus, responsible for causing febrile illness in the Belgian Congo. As a result, the virus was designated Crimean-Congo hemorrhagic fever virus (CCHFV).

Methods: Current treatment for Crimean-Congo hemorrhagic fever (CCHF) relies on supportive care, close monitoring of blood and clotting factors, and replacement therapy as needed. Ribavirin, typically administered orally, is also used. While antiviral and antibody-based therapies for CCHFV have shown promise in preclinical settings, their effectiveness relies on well-equipped healthcare systems capable of quickly recognizing, diagnosing, and treating CCHFV infections. These therapies may be inaccessible to patients in regions with limited healthcare resources or who present with advanced disease. Over the years, various strategies have been explored to develop effective vaccines, ranging from inactivated virus formulations to nucleotide-based options such as DNA and mRNA vaccines.

Results: Although not all susceptible livestock and wild mammals are affected by the virus, it can cause serious hemorrhagic fever in humans. At present, there is no authorized vaccine or medication specifically designed for CCHF. Prevention primarily relies on implementing biosecurity measures. Ribavirin is the sole approved drug utilized in certain countries to manage the disease in humans, although recent studies have cast doubt on its effectiveness. CCHF exhibits similar clinical characteristics to other prevention hemorrhagic fevers. Following an incubation period of less than a week, patients experience sudden onset of fever, severe headache, muscle aches, nausea, diarrhea, and other general symptoms.

Conclusion: Despite the widespread geographic distribution of CCHFV and the large populations at risk, our understanding of the viral and host factors contributing to CCHFV pathogenesis remains incomplete. Further investigation into the functions of viral proteins is necessary, and the development of advanced molecular virology tools and improved animal models will provide crucial insights into the mechanisms of CCHFV disease. To protect at-risk populations in endemic areas,

preventative measures such as education, reducing tick exposure, treating livestock for tick infestations, livestock quarantine, and protective measures for high-risk activities must be implemented.

Keywords: Crimean Congo hemorrhagic - fever - prevention- viral - symptom

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CRISPR Technology in Type ١ Diabetes Treatment (Review)

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Introduction: Type ١ Diabetes (T١D) constitutes an autoimmune disorder that precipitates the obliteration of insulin-secreting β-cells within the pancreatic tissue. Existing therapeutic modalities, predominantly comprising insulin replacement, fail to target the fundamental etiology and may lead to various complications. CRISPR/Cas٩ represents an advanced genome-editing apparatus that employs a guide RNA (gRNA) to accurately direct the Cas٩ nuclease towards designated DNA sequences, engendering double-strand breaks. These breaks are amenable to cellular repair mechanisms, thus permitting gene knockout or insertion. The advent of CRISPR technology presents a novel and promising paradigm for the management of T١D, facilitating precise genetic modifications aimed at promoting both β-cell regeneration and modulation of the immune response. Methods: To gain a comprehensive understanding of the role of CRISPR in Type ١ Diabetes, a thorough literature search was conducted across PubMed, Google Scholar, and NCBI databases. This search identified ١٩ relevant articles that were carefully reviewed and analyzed to provide a deeper insight into this subject.

Methods: To gain a comprehensive understanding of the role of CRISPR in Type ١ Diabetes, a thorough literature search was conducted across PubMed, Google Scholar, and NCBI databases. This search identified ١٩ relevant articles that were carefully reviewed and analyzed to provide a deeper insight into this subject.

Results: β-Cell Regeneration: Investigators are probing the application of CRISPR to modify stem cells with the objective of differentiating them into insulin-secreting β-cells. This process entails the targeted alteration of genes that govern cellular differentiation and the production of insulin. Immune System Modulation: Through the utilization of CRISPR for the modification of immune system genes, it becomes feasible to mitigate the autoimmune assault on β-cells. This may involve the generation of cells that elicit a diminished immune response or the enhancement of the immune system's tolerance towards these cells. Advances in Cell Therapy: Preliminary investigations and clinical trials, such as those involving VCTX٢١١, indicate significant potential for CRISPR-enhanced cellular therapies. These studies concentrate on the development of β-cells capable of exhibiting improved survivability post-transplantation and evading immune-mediated rejection. Enhanced Gene Editing: CRISPR has facilitated the attainment of precise genetic modifications that augment the functionality and resilience of therapeutic cells. This advancement encompasses the enhancement of their resistance to immune assaults and the optimization of their insulin production efficacy.

Conclusion: CRISPR technology proffers a revolutionary strategy for the treatment of T١D by enabling meticulous genetic alterations. Although challenges persist, including the imperative to ensure safety and navigate ethical considerations, ongoing research continues to demonstrate promise in the quest to devise effective therapies that target the root causes of T١D. Subsequent investigations and clinical trials will be paramount in fully actualizing the potential of CRISPR in combatting this intricate disease.

Keywords: β-Cell, CRISPR/Cas٩, Type ١ Diabetes

CRISPR-Mediated Modulation of mRNA Expression in Breast Cancer Cells: Implications for Targeted Therapy (Research Paper)

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Introduction: Breast cancer remains a significant global health concern, necessitating the exploration of innovative therapeutic strategies. CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) technology offers precise control over mRNA expression levels, presenting a promising avenue for targeted therapy. This study investigates the efficacy of CRISPR-based mRNA modulation in breast cancer cells, focusing on specific genetic targets and therapeutic implications.

Methods: Patient-derived breast cancer cell lines representing different subtypes were subjected to CRISPR-mediated mRNA modulation targeting key oncogenes or tumor suppressor genes relevant to breast cancer pathogenesis. mRNA expression levels were quantified using quantitative real-time PCR before and after CRISPR-mediated modulation. Functional assays, including cell proliferation, migration, and apoptosis assays, were performed to assess the impact of mRNA modulation on breast cancer cell behavior.

Results: CRISPR-mediated mRNA modulation effectively altered the expression levels of targeted genes in breast cancer cells. Downregulation of oncogene mRNA expression, such as HER٢ (mean mRNA copies: ١٠٠٠ to ٢٠٠; p<٠,٠٠١), resulted in decreased proliferation and migration, while upregulation of tumor suppressor mRNA expression, such as BRCA١ (mean mRNA copies: ٢٠٠ to ٨٠٠; p<٠,٠٠١), led to enhanced apoptosis. These findings demonstrate the functional significance of CRISPR-mediated mRNA modulation in modulating breast cancer cell behavior.

Conclusion: The study highlights the therapeutic potential of CRISPR-based mRNA modulation as a targeted approach in breast cancer therapy. By precisely controlling gene expression levels, CRISPR technology offers a tailored strategy for disrupting oncogenic pathways and enhancing tumor suppressor functions specific to breast cancer. This research underscores the role of CRISPR-based mRNA modulation in advancing precision oncology interventions for breast cancer treatment.

Keywords: CRISPER, mRNA, Breast Cancer

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CRISPR/Cas۹ gene therapy in sickle cell disease. IS IT SAFE? (Review)

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Introduction: Sickle cell disease (SCD) is the most prevalent monogenic hematologic disorder, characterized by congenital hemolytic anemia resulting from an inherited point mutation in the β-globin gene on chromosome ۱۱. Despite the identification of the genetic basis of SCD in ۱۹۵۷, treatment options remain limited. Hematopoietic stem cell transplantation (HSCT) was seen as a potential cure, but only ۱۵٪ of donors were suitable. However, ex vivo engineering of autologous hematopoietic stem and progenitor cells, followed by transplantation of genetically modified cells, may offer a permanent cure for all patients, eliminating dependence on suitable donors and the risk of graft-vs-host disease. The advent of clustered regularly interspaced short palindromic repeats (CRISPR) and CRISPR-associated protein ۹ (Cas۹) systems have transformed the field by allowing precise targeting of genes. This study focused on clinical trials conducted on SCD patients using the CRISPR/Cas۹ gene editing method and its safety.

Methods: Data was obtained from MEDLINE, Scopus, and Web of Science databases via the following keywords: sickle cell disease, SCD, hemoglobinopathy, CRISPR/Cas۹, CRISPR, gene editing, gene therapy, complication, and side effects.

Results: After searching the terms mentioned, over ٦۰ articles were selected for the subsequent study. Twelve articles (including over ۲۰۰ patients) were selected for final examinations. We found out that ۷ major clinical trials are being conducted worldwide investigating the efficacy of CRISPR/Cas۹ for SCD treatment by targeting BCL۱۱A and HBB genes. As the results showed, all patients demonstrated clinically meaningful increases in total Hb and HbF, which occurred early and have been maintained over time, and almost all patients were free from vaso-occlusive crises for at least ۱۲ consecutive months. Several adverse effects were reported after engraftment of gene-modified hematopoietic stem cells, including nausea, vomiting, low blood cell counts, and organ toxicities, particularly in older patients; however, all these adverse effects were mentioned as busulfan-based myeloablative conditioning-related conditions. To date, no evidence of serious complications such as any malignancies has been reported.

Conclusion: Unlike older methods that used viral vectors potentially leading to acute side effects like leukemia by affecting genes related to cell growth and maturation, CRISPR/Cas۹ demonstrates promising results for treating hemoglobinopathies, including sickle cell disease and major β-thalassemia. While this treatment is novel, further monitoring is necessary to address any future complications.

Keywords: CRISPR/Cas۹, sickle cell disease, SCD, gene therapy

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CRISPR/Cas۹ genome editing approaches in cancer research (Review)

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Introduction: In cancer research, the CRISPR/Cas۹ technology, with its notable genome engineering accuracy, has displayed effectiveness as a powerful method. CRISPR technology's ability to target and change specific genes linked to cancer in oncogenes, tumor suppressor genes, and other related genes paves the way for cancer treatment and novel cancer research.

Methods: Scientific sites and sources such as Scopus, Google Scholar, and PubMed will be used to conduct this study. Also, the keywords CRISPR system, Genome editing, Cancer therapy, Preclinical studies, and Clinical trials will be used. Articles that are very old (before ۲۰۰۰) or do not have any of these keywords are excluded from the study.

Results: Recent studies in various tumor fields have explored potential uses of CRISPR/Cas۹ for gene-level treatment, and the development of personalized and targeted CRISPR/Cas۹ medicines could transform tumor treatment. Numerous preliminary tumor treatment studies have been conducted in relevant fields. CRISPR/Cas۹ may treat gene-level tumors.

Conclusion: However, CRISPR's clinical implementation in cancer therapy is still in its initial stages. This review elucidates the CRISPR technology and its role in cancer research, both pre-clinical and clinical. This could deepen researchers' understanding of cancer's genetic agents and lead to more advanced therapies.

Keywords: CRISPR system, Genome editing, Cancer therapy, Preclinical studies, Clinical trials.

Curcumin and sertraline can prevent the stress-induced changes in medial prefrontal cortex

(Research Paper)

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Introduction: Chronic stress induces morphological changes in the neurons of several brain regions, including medial prefrontal cortex (mPFC). This region is involved in variety of behavioral tasks, including learning and memory. Our previous work showed that stress impaired function. The present work extends the earlier work to study medial prefrontal cortex in stressed and non-stressed rats with or without sertraline or curcumin treatments using stereological methods. Sertraline is a selective serotonin reuptake inhibitor and curcumin is the main ingredient of turmeric with neuroprotective effects

Methods: n this study, ٤٢ male rats were randomly assigned to seven groups: stress + distilled water, stress + olive oil, stress + curcumin (١٠٠ mg/kg/day), stress + sertraline (١٠ mg/kg/day), curcumin, sertraline, and control groups. After ٥٦ days, the right medial prefrontal cortex was removed

Results: The volume of mPFC and its subdivisions and the total number of neurons and glia were estimated. The results showed ~٨٪, ~٨٪, and ٢٤٪ decrease in the volume of the mPFC and its prelimbic and infralimbic subdivisions, respectively. However, the anterior cingulated cortex remained unchanged. Also, the total number of the neurons and glial cells was significantly reduced (١١٪ and ٥٪, respectively) in stress (+distilled water or olive oil) group in comparison to the non-stressed rats (P<٠,٠١). However, no significant reduction was observed in the volume of the medial prefrontal cortex and its subdivisions as well as the total number of the neurons and glial cells in stress + sertraline and stress + curcumin groups in comparison to the non-treated stressed rats (P<٠,٠١)

Conclusion: The result indicated that treatment of rats with curcumin and sertraline could prevent the stress-induced changes in medial prefrontal cortex

Keywords: sertraline, curcumin, stress, cortex, stereology

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Curcumin can prevent the sodium metabisulfite-induced changes in the rats' deep cerebellar nuclei (Research Paper)

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Introduction: To evaluate the the possible neurotoxic effects of sulfite and the protective potential of curcumin on the deep cerebellar nuclei using stereological methods

Methods: The rats were randomly divided into five experimental groups (n=٦): Group I: distilled water, Group II: Olive oil, Group III: Curcumin (١٠٠ mg/kg/day), Group IV: Sodium metabisulfite (٢٥ mg/kg/day), and Group V: Sodium metabisulfite+curcumin. At the end of ٥٦ d, the right cerebellar hemispheres were removed and assigned to stereological studies. The total volume and total neuron number of deep cerebellar nuclei were assessed using Cavalieri and optical disector methods, respectively

Results: The data showed ~٢٠٪ and ~١٦٪ decrease was respectively observed in the total volume and the total neuron number of the deep cerebellar nuclei of the sulfite-treated rats in comparison to the distilled water group (P<٠,٠٤). However, no significant change was observed in the total volume and neuronal number of the deep cerebellar nuclei in sulfite+curcumin-treated rats and curcumin played a protective role against sulfite. Curcumin or its vehicle (olive oil) did not induce any significant changes

Conclusion: Curcumin, the main part of the turmeric, could prevent the structural changes induced in the deep cerebellar nuclei by sodium metabisulfite, a preservative agent, in rats

Keywords: Cerebellum; Curcumin; Deep cerebellar nuclei; Rat; Sulfite

Curcumin-Etoposide Synergy: Unveiling the Molecular Mechanisms of Enhanced Apoptosis and Chemoresistance Attenuation in Breast Cancer (Research Paper)

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Introduction: The combination of natural compounds has emerged as a potential strategy to combat cancer. Curcumin, a natural polyphenol, exhibits various anti-cancer properties, such as inducing apoptosis and arresting cell cycle progression. The present investigation aimed to examine the impact of curcumin and etoposide, both independently and in conjunction, on the initiation of apoptosis in cell lines of breast cancer.

Methods: Curcumin and etoposide-treated cell proliferation was assessed using MTT viability assays. The drugs' influence on cancer cell apoptosis was evaluated using Annexin V flow cytometry and caspase-۳ and ۹ activity assays. Quantitative real-time PCR was utilized for assessing the gene expression of Bax and Bcl-۲. The western blotting technique was employed to determine the quantity of p۵۳, p۲۱, Bax and Bcl-۲ proteins.

Results: A non-significantly effective dose of etoposide was chosen through the MTT assay and used in combination with ۷۵ µM of curcumin. Curcumin enhanced the effects of etoposide on cancer cell apoptosis by increasing caspase activities. Additionally, the combination of curcumin and etoposide exhibited a more significant reduction in the expression of the Bcl-۲ gene and the concomitant upregulation of Bax expression. Furthermore, the protein levels of p۵۳, p۲۱ and Bax were elevated upon treatment with the curcumin and etoposide combination compared to etoposide and curcumin alone, while the levels of Bcl-۲ protein were decreased, significantly.

Conclusion: Curcumin has the potential to enhance the apoptotic impact of etoposide on breast cancer cells. Therefore, we propose the aforementioned combination as a potential treatment for breast cancer.

Keywords: breast cancer, combination, curcumin, etoposide, apoptosis

Cutting-Edge Advances of Stem Cell Therapy in Cardiovascular Diseases: Investigating Mechanisms of Regenerative Medicine and Clinical Setting (Review)

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Introduction: Cardiovascular diseases (CVDs) remain the leading cause of mortality worldwide, underlining the vital necessity for innovative therapeutic approaches. Stem cell-based therapies hold momentous promise for CVDs treatment, paving the window to more personalized and operative interventions.

Methods: In this study, we used a variety of sources including PubMed/Medline, Google Scholar, Science Direct, Web of Science, and Scopus. The search was performed by using combinations of the keywords; stem cell, heart, cardiovascular diseases, regenerative medicine, and clinical trial.

Results: An in-depth understanding of the molecular mechanisms governing stem cell proliferation, differentiation, and migration has provided new approaches for more effective treatment. For instance, various signaling axes, such as Notch, Hippo-YAP, Wnt/β-catenin pathways, etc., have been recognized as critical regulators in the regeneration and repair of myocardium and control cell fate. Moreover, paracrine signaling due to exosomes and growth factors released by stem cells mediate tissue repair through regulating angiogenesis, fibrosis, and immune responses. Recently, bioengineering has developed biomaterials and scaffolds to enhance stem cell integration within a hostile ischemic environment, improving their retention and survival. With the development of gene-editing technologies, particularly CRISPR/Cas۹, stem cell function has also been further enhanced, enabling stem cells to be precisely modified to express cardioprotective genes. Nevertheless, challenges such as tumorigenicity, immune rejection, and scalability remain, mandating further research to harness stem cell potential in the treatment of CVDs fully. There is encouraging evidence of positive outcomes in different cardiovascular conditions in clinical settings. These trials have provided insight into the possibility of reducing mortality in patients suffering from acute myocardial infarction by using bone marrow-derived mononuclear cells. Furthermore, MSCs administration could recover left ventricular function and quality of life in clinical conditions.

Conclusion: Despite these progressions, the optimal cell type, dosage, timing, and route of administration remain subjects of debate. Standardizing trial designs and outcomes is also necessary due to the heterogeneity in trial designs and outcomes. Thus, to fully realize the potential of stem cells in cardiovascular medicine, further research is required to overcome these challenges.

Keywords: Stem Cell; Cardiovascular Diseases; Regenerative Medicine; Clinical Setting

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Cystic fibrosis diagnosis , treatment review article (Review)

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Introduction: Cystic fibrosis or cystic fibrosis (CF) is an autosomal recessive genetic disease characterized by a chronic course characterized by pancreatic exocrine insufficiency, chronic lung diseases, and increased concentrations of chlorine and sodium in sweat. This monogenic disease is the most common life-shortening disease. This article focuses on knowing and dealing with the causes and symptoms of the disease, type of diagnosis, treatment and health maintenance. It also contains guidance that is important and suitable for all people with CF regardless of age and eligibility for this disease.

Methods: CF is an autosomal recessive genetic disease caused by a mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. It is possible that they help to absorb sodium ions (Na+). As a result, the mucus and secretions of the organs such as the lungs, pancreas, liver, intestines and reproductive system become dehydrated and thickened, and they are also thicker and stickier than usual, which creates a suitable environment for microbial growth and blocks them and receives It makes it difficult for nutrients to pass through the digestive system, thus causing damage. CF causes several chronic complications in the pancreas, lungs and other body organs such as thick mucus, bacterial infection and inflammation, gradual decrease in lung function and finally, death.

Results: Recent clinical evidence suggests that to better understand and slow CF disease progression, it is important to consider not only specific pathogens, but also the role of the entire airway microbial communities or airway microbiota, including their interactions and functions.

Conclusion: CF causes several chronic complications in the pancreas, lungs and other body organs such as thick mucus, bacterial infection and inflammation, gradual decrease in lung function and finally, death. In addition, the amount of salt in sweat gland secretions also increases and in in fact, the salt needed by the body is excreted through sweat. Although CF has been observed in all races, it is predominantly a disease of Northern European populations.

Keywords: digestive system,lung,mucus,genetic and Cystic fibrosis

DCs Pulsed with Hypochlorous Acid-Treated Tumor Cell Lysates present antigens efficiently and induce CDʌ+ T cell activation through cross-presentation (Research Paper)

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Introduction: In the process of initiating and regulating immune responses, dendritic cells (DCs) play an important role as antigen-presenting cells. When dendritic cells are exposed to tumor cell lysates , they can stimulate T cells to recognize tumor-associated and tumor-specific antigens and generate an immune response against cancer. The purpose of this study, was to compare four different approaches for preparing breast tumor cell lysates for pulsing DCs.

Methods: To prepare tumor cell lysates from ٤T١ cells, four different methods were used, including freeze-thaw (FT), hypochlorous acid (HOCl), hyperthermia (HSP), and UVB irradiation (UV). Using flow cytometry and ELISA, we assessed the effects of these tumor lysates on DC maturation and cytokines secretion. Furthermore, DCs pulsed with different lysates were also evaluated for their ability to promote CDʌ+T cell proliferation and release cytokines.

Results: Our data demonstrate that DCs pulsed with lysate prepared by HOCl pulsed with HOCl exhibited more maturation surface biomarker expression (CDʌ٦) compared to DCs pulsed with freeze-thawed cells or unloaded DCs (control) (P<٠,٠,٥). Furthermore, activated DCs were also found to promote CDʌ+T cell proliferation and induce T cells responses by producing high levels of IFN-γ, while inhibiting IL-١٠

Conclusion: HOCl is capable of releasing tumor antigens while maintaining their ability to stimulate an immune response. .DC-based therapies may be designed based on the findings presented here, demonstrating a cross-presentation of antigens and specific activation of the immune system against breast cancer.

Keywords: Breast cancer; Dendritic cells; Tumor cell lysate; Hypochlorous acid

Decellularized sheep peritoneum: a good scaffold for in vitro cell culture (Research Paper)

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Introduction: The search for optimal biomaterials for tissue engineering and cell culture has led to the exploration of various natural scaffolds. This study investigates the potential of decellularized sheep peritoneum as a scaffold for in vitro cell culture. Decellularization, a process that removes cellular components while preserving the extracellular matrix, was applied to sheep peritoneum to create a biocompatible and non-immunogenic scaffold.

Methods: The decellularized tissue was characterized using histological, biochemical, and mechanical analyses to assess its structural integrity and cellular compatibility. Subsequent in vitro cell culture experiments were conducted to evaluate the scaffold's ability to support cell attachment, proliferation, and differentiation.

Results: The histological examination of hematoxylin and eosin and Masson's trichrome stained samples of decellularized and native peritoneum reveals complete decellularization while maintaining the extracellular matrix microarchitecture after ٤ days. Additionally, DAPI staining confirms the complete removal of DNA fragments from the tissue samples. Scanning electron microscopy shows that the ٣D ultrastructure of the peritoneum, characterized by a porous appearance, is well-preserved following decellularization. Microscopic analysis of in vitro cultured scaffolds indicates the viability of adipose-derived stem cells (ADSC).

Conclusion: The results indicate that decellularized sheep peritoneum provides a favorable microenvironment for cell growth, demonstrating its potential as a viable scaffold for tissue engineering applications. This study highlights the feasibility of using decellularized sheep peritoneum in biomedical research and its potential for future clinical use in regenerative medicine.

Keywords: decellularized sheep peritoneum, natural scaffolds, Adipose-derived stem cells

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Deciphering Molecular Mechanisms of Colorectal Cancer Metastasis: A Comprehensive Bioinformatics Analysis of Dysregulated Genes and Pathways (Research Paper)

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Introduction: Colorectal cancer (CRC) metastasis is a complex process involving dysregulation of multiple genes and pathways. This study employs a bioinformatics approach to unravel the molecular mechanisms underlying CRC metastasis, focusing on the identification of dysregulated genes and enrichment of pathways associated with metastatic progression. Understanding these molecular alterations is critical for the development of targeted therapeutic interventions to combat CRC metastasis and improve patient outcomes.

Methods: Gene expression data from CRC patients with and without metastasis were retrieved from publicly available datasets, including The Cancer Genome Atlas (TCGA) and Gene Expression Omnibus (GEO). Differential gene expression analysis was performed to identify genes differentially expressed between metastatic and non-metastatic CRC samples. Functional enrichment analysis, including gene ontology (GO) analysis and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis, was conducted to elucidate the biological processes and pathways dysregulated in CRC metastasis. Protein-protein interaction (PPI) network analysis was employed to identify key hub genes and potential regulatory networks associated with CRC metastasis.

Results: Analysis of gene expression data revealed a distinct gene expression signature associated with CRC metastasis, with numerous genes differentially expressed between metastatic and non-metastatic CRC samples. Functional enrichment analysis identified enrichment of biological processes related to cell adhesion, migration, invasion, and angiogenesis, highlighting their critical roles in metastatic progression. KEGG pathway analysis revealed dysregulation of pathways associated with epithelial-to-mesenchymal transition (EMT), extracellular matrix (ECM) remodeling, and PI۳K-Akt signaling in metastatic CRC. PPI network analysis identified hub genes, including key regulators of metastasis such as MMP۹, VEGFA, and CTNNB۱, and revealed potential regulatory networks governing CRC metastasis.

Conclusion: This comprehensive bioinformatics analysis provides novel insights into the molecular mechanisms driving CRC metastasis. Dysregulated genes and pathways identified in this study offer potential therapeutic targets for intervention in CRC metastasis. Targeting key molecules involved in EMT, ECM remodeling, and angiogenesis may hold promise for inhibiting CRC metastasis and improving patient outcomes. Further experimental validation of identified biomarkers and regulatory networks is warranted to translate these findings into clinically relevant therapeutic strategies for CRC metastasis.

Keywords: Colorectal Cancer (CRC) Metastasis, Hub Genes, KEGG Pathway Analysis, PPI Network

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Decreased Expression of BTG١ in Colorectal Cancer Tumor Tissue Compared to Adjacent Normal Tissue: Implications for Tumor Progression (Research Paper)

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Introduction: Colorectal cancer (CRC) is one of the most common malignancies worldwide, representing nearly ١٠٪ of all new cancer cases. It is a major cause of cancer-related deaths globally. The progression of CRC, including its invasion and metastasis, significantly influences clinical outcomes, survival rates, and the overall quality of life for affected patients. As such, identifying the molecular mechanisms and key targets responsible for CRC invasion and metastasis is critical in developing new therapeutic strategies. One of the genes of interest is B-cell translocation gene ١ (BTG١), a member of the TOB/BTG protein family, which has been shown to regulate cell proliferation, apoptosis, and the cell cycle. Previous studies suggest that BTG١ may play an essential role in inhibiting tumor development and progression through its involvement in various cellular processes such as DNA repair, transcriptional regulation, and cell division. BTG١ has been linked to several cancers, including gastric, kidney, liver, breast, and lung cancers, where it has been observed to have abnormal expression levels. The role of BTG١ in colorectal cancer, however, remains underexplored. Given the importance of BTG١ in regulating cellular processes related to cancer progression, this study aims to assess BTG١ gene expression in tumor tissues and adjacent normal tissues from patients with colorectal cancer, focusing on its potential role in CRC progression.

Methods: This study was conducted on a cohort of colorectal cancer patients, with samples collected from both tumor tissue and adjacent non-tumor tissue. Total RNA was extracted using standard protocols, and complementary DNA (cDNA) synthesis was performed. Quantitative Real-Time PCR (qRT-PCR) was used to measure the expression of BTG١. Primers specific for BTG١ were designed to span the exon-exon junction to ensure specificity. GAPDH was used as the reference gene for normalization of expression data. The qRT-PCR reactions were performed using SYBR Green Master Mix in a LightCycler® ٩٦ system. The relative expression levels of BTG١ were calculated using the ΔΔCt method, and comparisons between tumor and adjacent normal tissues were made. Statistical analysis was performed using SPSS v.١٦, and results were presented as mean ± standard deviation. Non-parametric tests, including the Mann-Whitney U test, were used for comparing BTG١ expression between the two tissue types, as the data were not normally distributed. A p-value of less than ٠,٠٥ was considered statistically significant.

Results: Our findings indicate a significant reduction in BTG١ expression in colorectal cancer tumor tissues compared to the adjacent normal tissues. The expression levels of BTG١ were markedly lower in the tumor samples, with a statistically significant difference observed between the two groups ($p < ٠,٠٥$). These results suggest that downregulation of BTG١ is a characteristic feature of colorectal cancer. Given BTG١'s role as an anti-proliferative gene that promotes apoptosis and regulates the cell cycle, the decreased expression observed in CRC tumor tissues may be associated with uncontrolled cellular proliferation and reduced apoptosis, which are hallmarks of cancer progression. Furthermore, BTG١'s involvement in processes such as DNA repair and transcriptional regulation may be impaired in colorectal cancer, contributing to genomic instability and enhanced tumorigenic potential.

Conclusion: The results of this study highlight the potential tumor-suppressive role of BTG١ in colorectal cancer. The significant reduction in BTG١ expression in CRC tumor tissues, compared to adjacent normal tissues, suggests that loss of BTG١ function may contribute to colorectal cancer development and progression. Previous studies in other cancers have demonstrated similar downregulation of BTG١, further supporting its role as a tumor suppressor gene across different cancer types. BTG١'s involvement in key cellular processes such as DNA repair, cell cycle regulation, and apoptosis underscores its importance in maintaining cellular homeostasis. Loss of BTG١ function may result in disrupted regulation of these processes, leading to increased cellular proliferation, resistance to apoptosis, and enhanced tumor progression in colorectal cancer. Moreover, BTG١'s influence on vascular endothelial growth factor (VEGF) expression and tumor neovascularization may also play a role in CRC metastasis. This study provides evidence for the downregulation of BTG١ in colorectal cancer, highlighting its potential role as a tumor suppressor gene. The reduced expression of BTG١ in tumor tissues suggests that it may be involved in regulating cellular processes that prevent tumor progression. Further research is needed to explore the molecular mechanisms underlying BTG١'s role in colorectal cancer and its potential as a therapeutic target. Targeting BTG١-related pathways may offer new avenues for developing treatment strategies aimed at limiting tumor growth and metastasis in colorectal cancer.

Keywords: Colorectal cancer, BTG١, gene expression, qRT-PCR.

Deep reinforcement learning to optimize fractional radiotherapy in head and neck cancer

(Research Paper)

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Introduction: Radiation therapy is one of the main approaches to the treatment of head and neck cancer. Radiotherapy uses ionizing radiation to selectively kill cancer cells and seeks to preserve as much as possible nearby healthy cells. Treatment planning is a crucial step in achieving this goal and enhancing the quality of treatment. However, the current method, which continuously delivers the dose, does not take into account the specific characteristics of the tumor that may affect the treatment outcome. The reinforcement learning (RL) method can be used to overcome these limitations. Optimization is achieved through sequential decision problems in the RL method, unlike the supervised learning method. Deep reinforcement learning (DRL) is the form of deep reinforcement learning that has gained popularity in recent years.

Methods: To solve the problem as efficiently and effectively as possible, an optimization RL agent's main objective is to find an optimal objective. According to the classifications introduced in previous articles, the methods used by RL to find an optimal goal are usually classified into the following two modes. ۱. Value-based approaches ۲. Approaches based on goal search We focus on the former in this research because they typically show better efficiency and stable performance, while the latter can be optimized directly. Value-based approaches rely on a value function that estimates the ideal for following a given goal and is gradually modified by an agent through environmental detection. A probability function is called a state-value function. Due to the risks associated with radiation therapy, in vitro models and to a large extent in vivo models are difficult to implement, and also require a lot of time and money. To address such issues, we propose a computational model that represents the evolutionary dynamics of a radiotherapy process using data directly extracted from patients' CT scans.

Results: The most common model for predicting the radiobiological response of the cell population is the linear-quadratic (LQ) model, which is currently also used in clinical practice to plan radiotherapy treatment, but despite its generality and comprehensiveness, the LQ model is inappropriate for the RL approach because the factors It does not take into account important secondaries such as dose rate, rate of radiation damage repair, and dose fractionation. Also, this model does not consider the temporal component (time effect), because it does not provide an overview of the temporal evolution of the system. Now, to overcome these limitations, we have come up with the Γ-LQ model, which allows studying the evolution of a cell population during the entire treatment by introducing a set of ordinary differential equations (ODEs) that extend the lifetime. But still the Γ-LQ model is limited in reality because it does not consider cell regrowth, in

fact there is another important secondary effect that we modeled using the Gompertz ODE model. Among several mathematical models that describe the growth of the tumor population, this model considers the decrease in the growth rate with the increase in tumor volume, and this is the best studied option.

Conclusion: This research not only provides a personalized treatment for volume adaptation, but also introduces a virtual radiotherapy environment for daily fractionation based on a set of ordinary differential equations that model tissue radiosensitivity by combining the effect of radiotherapy treatment and cell growth. Research parameters are estimated from CT scans that are routinely collected using a particle swarm optimization algorithm. This allows the DRL to learn the optimal behavior through an iterative process of trial and error with the environment. In this research, we came to the conclusion that the DRL approach can adapt to the radiation therapy process, optimize its behavior according to different functions, and finally perform better the current clinical practice.

Keywords: AI, Deep reinforcement learning, swarm optimization SCLC, Radiation therapy, Tumor treatment optimiz

Delivery of htsFLT۰۱ to YY۹ Cells by MiRGD peptide and Graphene Quantum Dots Nanoparticles

(Research Paper)

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Introduction: Retinoblastoma is a common intraocular malignancy that affects children. Vascular endothelial growth factor (VEGF) is a potent proangiogenic factor highly expressed in retinoblastoma. Inhibiting angiogenesis has shown promise in killing retinoblastoma cells, making anti-angiogenic therapy a potential new treatment strategy. htsFLT۰۱ is a fusion protein that can neutralize mouse and human VEGF and PlGF. MiRGD peptide contains various motifs, can penetrate cancerous tissue, and bind to overexpressed receptors in tumor cells. Graphene quantum dots have great potential in bio-imaging applications due to their biocompatibility, low cytotoxicity, and tunable fluorescence properties.

Methods: The htsFLT۰۱ plasmids were cloned in XL۱۰ bacteria and extracted using an anion exchange affinity column per the Favorgen Maxi preparation kit protocol. BL۲۱ bacteria containing the MiRGD gene were cultured in a ۲xyt medium and induced with IPTG at a final concentration of ۰٫۵ mM. The bacterial lysate was then transferred to a Ni-NTA chromatography column with an increasing imidazole and decreasing urea gradient. After observing the peptide bands on a ۱۵٪ SDS-PAGE gel, the purified peptide was desalted by dialysis. Graphene quantum dots were produced using the hydrothermal method with citric acid and urea. Their absorption and emission wavelengths were examined using Bio Tek cytation, and their functional surface groups were analyzed using FTIR. In the next step, ۱٫۰ µg plasmid was mixed with different amounts of the purified peptide at different nitrogen-to-phosphate ratios and incubated at room temperature for ٤۰ minutes. Various concentrations of GQDs were then mixed with the prepared pDNA/MiRGD complexes, and this step was performed on ice. These mixtures were incubated at ٤ °C with controlled agitation overnight. The formation of the complexes was preliminarily investigated using a gel retardation assay. Finally, DLS was conducted to determine the size and charge of GQDs,

MiRGD, and the complexes. The human RB cell line Y٧٩ was maintained in RPMI ١٦٤٠ medium containing ١٠٪ fetal bovine serum and ١٪ penicillin/streptomycin and was placed in a ٣٧°C, ٥٪ CO٢ incubator.

Results: The agarose gel electrophoresis results showed that the plasmid has good quality. The presence of the peptide band was confirmed using a ١٥٪ Tris-Glycine SDS-PAGE. The GQDs Cytation exhibited absorption at ٣٣٠ nm and emission at ٤٤٠ nm wavelengths. Gel retardation assays using acrylamide-based gels demonstrated stable dual and ternary complexes. Agarose-based gel retardation assays, followed by ethidium bromide staining, confirmed the binding of pDNA to the complexes. Dynamic Light Scattering determined the charges of GQDs, MiRGDs, and the complexes as -٢٣, +٦, and +١١, respectively.

Conclusion: We will conduct additional molecular investigations after identifying the optimal dose and timing for treating cells with the nano complex using the MTT assay. These will include apoptosis flow cytometry and real-time PCR to assess the final impact of the targeted gene delivery by the nano complex on inhibiting the retinoblastoma cell line by reducing angiogenesis.

Keywords: Retinoblastoma – gene delivery – peptide – nanoparticles

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Design and Development of Smart Nanocarriers for Targeted Delivery of Anticancer Drugs: From Basic Concepts to Clinical Applications (Research Paper)

Mojtaba Rashidi Mosleh,[۱,*] Majid Mesgartehrani,[۲]

۱.
۲.

Introduction: The development of smart nanocarriers for targeted drug delivery has revolutionized cancer therapy by enhancing drug efficacy while minimizing off-target effects. These advanced systems leverage nanotechnology to achieve precise tumor targeting, controlled drug release, and improved pharmacokinetics. This study explores the design principles, mechanisms, and clinical applications of smart nanocarriers in delivering anticancer drugs.

Methods: A comprehensive analysis was conducted, integrating data from experimental studies, computational modeling, and clinical trials. Nanocarriers such as liposomes, polymeric nanoparticles, dendrimers, and micelles were evaluated for their ability to encapsulate and deliver chemotherapeutic agents. Functionalization strategies, including ligand-mediated targeting and stimuli-responsive drug release, were examined to enhance specificity and efficacy. The study also assessed preclinical and clinical outcomes of nanocarrier-based therapies.

Results: Smart nanocarriers demonstrated superior tumor-targeting capabilities through active targeting mechanisms, such as ligand-receptor interactions and passive targeting via the enhanced permeability and retention (EPR) effect. Stimuli-responsive systems, triggered by pH, temperature, or enzymatic activity, enabled controlled drug release in the tumor microenvironment. Clinical data revealed significant improvements in therapeutic outcomes, including reduced toxicity and enhanced tumor suppression, particularly in patients treated with ligand-functionalized liposomes and polymeric nanoparticles.

Conclusion: Smart nanocarriers offer a transformative approach to cancer therapy, addressing the limitations of conventional drug delivery systems. By combining advanced functionalization techniques with tailored drug release mechanisms, these nanocarriers provide a promising platform for personalized and precision oncology. Future efforts should focus on optimizing scalability, regulatory compliance, and cost-effectiveness to facilitate their widespread clinical adoption.

Keywords: nanotechnology, tumor, Anticancer Drugs

Design of multi-antigen vaccine based on mRNA platform against cytomegalovirus and evaluation of expression of vaccine antigens at protein level in Vitro (Research Paper)

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Introduction: Cytomegalovirus is a widespread infection that is prevalent globally. In healthy individuals, this infection typically remains asymptomatic due to its slow replication, immune system inhibition, and suppression, but persists in the body indefinitely following initial infection. Mononucleosis is the most common complication resulting from this virus in healthy individuals. However, cytomegalovirus is considered a hazardous pathogen for those with weakened or suppressed immune systems, including organ transplant recipients, AIDS patients, premature infants, and individuals with various malignancies. At present, there is no approved vaccine available against CMV. Given the recent surge in pharmaceutical sanctions and the associated challenges and costs associated with accessing vaccines produced abroad, it would be difficult and expensive for the people of Iran to obtain such a vaccine. In light of these circumstances and the paramount importance of this subject matter, our objective in this study is to develop an mRNA vaccine against cytomegalovirus.

Methods: Initially, the desired antigens were meticulously selected by thoroughly scrutinizing scientific sources and utilizing immunoinformatic methods. Subsequently, an appropriate genetic construct was designed to express the chosen antigens, followed by the design of a suitable clonal vector for the genetic construct. The vector was then procured from Gene Universal for synthesis. Upon receipt of the designed vector, the appropriate cell was prepared and the vector was transformed into it. Bacteria containing the desired vector were then identified and cultured. The cloned plasmid was extracted and linearized using the appropriate restriction enzyme. An IVT reaction was performed using linearized DNAs. Thereafter, if the desired mRNA was properly synthesized, it was extracted and labeled. The protein expression of mRNAs in specific cell lines was measured using the western blot method.

Results: Upon receipt of the intended plasmids and their subsequent cloning in bacterial cells, it was observed that the insert sequence had been correctly integrated. Subsequently, these plasmids was subjected to purification and concentration measurement via nanodrop, rendering them suitable for employment in the in vitro transcription (IVT) reaction. After purification and encapsulation of mRNA and their treatment on cell lines and performing western blot and Flow cytometry , it was observed that the proteins had an acceptable expression.

Conclusion: According to the obtained results, it is concluded that the synthesized mRNAs have the ability to be expressed into protein and create antigens related to the cytomegalovirus virus, which probably has the potential to stimulate the immune system.

Keywords: Cytomegalovirus, mRNA vaccine

Determination of diagnostic value of CRP, cortisol and pro-calcitonin of cerebrospinal fluid in differentiation of types of meningitis (Research Paper)

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Introduction: Background Meningitis which refer to inflammation of leptomeningeal space is a dangerous condition. According to its etiological factor categorized into septic and aseptic meningitis. Septic meningitis need early therapeutic intervention thus differentiation of the type of meningitis could prevent neurological sequelae. Due to the delay in reporting the results of cerebrospinal fluid cultures, which are the gold standard diagnostic method, the use of rapid laboratory diagnostic tests will be handy. Objective This study was conducted to determine the diagnostic value of CRP, cortisol and procalcitonin (PCT) of cerebrospinal fluid (CSF) in differentiating the types of meningitis.

Methods: Methods This is a cross-sectional analytic study implanted in Shahid Beheshti hospital of Kashan city from Jan. ٢٠٢٣ to Jul. ٢٠٢٤. After obtaining the approval of the ethics committee (IR.KAUMS.MEDNT.REC.١٤٠٢,١٠٠); all patients` CSF samples who were taken with suspicion of meningitis collected from laboratory center. CSF pattern analyzed and samples with pleocytosis more than ٥ cells/mm٣ included in study. Patients with immune deficiency or autoimmune diseases, adrenal insufficiency, hypothalamic–pituitary axis disorders, cirrhosis, thyroidectomy and previous antibiotic and corticosteroid therapy excluded. After determining demographic information of patients, CSF samples analysis were carried out to determine CRP, cortisol and PCT level. By evaluating of CSF pattern along the clinical diagnosis, sensitivity and specificity of PCT, cortisol, and CRP of CSF tests in differentiating types of meningitis obtained. The receiver-operating characteristic (ROC) curve was used for determination of the cut off levels using SPSS software and other statistical tests was done.

Results: Results Out of ٦٨ participants in this study, ٤١ (٦٠,٢٩٪) cases were male and ٢٧ (٣٩,٧٪) were female. ٣٤ cases were diagnosed as septic and aseptic meningitis equally. Mean of age in septic meningitis was ٤٤,٥٩ years and ٣٧,٠٦ in aseptic group. Cut off level of PCT was ٠,٣٨ ng/mL with sensitivity and specificity of ٩٣,٩٪ and ٤١,٢٪ respectively in this point. Cut off levels for cortisol was obtained ٠,٩٩ µg/dL in the ROC curve. Sensitivity and specificity of cortisol was ٨١,٨٪ and ٣٢,٤٪ respectively. Sensitivity of CRP was ٦٤,٧٪ with specificity of ٣٢,٤٪ in cut off level of ٢,٥ mg/L in the ROC curve.

Conclusion: Conclusion CSF-PCT, cortisol and CRP has suitable diagnostic value in distinguishing between bacterial from aseptic meningitis especially in cases of negative bacterial culture of the blood and spinal fluid. Because the results of this research are in agreement with previous studies thus we recommend their usage in the clinical setting.

Keywords: meningitis, procalcitonin, CRP, cortisol, CSF

Determination of multiple antibiotic resistance patterns and identification of class I and II integrons in Staphylococcus aureus isolates in Gilan. (Research Paper)

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Introduction: Studies show that several different mechanisms including mobile genetic elements consisting of plasmids, transposons and integrons play an important role in acquiring and spreading antibiotic resistance genes . Integrons are one of the mobile genetic factors that are able to can carry and spread antibiotic resistance genes among these bacteria, and their horizontal transfer among bacteria is one of the most important ways of spreading resistance genes and creating resistant strains It is medicine. The purpose of this study is to determine the pattern of antibiotic resistance in clinical isolates of Staphylococcus aureus in Gilan and to investigate the gene class I and II integrons in isolates with multiple antibiotic resistance.

Methods: Sampling and isolation of bacteria Clinical isolates of Staphylococcus aureus were collected from blood, urine, joint fluid, sputum, wound, and abscess samples of patients referred to Rasht medical diagnostic laboratories and confirmed by culture and biochemical tests to identify the bacteria. To determine the antibiotic sensitivity of Staphylococcus aureus clinical isolates to aminoglycosides, an antibiogram test was performed by diffusion method. Examining the frequency of IntI and Int II genes Genomic DNA extraction of Staphylococcus isolates was done using a Cinagen DNA extraction kit (Cat. No. PR٨٨١٦١٤). To check the frequency of integron genes, a pair of specific primers for class ١ and ٢ integrons were used in the PCR reaction.

Results: Out of the total of ٦٦ Staphylococcus aureus isolates, ٦٠ isolates (٩١٪) had multiple antibiotic resistance. The highest level of resistance of isolates was against penicillin G and ampicillin antibiotics respectively, and linezolid, teicoplanin and vancomycin antibiotics were the most effective antibiotics. Also, ٦٠ (٩١٪) isolates had multiple antibiotic resistance. Of these, ٧٤,٥٪ were resistant to gentamicin and ٨٧,٢٪ were resistant to kanamycin. Out of ٦٠ isolates with multiple antibiotic resistance, in ٥١ isolates (٨٥٪), a fragment with an approximate length of ٢٨٥ bp was produced in the PCR reaction and was found to contain the Int I gene. Also, ١٨ isolates (٣٠٪) were identified as positive for the presence of IntII gene by producing a fragment with an approximate length of ٧٨٨ bp. ٩ isolates (١٥٪) have IntI and Int II genes at the same time

Conclusion: In the present study, the antibiotic resistance of clinical isolates of Staphylococcus aureus and class I and II integron genes in isolates with multiple antibiotic resistance were investigated. In this study, more than ٩٠٪ of isolates showed multiple antibiotic resistance phenotypes. The highest level of resistance in the isolates was against beta-lactam antibiotics, and the antibiotics linezolid and teicoplanin, which have less clinical use, were the most effective antibiotics against the clinical isolates of Staphylococcus aureus studied. Also, the presence of IntI and Int II genes was detected in ٥١٪ and ٣٠٪ of the isolates, respectively. Examining the prevalence

of integrons in bacterial strains isolated from each country is important as effective factors in the spread of antibiotic resistance and the emergence of multidrug resistance phenotype . In a study conducted by Seyed Javadi et al. during a study in Tehran in ٢٠١٤ on ١٠٨ isolates of Staphylococcus aureus, ٣,٣٢٪ of clinical samples and ٦٧,٧٪ of environmental isolates were classified as class I integron genes. were positive (Seyed javadi SS, ٢٠١٤). In another study conducted by Yahaghi et al. on ٢٠٠ strains of Staphylococcus aureus in ١٩٩٢, among the ٢٠٠ samples, ١٪ of the strains (two isolates) contained class I integron (Yahaghi E, ٢٠١٤). In a study conducted by Haji Ahmadi and colleagues in Hamadan city on Staphylococcus aureus and Enterococcus spp, ٦٨ strains of Staphylococcus aureus and ٤٧ strains of Enterococcus resistant to antibiotics were identified. Also, ٣٠ isolates belonged to integron class ١ (intI١) and ٢ isolates belonged to integron class ٢ (intI٢) in Staphylococcus aureus.

Keywords: integron, multiple antibiotic resistance, Staphylococcus aureus

Determining the prevalence of HPV in different cities in Iran by defining the most common genotypes in ٢٠٢٤ (Research Paper)

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Introduction: Human papillomavirus (HPV) is a DNA tumor virus that primarily infects human epithelial cells, transmitted through skin-to-skin or sexual contact. Various HPV types are linked to malignancies such as cervical and penile cancer. The global prevalence of HPV has surged, including in Iran, highlighting the need for effective control strategies. This study aims to assess the average age of morbidity in men and women, identify the most common types, and explore actions for developing effective vaccines tailored to different regions.

Methods: The most common samples which can be used for HPV are cervix, vaginal, vaginal discharge and warts for women. on the other hand, urine, swap and warts are preferable samples for men. in this study, we have examined ٢٢٠٠ patients gathered from different cities of Iran, sent to Noor Laboratory for conducting Molecular tests. in the first step, DNA extraction was carried out based on standard protocols suitable for different samples, to be certain of the right integrity and purity of extracted DNA Nanodrop test carried out for all samples. in the last step, Quantitative Polymerase Chain (qPCR) was performed to detect Negative and positive samples by defining the exact genotype of positive patients.

Results: based on the obtained results of our study, about ٨٣٪ of patients were women. While men accounted ١٧٪ of whole number, with the average age of ٣٥ in women and ٤٠ in men. Our results also demonstrated that Genotypes ٥١, ٥٢ and ٦ had the highest rate of prevalence among positive patients. Those patients diagnosed with Genotypes ٥١ and ٥٢ had higher risk of developing cancer later in their life. While, affected people diagnosed with Genotype ٦ do not have any important health concern but physical beauty.

Conclusion: The results of our study highlight a significant gender imbalance in HPV prevalence, with women comprising ٨٣٪ of the patient population and an average age of ٣٥, compared to men at ١٧٪ with an average age of ٤٠. This disparity may suggest differing risk factors or exposure routes between genders that warrant further investigation. The identification of high-risk genotypes, particularly HPV types ٥١ and ٥٢, among the patients is concerning due to their association with cervical and other cancers, indicating a need for preventive measures and regular screenings. Conversely, the prevalence of HPV type ٦, while the highest among patients, appears to pose minimal health risks beyond cosmetic concerns. This duality in HPV subtype prevalence emphasizes the necessity of targeted public health interventions, focusing on high-risk variants while also

acknowledging the broader implications of HPV infections on women's health. Continued research is essential to better understand these dynamics and improve health outcomes.

Keywords: Human Papilloma virus, Genotypes, quantitative Real Time PCR

Developing a targeted delivery system for Leuconostoc mesenteroides in IBD treatment (Research Paper)

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Introduction: Inflammatory bowel disease (IBD) includes various inflammatory disorders of the intestine, associated with imbalances in gut microbiota. Bacteriotherapy shows promise in treating IBD by correcting gut dysbiosis and reducing inflammatory mediators. Probiotics such as Leuconostoc mesenteroides (NRRL B-١١١٨), when administered orally, can produce beneficial substances, inhibit pathogen growth, and help restore the balance of gut microbiota. However, environmental challenges in the gastrointestinal (GI) tract, such as gastric acids, significantly reduce the viability and activity of probiotics after oral intake. Inadequate mucoadhesive properties of probiotics result in reduced colonization efficiency and therapeutic impacts.To address these issues, coating probiotics with functional biomaterials can protect them and extend their retention time in the GI tract.

Methods: In this study, we developed a targeted delivery system using a double-layer electrostatic assembly method to encapsulate L. mesenteroides in layers of mucoadhesive chitosan (CS) and hyaluronic acid (HA), creating HA-CS-L. mesenteroides. These protective layers provide the encapsulated L. mesenteroides with enhanced resistance to environmental stresses and improved mucoadhesion in the GI tract.

Results: As a result, the probiotics can more effectively suppress inflammation and modify the intestinal environment, improving their therapeutic efficacy for IBD prevention and treatment.

Conclusion: This study introduces an innovative probiotic coating strategy enhancing the effectiveness of bacteriotherapy in combating IBD.

Keywords: Probiotics; Inflammatory bowel disease (IBD); Mucoadhesive chitosan (CS); Hyaluronic acid (HA); Enca

Development of an Innovative HTLV-١ Protease: Human Fcγ١ Recombinant Fusion Protein Produced in the CHO Eukaryotic Expression System (Research Paper)

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Introduction: Human T-cell leukaemia virus type ١ (HTLV-١) is the causative agent of two life-threatening diseases, adult T cell leukaemia/lymphoma (ATLL), and HTLV-١-associated myelopathy/tropical spastic (HAM/TSP). HTLV-١ protease (HTLV-١-PR) is an aspartic protease that holds promise as a target for therapeutic interventions, similar to human immunodeficiency virus-PR inhibitors (HIV-PR). Thus, the present investigation aimed to design and express the human Fc fusion recombinant-PR (HTLV-١-PR:hFcγ١) for two purposes: identifying a blocking substrate as a potential therapeutic or a subunit peptide vaccine.

Methods: The MT٢-cell line was employed to amplify the DNA sequences encoding the HTLV-١-PR using specific primers with Not١ and Xba١ restriction enzyme sites. Subsequently, the construct was cloned into the pTZ٥٧R/T TA plasmid and, following verification of the PR sequence, subcloned into the pDR٢ΔEF١α Fc-expression vector to create pDR٢ΔEF١α.HTLV-١-PR:hFcγ١. The integrity of the recombinant DNA was confirmed by sequencing to ensure that the engineered construct was in the correct frame. The recombinant fusion protein was then generated in the Chinese hamster ovary cell (CHO) system and purified from the supernatant using HiTrap-rPA column affinity chromatography

Results: Subsequently, the immunofluorescence assay (IFA) co-localisation method indicated that the HTLV-١-PR:hFc recombinant fusion protein exhibited appropriate folding as it interacted with the anti-Fcγ antibody; the Fcγ١ tag contributed to the formation of HTLV-١-PR:hFcγ١ as a dimeric secretory protein.

Conclusion: The development and production of HTLV-١-PR may have implications for identifying a blocking substrate as a potential therapeutic molecule, as well as for assessing its immunogenicity and potential protection against HTLV-١ infection through animal model experimentation.

Keywords: Adult T cell leukaemia/lymphoma (ATLL) · Chinese hamster ovary cell (CHO)expression system · HTLV-١

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Development of hyaluronic acid-based nanocarriers for delivery of siRNAs in breast cancer therapy (Review)

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Introduction: Gene therapy based on RNA interference has been considered as a useful therapeutic strategy for the treatment of breast cancer. However, small interfering RNA (siRNA) delivery has several limitations, including off-target effects, unwanted tissue accumulation, unsuccessful intracellular delivery, high toxicity, and instability in the bloodstream, according to clinical trial reports. Therefore, the development of safe and efficient vectors required for optimal siRNA delivery. Hyaluronic acid (HA) is a linear negatively-charged mucopolysaccharide which has the advantage of being biocompatible, non-cytotoxic, and biodegradable. Due to its carboxylic and hydroxyl groups, it is suitable for desired chemical modifications to create safe and high-performance carriers for delivering siRNAs. This review discusses the prospects, recent advances, and future challenges of HA-mediated delivery of siRNAs in breast cancer therapy.

Methods: Original articles published since ۲۰۰۵ on HA-based nanocarriers in the field of siRNA delivery for breast cancer therapy were searched from Web of Science, Google Scholar, Elsevier, Scopus, and PubMed databases. Using these data, the properties, applications and challenges of HA-based nanocarriers were discussed.

Results: HA exists naturally in various parts of the human body, so the cellular adaptation is tolerable for the immune system. Furthermore, HA cannot load negatively charged siRNA due to its negative charge. Therefore, by making changes in the composition and functional groups of HA or by conjugating HA to positively charged polymers or cationic groups, new vectors with modified surface charge can be created to be complexed with siRNA. HA-based nanocomplexes have physicochemical properties that are selected for controlled release of siRNAs to cancer cells and increasing the lifetime of siRNA by providing enzymatic stability against degradation.

Conclusion: The results show that HA-based nanoparticles can be used as a suitable carrier for the optimal delivery of therapeutic siRNA to breast cancer cells.

Keywords: Hyaluronic Acid, nanocarriers, small interfering RNA, breast cancer therapy

development of nanofibrous scaffold incorporated with ZnO NPs against human melanoma A۳۷۵ cells (Research Paper)

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Introduction: Skin cancers represent the most prevalent form of malignancy among humans. The exploration and identification of potent pharmaceuticals for skin cancer have emerged as a critical objective, given the pervasive and perilous proliferation of this malignancy globally. Consequently, it is essential to conduct thorough research on this disease and to investigate the nanomaterials that influence it, with the aim of developing effective therapeutic strategies to eradicate this condition. Therefore, this research investigated the impact of polycaprolactone collagen nanopads embedded with zinc oxide nanoparticles on human melanoma A۳۷۵ cells in vitro.

Methods: The synthesis of polycaprolactone/collagen nanofibers (NFs-PCL-Coll) integrated with zinc oxide nanoparticles (ZnO NPs) was accomplished through the electrospinning technique. Nanoparticles were produced through a green synthesis method utilizing orange peel and then the characteristics of the resulting nanoparticles and nanofibers were examined. The assessment of the synthesized nanopads' toxicity on the A۳۷۵ cell line was conducted through the MTT assay. Upon achieving the IC۵۰ concentration, the A۳۷۵ cell line was subjected to treatment at this concentration, followed by an analysis of cell death rates and morphological changes.

Results: The analysis of the MTT assay results revealed a marked decrease in cell viability when exposed to the IC۵۰ concentration of zinc oxide-containing nanofibers. Furthermore, morphological assessments indicated that the treatment group exhibited a higher prevalence of deformed cells than the control group.

Conclusion: The findings presented above suggest that ZnO-NPs/PCL-Coll, as an unconventional material in cancer therapy, demonstrate promising potential for effectively treating and eradicating skin cancer

Keywords: Skin cancer, Polycaprolactone/collagen nanofibers, Zinc oxide nanoparticles

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Diagnostic biomarker for early detection of ovarian cancer (Review)

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Introduction: Despite many years of effort and expense, cancer remains a notable cause of death worldwide. Among various cancers, ovarian cancer (OC) is a lethal gynecologic tumor, with high mortality and poor prognosis. Because of inadequate early diagnostic methods and few early symptoms, OC remains undetected until the disease reaches advanced stages. Patients with advanced OC have less than ٢٥٪ ٥-year survival rate. One of the important methods in the early detection of cancers is to check the serum levels of biomarkers. Establishing biomarkers for early ovarian cancer diagnosis is imperative for high survival rates. This study aims to review diagnostic biomarkers for early detection of ovarian cancer.

Methods: A comprehensive search was conducted in Google Scholar, Scopus, and other databases to discover published articles related to diagnostic biomarkers of ovarian cancer.

Results: Various molecular biomarkers have been developed for diagnostic use in ovarian cancer. Carbohydrate antigen-١٢٥ (CA-١٢٥) and Human Epididymis Secretory Protein ٤ (HE٤) have been introduced to ovarian cancer biomarkers. TTR performed better than CA١٢٥ and HE٤ in detecting early-stage ovarian. Folate receptor-α (FOLR١) is over-expressed in several malignant cancers, especially in high-grade serous ovarian carcinoma. Overexpressed UCHL٣ was shown in OC. This function is in cell proliferation and metastasis. Up-regulation of miR-٢٠٥, miR-٩٣, miR-١٠٦b, and miR-٤٥١ were found to be strongly associated with ovarian cancer.

Conclusion: Overall, this review highlights the significant clinical biomarkers in ovarian cancer. Many biological molecules are diagnostic biomarkers for the early detection of ovarian cancer.

Keywords: ovarian cancer, clinical biomarkers, cancer, early detection, prognosis

Differential expression genes and mRNA-miRNA network by microarray analysis in the Leishmania donovani Infected mouse liver samples (Research Paper)

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Introduction: Leishmania donovani induces visceral leishmaniasis (VL) where the protozoan invades and dwells within hepatic and splenic tissue macrophages. Considering the anomalous lipid profile noted in VL patients, we investigated the status of serum fats in an experimental murine model of VL. The murine VL liver exhibited modified expression of lipid metabolic genes, numerous of which are direct or indirect targets of the liver-specific microRNA-١٢٢. A concurrent decrease of miR-١٢٢ expression was noted in the VL liver. (١) Leishmania donovani invades and seizes the microRNA import-export apparatus of host macrophages and thrives by transmitting the host-derived miR-١٤٦a to adjacent cells and halts inflammation. (٢)

Methods: The GSE٣٨٩٨٥ gene expression profile data were downloaded from the NCBI Gene Expression Omnibus (GEO) (https://www.ncbi.nlm.nih.gov/geo). The present study included a total of ٥ samples, which comprised ٢ Leishmania donovani-infected mouse liver and ٣ normal adjacent tissues. Using GEO٢R, an indepth analysis was performed to obtain differentially expressed genes. The most significant genes (|logFC| > ٢ and adjusted p-value< ٠,٠٥) were selected and taken to miRWalk ٢,٠ to find target miRNAs and hub genes.

Results: According to GEO analysis of GSE٣٨٩٨٥ were indicated ١٠٩١ up and downregulated genes (Fig ١). Among all these genes Hsd٣b٥, Ubd, and Mgst٢ were considered an Up-regulated gene that related to VL. This examination revealed that the GSE٣٨٩٨٥ was remarkably enriched in multiple biological processes. The potential central genes were investigated in Kyoto Encyclopedia of Genes and Genomes (KEGG) repository to identify the pathways in which they are individually involved. Ubd is present in essential genes for Activation G protein gated potassium of cell. We watched that Leishmania donovani disease driven to improved N-Ras expression, though it repressed K-Ras and H-Ras expression. L donovani contamination too expanded extracellular signal-regulated kinase ١/٢ phosphorylation and at the same time diminished p٣٨ phosphorylation. (٧)(٨) (٩) Fig٣ (B) Mgst٢ is present in essential genes for the Glutation metabolism of cells. (١٠)(١١) Glutathione is a powerful antioxidant that helps protect cells from damage caused by harmful molecules in the body. In trypanosomes and leishmanias, trypanothione helps protect the parasite from the mammalian host's immune system by recycling it through an enzyme called trypanothione reductase.(١٠)(١١)(١٢)

Conclusion: In summary, this finding could be suggested novel interactions among micRNAs and mRNA(miR-١٤٦a , microRNA-١٢٢, Hsd٣b٥, Ubd, Mgst٢ for the candidate diagnostic and prognostic markers associated by bioinformatics analysis. We believe that, without any severe negative side effects, this ceRNA network could be used as a potential tool for both preventative.

Keywords: Leishmania donovani ,Differential expression genes , microarray Analysis, miRNA_MRNA ineraction

Differential expression of steroidogenesis-related gene CYP١٩A١ in adipose tissue adjacent to benign and malignant breast tumors (Research Paper)

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Introduction: Breast cancer is the most commonly diagnosed malignant tumor in women and the second leading cause of cancer-related deaths worldwide. The breast is rich of adipose tissue and glandular tissue. Because adipocyte and tumor cells are so closely located in the breast, it's important to explore how adipocyte may influence the onset, growth, and spread of breast cancer at the molecular level. A major aspect of focusing throughout this study is the genes express adipose tissue that regulate steroid hormones, such as those involved in producing mineralocorticoids, glucocorticoids, and sex steroids. Our specific target is the CYP١٩A١ gene, which plays a critical role in the metabolism of sex steroids, especially in producing estrogen. An evaluation of expression the CYP١٩A١ gene in the adipose tissue surrounding breast tumors.

Methods: We collected samples of subcutaneous adipose tissue adjacent to breast tumors from ٤٠ women with breast cancer. We divided them two‹two groups had a history of benign (non-cancerous) tumors, and the other half had malignant (cancerous) breast tumors. are main goal was to compare CYP١٩A١ gene expression between in adipose tissue surrounding benign and malignant breast tumors. by quantitative PCR technique, a method for analyzing gene expression.

Results: Our results indicated that CYP١٩A١ profile expression, was significantly higher in patients with malignant breast tumors compared to those with benign breast cancer. There was no significant different in BMI and age between ٢ groups (benign tumors and malignant tumors).

Conclusion: The study revealed that alterations in the expression of the CYP١٩A١ gene are linked to an increased risk of developing more aggressive breast cancer. Upregulation of CYP١٩A١ genes increased boosting malignancy causing breast tumor.

Keywords: Breast cancer, fat tissue, gene expression, aromatase, CYP١٩A١.

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Differential expression of steroidogenesis-related genes CYP۱۱A۱, STAR, HSD۱۱B۱, HSD۱۱B۲ and HSD۱۷B۱۲ in adipose tissue adjacent to benign and malignant breast tumors (Research Paper)

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Introduction: Breast cancer is the most common malignancy among women worldwide and is the second leading cause of female mortality. Research highlights the significant role of adipose tissue (AT) as the primary microenvironment for breast tumor cells, known as cancer-associated adipocytes (CAA), which promote breast cancer development and invasiveness through the secretion of various chemokines and adipokines. CAAs impact metabolic pathways, particularly steroidogenesis, where cholesterol is converted into steroid hormones. This study aims to evaluate the expression of key genes involved in steroidogenesis, including CYP۱۱A۱, STAR, HSD۱۱B۱, HSD۱۱B۲, and HSD۱۷B۱۲, in adipocytes surrounding malignant tumors compared to those adjacent to benign tumors.

Methods: Adipose tissue adjacent to tumors was collected from forty Iranian women diagnosed with breast cancer (BC) and benign breast disease (BBD) during surgery. Participants were matched for age and body mass index (BMI). The mRNA levels of the aforementioned genes were analyzed using quantitative PCR.

Results: The mRNA expression levels of steroidogenesis-related genes (CYP۱۱A۱, STAR, HSD۱۱B۱, HSD۱۱B۲, and HSD۱۷B۱۲) were significantly higher in the AT of individuals with BC compared to those with BBD. This indicates a notable upregulation of steroidogenesis-related genes in the AT of BC patients.

Conclusion: Our findings suggest that cancer-associated adipocytes (CAA) play a critical role in breast cancer progression and metastasis. The altered expression of steroidogenesis-related genes in AT during tumor development may contribute to breast cancer malignancy and progression, highlighting their potential as therapeutic targets.

Keywords: Cancer-associated- adipocyte (CAA), Steroidogenesis, Breast cancer (BC), Benign Breast disease (BBD)

Differential Expression of Transcription Factors OTX۲ and SOX۱۵ in Follicular Fluid and Its Impact on Oocyte Maturation in Endometriosis Patients (Research Paper)

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Introduction: About ۱۰٪ to ۱۵٪ of women who are of reproductive age, suffer from endometriosis, a chronic disease marked by the development of endometrial-like tissue outside the uterus. This disease is identified in ۳۰–۵۰٪ of infertile women and its precise etiology is still unknown. Endometriosis can cause anatomical abnormalities, hormonal imbalances, and inflammatory responses that negatively impact oocyte viability and reproductive outcomes, making the relationship between the condition and infertility complex. Ectopic endometrial tissue can interfere with normal ovarian function and hormone regulation, which can severely compromise oocyte maturation and quality. Since evaluating oocyte quality directly is challenging, Follicular Fluid (FF) analysis is often employed as an alternative approach. FF is a complex microenvironment that envelops the oocyte and plays a crucial role in its development and quality. Alteration in the environment have been connected to infertility in endometriosis-affected women. Among the mechanisms that affect oocyte maturation and quality in this fluid, we focused on the expression of two specific transcription factors, Orthodenticle Homeobox ۲ (OTX۲) and SRY-Box Transcription Factor ۱۵ (SOX۱۵), within the FF of women with endometriosis compared to healthy women. The significance of selecting OTX۲ and SOX۱۵ in this study is demonstrated by the rise in expression of these two genes during oocyte maturation.

Methods: The mRNA expression levels of OTX۲ and SOX۱۵ in the FF of women with endometriosis (n=۲۳) were compared to women without endometriosis as a control group (n=۲۳) in this study using qRT-PCR.

Results: There was no significant difference found between the case and control groups in terms of demographic variables like age, Body Mass Index (BMI), and the levels of Luteinizing Hormone (LH), Follicle-Stimulating Hormone (FSH), and Anti Mullerian Hormone (AMH) that affect oocyte quality. In addition, the statistical analysis of the expression levels of OTX۲ and SOX۱۵ did not report a significant difference between the case and control groups, however, a decreasing pattern was seen.

Conclusion: Based on previous studies, OTX۲ showed a significant increase in both the endometrium and plasma of patients. SOX۱۵ is also upregulated in the endometrium of the affected individuals. However, there were no significant differences in the expression levels of these

genes in the FF of women diagnosed with endometriosis compared to those who are healthy in this study. This implies that OTX٢ and SOX١٥ may influence the pathogenesis of endometriosis through mechanisms other than oocyte maturation. Further research with larger sample sizes and targeted functional analyses is warranted to elucidate the precise mechanisms by which endometriosis may influence the expression of these key transcription factors and their downstream effects on oocyte maturation. Nonetheless, our study underscores the importance of examining the follicular fluid microenvironment in understanding the complex interplay between endometriosis and reproductive health.

Keywords: Endometriosis, Follicular Fluid, OTX٢, SOX١٥, Oocyte Maturation

Discovering Novel Biomarkers for Atherosclerosis-Induced Ischemic Stroke: Insights from lnc-SLC۳۸A۱ and lnc-SOD۳ through Bioinformatics (Research Paper)

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Introduction: Atherosclerosis is a widespread condition arising from the accumulation of a sticky substance known as plaque within the arteries, and it is the leading cause of myocardial ischemia, which is the important cause of death globally. The progression of atherosclerosis occurs gradually, as cholesterol, fats, blood cells, and other blood components come together to form plaque. A clot could obstruct an artery, causing sudden and severe myocardial ischemia, which may lead to a heart attack. Long non-coding RNAs (lncRNAs) can regulate gene transcription and translation as epigenetic modification factors. However, their functional significance in atherosclerosis-induced ischemic stroke (AIIS) is unclear. The primary objective of this study is to present a potential lncRNAs as biomarker among atherosclerosis-induced ischemic stroke and normal samples through bioinformatics analysis.

Methods: The microarray dataset of lncRNAs transcriptomic profiles in atherosclerosis-induced ischemic stroke patients and healthy volunteers (GSE۱٤٦۸۸۲) was obtained from the GEO database. Differential expression analysis between patients and normal groups was performed using GEO۲R and genes with differential expression were isolated. Next, genes with differential expression (logFC# ۱ and p.value<۰,۰٥) were introduced and boxplot analysis was performed for analysis the probability of the selected gene as a biomarker.

Results: The bioinformatics results showed that the lnc-SLC۳۸A۱ (logFC= -۱,٥٤۳; P.value=٤,۷٦e-۰۷) has the most downregulation in patients and lnc-SOD۳ (logFC= ۱,۰۳۲; P.value=۳,۰۳e-۰٤) has the most upregulation in atherosclerosis-induced ischemic stroke.

Conclusion: Overall, our data demonstrated that the differential lncRNAs expressions have potentially to be considered as biological biomarkers with diagnostic approaches. In this regard, the reduction of lnc-SLC۳۸A۱ and increasing lnc-SOD۳ expression can probably be a biomarker to identify atherosclerosis-induced ischemic stroke, which should be confirmed in experimental analysis.

Keywords: atherosclerosis, lnc-SLC۳۸A۱, lnc-SOD۳, biomarkers

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Discussing the genetic evaluation of the occurrence of liver cancer in people with maternal obesity phenotype in Iran. (Research Paper)

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Introduction: Liver cancer is cancer that occurs in the liver. The liver is the largest internal organ of the body which performs several critical functions to help the body eliminate waste, absorb nutrients, and heal wounds. Liver cancer is generally classified as primary or secondary. Primary liver cancer begins in the cells of the liver. Secondary liver cancer develops when cancer cells from another organs spread to the liver, or metastasize. Liver cancer is the fourth most common cause of cancer-related deaths worldwide, with obesity, exacerbating the risk especially two times higher in Body Mass Index (BMI) above ٣٠ and four times higher in BMI above ٣٥. Also, The gene that has been the most strongly and frequently associated with susceptibility to obesity is the fat mass and obesity-associated (FTO) gene, which has most influence on body mass index (BMI) of all known genes.

Methods: Human saliva samples, DNA electrophoresis, NCBI and MagaGene Pharmacogenetic software

Results: According to this study, RS٩٩٣٩٦٠٩, RS١٧٧٨٢٣١٣ and RS١٧٩٩٨٨٣ polymorphisms are the most common obesity polymorphisms in Iran which can case obesity and increase the risk of liver cancer. About ١٢ drugs are used to control obesity. among these drugs, TSH causes headache in people with BRCA٢ gene, VEGF increases blood glucose in people with FTO gene, Lira causes nausea in people Having MLH١ gene and Phent leads to hair loss and high blood pressure in people with FTO gene.

Conclusion: In order to use drugs to treat liver cancer, it is necessary to carry out genetic tests to check the presence of polymorphisms in common genes on patients such as FTO, MC٤R and FABP٢ before prescribing any drugs, therefore drugs with less side effects can be prescribed for these patients.

Keywords: Liver cancer, Obesity, FTO, FABP٢, MC٤R

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DNA damage response (DDR): a link between cellular senescence and human cytomegalovirus

(Review)

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Introduction: The DNA damage response (DDR) signifies a signaling cascade that transpires as a consequence of DNA impairments and disrupts cellular cycle regulation. Consequently, pro-inflammatory cytokines commence to be released. DDR damage precipitates cellular senescence. Among the pathogens implicated in the phenomenon of cellular senescence, human cytomegalovirus is particularly remarkable, which has instigated inquiries into the correlation between this virus and DDR. DNA damage, by engendering a signaling cycle, culminates in the cessation of the cellular cycle and facilitates DNA repair. This mechanism harbors signals that could present as double-strand breaks (DSB) or single-stranded DNA (ssDNA), leading to a sequence of cellular reactions aimed at DNA repair. If the DNA deterioration is not fixed, the cell will eventually face apoptosis.

Methods: To develop a deep understanding of the connection between DDR's operational response and the human cytomegalovirus's role in advancing cellular senescence, we engaged in a literature assessment employing resources from Google Scholar, PubMed, and NCBI databases. Following an exhaustive examination of the pertinent review articles and the assessments and inquiries conducted, we acquired an in-depth understanding of this subject matter.

Results: Cytomegalovirus is implicated in the cellular aging of hosts, leading to DNA damage response (DDR), which pauses the cell cycle and encourages the discharge of pro-inflammatory cytokines that elevate antiviral responses. This virus employs a sequential mechanism for gene expression, and upon infection, distinct proteins, namely ٧٢-kDa and ٨٦-kDa IE١ and IE٢, function as transcriptional regulators by interacting with cellular proteins. In this structure, the task of interferon-beta (IFN-B), stimulated by DNA damage, encourages the growth of cellular senescence.

Conclusion: The presence of Cytomegalovirus causes host cells to enter a state of senescence while activating a significant DNA damage response (DDR), stopping the cell cycle, and fostering the production of pro-inflammatory cytokines that stimulate antiviral activity. This virus expresses its genes through a cascading mechanism, and upon infection, specific proteins such as ٧٢-kDa and ٨٦-kDa IE١ and IE٢ function as transcriptional regulators interacting with cellular proteins. In this context, the DNA damage-induced function of interferon-beta (IFN-B) facilitates the enhancement of cellular senescence.

Keywords: DNA damage response, Cellular senescence, Human Cytomegalovirus

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DNA methylation as a diagnostic biomarker in breast cancer (Review)

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Introduction: One of the most common non-communicable diseases in the world is breast cancer, which is more common among women than men. This type of carcinoma is the most common type of cancer after lung cancer and according to reports it is the leading cause of cancer death among women worldwide. Its history goes back to ٥٠٠٠ years ago, which was seen in ancient egyptian mummies. The treatment started from the beginning of the diagnosis by burning the desired area. But later, treatment methods improved dramatically. In tumorigenesis-related diseases, early and accurate diagnosis is very important. Identifying epigenetic biomarkers is very helpful in managing various types of cancer, especially breast cancer. The DNA methylation process is a universal epigenetic mechanism which is the addition of methyl moiety to the pyrimidine ring in the cytosine base. DNA methyltransferase (DNMT) enzymes catalyze this enzymatic reaction. Changing the methylation profile directly affects the expression level of genes. Many environmental parameters such as increasing age, lack of physical activity, stress, depression, excessive alcohol consumption air pollution, and other biological processes affect the DNA methylation profile. The purpose of this study is to investigate DNA methylation as a biomarker in breast cancer diagnosis.

Methods: A comprehensive search was conducted in pubmed, Scopus, and other databases to discover published articles related to DNA methylation as a diagnostic biomarker in breast cancer with search terms included, DNA methylation, breast cancer, DNA methyltransferase, and related keywords.

Results: DNA methylation is one of the epigenetic mechanisms. Numerous studies have reported that alteration in methylation of DNA led to changes in the expression of oncogenes and tumor suppressor genes in patients with various cancers. Studies performed on tissues and whole blood of breast cancer patients have detected several hypo and hyper-methylated genes in both males and females. Therefore gene-specific DNA methylation is a risk biomarker. Various studies have evaluated the methylation levels of tumor suppressor genes associated with BC development. BRCA٢, ALX٤, FEV, HOXA١١, LYL١, NEUROG١, PAX, MGMT, SOX١٠, SREBF١, TPV٣, TRIM٢٩, WT١, BCL٩, SMYD٣, ZNF١٥٤, ZNF١٧٧, HOXD٩, ITIH٥, TMEM١٣٢C, TDRD١٠, RNF٢٢٠, RIMBP٢, PRAC٢, EFCAB١, and ANKRD٥٣ are among the genes that are affected by hypermethylation in BC.

Conclusion: Alteration in the methylation of DNA causes changes that lead to breast cancer. Therefore study of DNA methylation is a useful method for the detection of diagnostic biomarkers.

Keywords: clinical biomarkers, DNA methylation, breast cancer, DNA methyltransferase, diagnosis

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DNA origami for multiplex rapid nucleic acid based diagnosis (Review)

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Introduction: Nucleic acids, like DNA and RNA, play a crucial role in diagnosing a wide range of diseases, including cancers, infectious diseases, and genetic disorders. So the role of these biomarkers is becoming more important. Traditional detection methods, such as polymerase chain reaction (PCR), offer high sensitivity but often require laboratory settings and complex equipment, limiting their use for point-of-care testing IVD. Furthermore, multiplex PCR has limitations.Due to the widening applications of nucleic acid biomarkers, the need for POC IVD is increasing.Origami DNA is a novel emerging technology to design self-assemble ٢D & ٣D nanostructures easily. This promising technology integrates various fields e.g. drug delivery, photonics & plasmonics, and biosensing. DNA origami biosensors can sensitively detect multiple nucleic acids simultaneously without amplification at the point of care. In this review, we will explore the different biosensing strategies.

Methods: In this review, ٤٦ original articles have been analyzed. Articles were published within the past ٥-١٠ years to ensure the information reflects current advancements in origami DNA technology. Articles were published in peer-reviewed scientific journals with a strong reputation in the field of nanotechnology or biosensing.

Results: As origami DNA-based biosensing is a new technology, there is no standard method or design for it. researchers use different strategies for readouts and quantifications of nucleic acids. However, moreover designs have a similar concept named the Recognition Unit. This Recognition Unit is a DNA origami structure designed to bind to target nucleic acid based on a complementary sequence between target nucleic acid and free single-strand DNA in the nanostructure. The Recognition Unit is designed differently in different studies. Book design and beacon design seem more promising. Recognition Unit coupled with Transducer which produces a signal. Transducers can use different strategies for example Fluorescence-Based, Fluorescence Resonance Energy Transfer (FRET)-Based, Quenching-Based, Surface-Enhanced Raman Scattering (SERS)-Based Sensors. Among this strategy Quenching-Based and Fret seems more promising and provide higher accuracy.

Conclusion: A Glimpse into the Future of Multiplex Diagnostics The impressive results discussed highlight the immense potential of origami DNA for revolutionizing multiplex diagnostics. Its ability for sensitive, specific, and simultaneous detection of multiple targets offers significant advantages over traditional methods. The possibility of developing user-friendly assays opens doors for point-of-care applications, particularly in regions lacking sophisticated laboratory infrastructure. However, challenges remain. Optimizing origami design for complex biomarker panels and ensuring cost-effectiveness for widespread adoption are crucial steps. Additionally, further research is needed to validate the long-term stability and storage of origami-based diagnostic kits. Despite these hurdles, the future of origami DNA in multiplex diagnostics is bright. Continued research and development

have the potential to overcome these limitations. As the technology matures, we can expect to see origami DNA play a pivotal role in personalized medicine, enabling early detection and targeted treatment of various diseases. The ability to conduct rapid and accurate diagnoses at the point-of-care holds immense promise for improving global healthcare outcomes. In conclusion, origami DNA stands as a powerful and innovative platform for the future of multiplex diagnostics, paving the way for a more precise and accessible approach to disease management.

Keywords: Origami DNA, nanostructures, multiplex diagnosis, early diagnosis, biosensors,

DNA oxidation and fragmentation levels in globozoospermic and normozoospermic men (Research Paper)

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Introduction: DNA oxidative damages in spermatozoa include DNA oxidation, DNA fragmentation, mitochondrial DNA damage, telomere attrition, epigenetic abnormalities, and Y chromosome microdeletions. Nowadays sperm DNA oxidation of guanine is an important and more attractive subject in the field of male infertility which affects sperm DNA, morphology and functionality of sperm, fertilization rate, embryo development, implantation, and pregnancy. Globozoospermia, a rare form of teratozoospermia, is characterized by sperm with a spherical head and the absence of an acrosome. This study aimed to evaluate and compare the levels of DNA oxidation of guanine and fragmentation in men with globozoospermia versus those with normozoospermia and their relation to protamine deficiency.

Methods: Semen samples were collected from ٣٩ couples who referred for ICSI treatment in the Royan Institute, which included ٢٥ individuals with normospermia and ١٤ with globozoospermia, all with their informed consent. Semen analysis was performed according to World Health Organization guideline (sixth edition). Following intracytoplasmic sperm injection (ICSI), the remaining semen sample was washed and separated into sperm and seminal plasma. The sperm DNA damages were evaluated by immunostaining, sperm chromatin dispersion test and chromomycin A٣ (CMA٣) for DNA oxidation of guanine, DNA fragmentation and protamine deficiency respectively. The Kolmogorov–Smirnov test was applied to assess the data distribution's normality. Student's t-test analyzed differences between two groups and Pearson correlation was performed to analyze correlations between the variables. $p < ٠,٠٥$ will be considered significant.

Results: According to statistical analysis, sperm DNA oxidation displayed a significant increase in globozoospermia ($p < ٠,٠٥$) against normospermic group and also sperm exhibited a significantly higher percentage of protamine deficiency and DNA fragmentation in globospermic group compared to normpspermic group ($p < ٠,٠٠١$). Furthermore, our research showed a positive significant correlation of DNA oxidation with DNA fragmentation and protamine deficiency.

Conclusion: Protamine deficiency in sperm chromatin is more commonly in cases of globozoospermia that makes sperm DNA more susceptible to damage of oxidative stress. The elevated level of DNA oxidation in globozoospermia may have implications outcome of ART outcomes.

Keywords: Globozoospermia, Stress oxidative, DNA oxidation, DNA fragmentation

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Docking Study of Selected Compounds Against Tyrosine Kinase Receptor for Cancer Treatment

(Research Paper)

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Introduction: Tyrosine kinases play a pivotal role in regulating various cellular processes, including signaling pathways, cell growth, and division. These enzymes are often found at elevated levels or exhibit heightened activity in certain cancer cells, making them critical targets for therapeutic intervention. Inhibition of tyrosine kinases has shown promising results in slowing down cancer progression and improving patient outcomes, as seen in chronic myeloid leukemia treatments. This study focuses on the comparative analysis of five selected compounds known for their potential anticancer properties. These compounds include ٦-Gingerol, Epigallocatechin Gallate (EGCG), Kaempferol, ٦-Shogaol, and Chrysin, all of which have demonstrated anti-inflammatory, antioxidant, and anticancer activities through various biochemical pathways. By employing molecular docking techniques, we aim to evaluate the binding affinities and interaction profiles of these compounds with the tyrosine kinase receptor, with the goal of identifying the most potent inhibitor. The results of this study could provide valuable insights into the structure-activity relationships of these compounds, potentially guiding future drug development efforts.

Methods: The three-dimensional structures of the tyrosine kinase receptor and the five selected compounds were retrieved from the Protein Data Bank (PDB). Prior to molecular docking, the structures were prepared using ChemBioDraw and Chem٣D software to ensure the accuracy of the molecular conformations. Molecular docking simulations were conducted using Chimera and AutoDock Vina, which enabled the identification of the optimal ligand-receptor conformations for each compound. The docking analysis included the evaluation of binding modes, hydrogen bonding, and hydrophobic interactions between each compound and the tyrosine kinase receptor. To further validate the results, the Protein-Ligand Interaction Profiler (PLIP) was used to analyze the key interactions formed at the receptor's active site. The docking scores and binding energies obtained from Chimera and AutoDock Vina were used to rank the compounds according to their potential inhibitory effects on the tyrosine kinase receptor.

Results: Docking studies were performed on all selected compounds against the tyrosine kinase receptor. The results indicated that three of these compounds exhibit promising inhibitory potential

against the target protein, showing favorable interactions such as hydrogen bonding, desolvation energy, optimal RMSD values, and stabilizing factors including salt bridges, hydrophobic interactions, π-stacking, and π-cation interactions. Among the docked compounds, ٦-Shogaol and Kaempferol demonstrated the lowest binding energies of -٧,٢٣ KJ/mol and -٧,٤٣ KJ/mol, respectively, indicating strong interactions with the protein target. On the other hand, EGCG, Chrysin, and ٦-Gingerol showed binding energies of -٨,٥ KJ/mol, -٧,٥ KJ/mol, and -٦,٥ KJ/mol, respectively. Despite its slightly higher binding energy, ٦-Gingerol exhibited significant hydrogen bonding, which suggests a stable interaction with the receptor. This was considered an important factor in identifying it as a strong candidate for further study.

Conclusion: The docking study identified three compounds with significant inhibitory potential against the tyrosine kinase receptor. ٦-Shogaol and Kaempferol emerged as top candidates due to their low binding energies, suggesting strong interactions with the protein target. However, ٦-Gingerol was recognized for its hydrogen bonding interactions, which contribute to its stability despite a slightly higher binding energy. These findings ,similar to several studies provide a theoretical basis for the rational design of new pyrazole derivatives as potential cancer inhibitors, highlighting the potential for further development of targeted therapies against tyrosine kinase.

Keywords: Tyrosine kinase, Protein-ligand docking, Anticancer docking, Herbal compounds

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Down-Regulation DNER (Delta/Notch Like EGF Repeat Containing) Gene in Patients with multiple sclerosis and relationship with High Disability (Research Paper)

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Introduction: Multiple Sclerosis (MS) is an autoimmune inflammatory and demyelinating disease of the central nervous system (CNS), influenced by various environmental and genetic factors. The DeNotch-like EGF-related Receptor (DNER) gene, due to its role in the growth and differentiation of neurons, may play a significant role in CNS-related diseases, including MS. Therefore, the aim of this study is to investigate the changes in DNER gene expression in MS and its relationship with clinical and demographic factors such as gender, duration of illness, and degree of disability.

Methods: This descriptive-analytical study was conducted in ٢٠٢٤ in Shahrekord to evaluate the relative expression of the DNER gene. The study sample included ١٠٠ individuals, consisting of ٥٠ people with MS as the case group and ٥٠ healthy individuals as the control group, from whom blood samples were collected. RNA extraction and complementary DNA (cDNA) synthesis were then performed, followed by the determination of the relative expression of the DNER gene using real-time PCR. The data were analyzed using statistical methods such as t-test and ANOVA.

Results: The findings indicated that DNER gene expression was significantly decreased in MS patients compared to the control group (P<٠,٠٠١). Additionally, this decrease in gene expression was observed with the prolongation of the disease duration and in cases of severe disability (p<٠,٠٥).

Conclusion: The DNER gene is expressed in developing and mature CNS (Central Nervous System) neurons and also aids in the maturation of glial cells through the activation of the Notch pathway. This study demonstrated a significant reduction in DNER gene expression in Multiple Sclerosis (MS) patients compared to healthy controls, suggesting a potential role for DNER in MS pathology. The correlation between reduced gene expression and increased disease severity indicates that DNER could serve as a biomarker for disease progression, highlighting its importance for further research and potential therapeutic targeting.

Keywords: Multiple Sclerosis; DNER gene; Gene Expression

effect of antibody-drug conjugates in breast cancer treatment (Review)

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Introduction: Breast cancer (BC) continues to be an incurable condition and represents a significant contributor to cancer-related mortality among women globally. In addition to endocrine and targeted therapies, chemotherapy is frequently utilized as a treatment modality for this malignancy. Recently, a novel class of anticancer agents known as antibody-drug conjugates (ADCs) has emerged, enabling the targeted delivery of chemotherapeutic agents to solid tumors. ADCs are composed of three fundamental elements: an antibody that specifically binds to a target antigen, a cytotoxic payload, and a linker that connects the antibody to the payload. Trastuzumab emtansine (T-DM1) was the inaugural ADC to receive approval for use in breast cancer. Subsequently, two additional ADCs, trastuzumab deruxtecan (T-DXd) and sacituzumab govitecan (SG) have also obtained regulatory approval for breast cancer treatment. Both T-DXd and SG have exhibited bystander effects and remarkable tumor control in this context. Clinical trials indicate that T-DM1, T-DXd, and SG can be effective in the management of breast cancer; however, they may encounter certain challenges in their application.

Methods: This study was conducted through a comprehensive search of the PubMed, Web of Science, Scopus, and Google Scholar databases, utilizing scientific articles obtained from these sources.

Results: Antibodies, or immunoglobulins, are proteins synthesized by the humoral immune system in response to foreign antigens. T-DM1 is an antibody-drug conjugate (ADC) that combines the antibody trastuzumab with the microtubule inhibitor emtansine, utilizing a drug-to-antibody ratio (DAR) of 1:3,5. This conjugation occurs through a non-reducible thioether linker, which maintains stability in both systemic circulation and the tumor microenvironment. Due to the positive charge and membrane impermeability of emtansine upon its release into the cell, T-DM1 exhibits no bystander effect, meaning it does not impact adjacent non-target cells. The mechanism of action for T-DM1 is consistent with that of other ADCs; it first targets and binds to HER2 receptors on the surface of cancer cells. Subsequently, the complex is internalized via endocytosis, where it is transported to lysosomes for degradation. The active agent, DM1, is then released and binds to microtubules, disrupting their function, halting the cell cycle, and ultimately leading to cell death. T-DM1 is currently approved for use in both adjuvant and second-line metastatic settings for HER2-positive (HER2+) breast cancer. Deruxtecan, a derivative of exatecan mesylate, functions as a topoisomerase I inhibitor with approximately tenfold greater activity than 7-ethyl-10-hydroxycamptothecin (SN38), the active metabolite of irinotecan. The payload of T-DXd is linked via a tetrapeptide-based cleavable linker, which confers high stability in plasma. Deruxtecan's membrane permeability facilitates its diffusion from the target cell, allowing it to exert cytotoxic effects on neighboring cancer cells through a bystander effect. T-DXd is approved for use in second-

line treatment and for patients previously treated with T-DM١ for metastatic HER٢+ breast cancer. Clinical studies have demonstrated that T-DXd significantly outperforms T-DM١ in terms of progression-free survival, overall survival, and objective response rates. Sacituzumab govitecan (SG) is a humanized monoclonal antibody targeting trophoblastic cell-surface antigen-٢ (TROP-٢), a receptor identified in trophoblasts four decades ago. Sacituzumab is linked to the topoisomerase I inhibitor SN-٣٨ via a hydrolysable linker. Similar to T-DXd, SG possesses a high DAR of ٧,٦:١ and also exhibits a bystander effect. It is approved for use in the third-line setting for metastatic triple-negative breast cancer (mTNBC) and in later lines of therapy for metastatic hormone receptor-positive (HR+) HER٢-negative breast cancer. When comparing sacituzumab govitecan (SG) to trastuzumab deruxtecan (T-DXd) for the treatment of metastatic breast cancer, particularly in HER٢-low and triple-negative subtypes, SG presents stronger clinical evidence of superiority in specific patient populations. While both agents demonstrate efficacy, SG may be favored in HER٢-zero patients and in certain treatment sequences. The advent of these ADCs offers a more optimistic outlook for the future treatment of breast cancer.

Conclusion: The advent of ADCs in the treatment of breast cancer marks a significant advancement, as these therapies can now target specific cancer antigens beyond HER٢. This development represents a move towards more personalized treatment approaches, although it may also present its own set of challenges. Ongoing efforts to develop next-generation ADCs are expected to enhance their precision, efficacy, and safety, thereby holding considerable promise for the future of breast cancer therapy.

Keywords: Breast Neoplasms, Immunoglobulins, Immunoconjugates, Ado-Trastuzumab Emtansine.

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Effect of antioxidant activity of nanochitosan carrying the extract of Lepidium draba L plant on the liver tissue of rat infected with Staphylococcus aureus (Research Paper)

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Introduction: Today, nanocarriers are of particular importance, because they can improve the bioavailability and efficacy of the compound by passive or active targeting to damaged tissues. On the other hand, medicinal plants are good candidates for the treatment of diseases, and one of the most valuable medicinal plants of the shabbo family is the Lepidium draba L plant. Chitosan is a non-toxic, renewable nanocarrier that acts as a compatible and effective biological material. The purpose of this research. Investigating the effect of antioxidant activities of nanochitosan carrying the extract of Lepidium draba L plant on liver tissue infected with Staphylococcus aureus bacteria in male Wistar rats

Methods: In this experimental study, ۲۸ male Wistar rats were divided into four groups, including the control group, infected with Staphylococcus aureus (۱۰۸ CFU/ml), recipient of nanochitosan (۱ ml) and the infected model + recipient of nanochitosan carrying the extract of Lepidium draba L plant (۲۰۰ mg/ kg) were divided. Induction of infection was done by intraperitoneal injection and receiving the extract of plant-carrying nanochitosan for ۳۵ days by gavage method. After the treatment and dissection of the animals, the liver tissue was extracted to check the level of antioxidant activity of TAC and MDA in different groups. Data analysis in different groups was done with SPSS software and one-way variance statistical test and $p<۰,۰۵$ was considered significant.

Results: The results showed a significant change in the level of antioxidant activity of TAC and MDA in the infected groups compared to the control group. While the increase of TAC activity and the decrease of MDA in the treatment groups compared to the infected group were shown significantly.

Conclusion: Based on the obtained results, nano-chitosan carrying the extract of Lepidium draba L plant showed a modulating effect on the antioxidant activity of the liver tissue of rat infected with bacteria. Therefore, it can probably be used as a promising therapeutic tool, although it is suggested that gene pathways, molecular pathways and tissue changes should be taken into consideration in the next investigations.

Keywords: Nanochitosan, Lepidium draba L plant , TAC, MDA, liver, Staphylococcus aureus, Rat

Effect of Green tea (Camellia sinensis) Supplementation on liver enzymes: A Systematic Review of Clinical Trials (Review)

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Introduction: Green tea, which is derived from the leaves of *Camellia sinensis*, is widely known for its health benefits, such as its antioxidant and anti-inflammatory properties. It has been suggested that consuming green tea may have a positive impact on liver function by affecting certain liver enzymes, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma-glutamyl transferase (GGT). Elevated levels of these liver enzymes are often indicative of liver damage or dysfunction. Despite the increasing interest in this topic, the precise effect of green tea on liver enzymes is still unclear. This systematic review seeks to assess the existing clinical evidence regarding the effect of green tea on liver enzymes.

Methods: A comprehensive search was conducted using PubMed, Google Scholar, Scopus, and Medline databases. The search focused on randomized controlled trials (RCTs) examining the effects of green tea on liver enzymes in human subjects. Keywords used included "green tea," "liver enzymes," "ALT," "AST," "ALP," "GGT," and "RCT." Studies were screened based on inclusion criteria, including human clinical trials, green tea intervention, and reported liver enzyme outcomes. A total of ١٠ RCTs were identified and included in the review. Data from these studies were extracted, and a qualitative synthesis was performed.

Results: Among the ١٠ RCTs included in the review, eight studies reported a statistically significant beneficial effect of green tea on liver enzyme levels. These studies demonstrated reductions in ALT, AST, and GGT levels, suggesting a hepatoprotective effect of green tea. The potential mechanisms discussed include green tea's antioxidant properties, which may reduce oxidative stress in the liver, and its ability to modulate inflammatory responses. In contrast, two studies found no significant impact of green tea on liver enzymes. These studies reported that green tea did not result in any substantial changes in liver function markers compared to placebo. Possible explanations for the lack of effect in these studies include differences in study populations, green tea dosages, and study durations.

Conclusion: The majority of RCTs reviewed in this systematic analysis suggest that green tea may have beneficial effects on liver enzyme levels, supporting its role as a potential hepatoprotective agent. However, the presence of conflicting results in a minority of studies highlights the need for further research, particularly to clarify the dose-response relationship and to identify subpopulations

that may benefit most from green tea consumption. Future studies should aim to standardize green tea formulations and dosages to allow for more consistent comparisons across trials.

Keywords: Green tea, Liver enzymes, Hepatoprotection, Randomized controlled trials (RCTs), Systematic review.

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Effect of SKEO on inflammatory genes using real-time polymerase chain reaction. (Research Paper)

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Introduction: Essential Satureja Khuzestanica oil (SKEO) and the monoterpene Carvacrol have anti-inflammatory properties, albeit without specifying the precise mechanism of its efficacy. Prostaglandin is one of the main mediators of inflammation regulated by the cyclooxygenase gene and nitric oxide synthase gene. This study examined the effects of SKEO and Carvacrol on the expression of the cyclooxygenase and nitric oxide synthase gene in the LPS-stimulated cell line.

Methods: Fresh parts of the plant were processed to prepare SKEO. Different doses of SKEO and Carvacrol were then used to treat an LPS-stimulated cell line. Following RNA extraction, gene expression analysis was conducted using real-time polymerase chain reaction.

Results: Results: In the LPS-stimulated macrophage cell line, essential S. Khuzestanica oil significantly reduced cyclooxygenase and nitric oxide synthase gene expression in a dose-dependent manner. Carvacrol had a lesser effect. Notably, essential S. Khuzestanica oil exhibited a significantly stronger inhibitory effect on cyclooxygenase and nitric oxide synthase gene expression than Carvacrol.

Conclusion: The decrease in cyclooxygenase and nitric oxide synthase gene expression indicates that S. Khuzestanica oil could be beneficial for managing inflammation-related conditions. Future research should focus on optimizing the dosage and formulation of SKEO to enhance efficacy and reduce side effects. These encouraging results emphasize the necessity of integrating herbal remedies into conventional treatment regimens, paving the way for innovative anti-inflammatory strategies.

Keywords: Essential oil, gene expression, inflammation, SKEO, LPS-stimulated macrophage

Effects of astaxanthin on learning and memory disorders, anxiety-like symptoms, and depression induced by ethanol in mice brain (Research Paper)

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Introduction: ۱. Introduction Ethanol is a colorless, volatile, flammable, odorless, antiseptic, and psychoactive liquid that is the main ingredient of alcoholic beverages. Ethanol has many harmful effects on the brain, including memory loss, and impaired motor and cognitive function caused by neurodegeneration due to increased oxidative stress. Some of the main effects of ethanol are learning and memory impairment, anxiety, and depression. Antioxidants are compounds with the ability to deal with oxidative stress and reduce its effects on people's health. These compounds protect the body against free radical damage. Astaxanthin (ATX) is a lipophilic terpene composed of carbon precursors and a natural red-orange oxy-carotenoid pigment, which is considered a fat-soluble xanthophyll carotenoid.

Methods: ۲. Methods Thirty five ۲۵-۳۰ grams mice in the weight range were purchased from Pasteur Amol Institute and were kept under standard conditions of ۲۳ ± ۲ °C and ۱۲ hours of light and dark cycle in the animal room of the Faculty of Biology. Mice were randomly divided into ۵ groups of ۷: ۱- Control, did not receive any drug. ۲- Positive control, received ۲۰ mg/kg astaxanthin by gavage. ۳- Ethanol, received ۲۰٪ ethanol by gavage. ٤- AST ۱۰, which first received ۲۰٪ ethanol and ۲ hours later received ۱۰ mg/kg astaxanthin by gavage. ۵- AST ۲۰, which first received ۲۰٪ ethanol and ۲ hours later received ۲۰ mg/kg astaxanthin by gavage. ۲,۱. Novel Object Recognition Test (NORT) NORT is a behavioral test that investigates different aspects of memory and learning in rodents and evaluates their ability to investigate a new object. This test is completed in three ۵-minute stages: Habituation stage: the animal is placed in an empty box to get familiar with the environment. Acquaintance phase: First, two identical objects were placed on both sides of the box, and then the animal was placed inside the chamber and in the middle of the two objects to explore. Memory test phase: In this phase, one of the objects in the box was replaced with a new object with different appearance characteristics, and the animal was returned to the box to explore. Exploration was described as smelling or touching objects. Results were described as a discrimination index: the percent of novel object exploration time to the whole exploration time. ۲,۲. Open Field Test (OFT) The open-field test is used to evaluate the level of anxiety and motor activity. To perform this test, we place the animal in one of the quadrants of the device so that it can move freely in the box. The duration of this test is about ۵ to ۱۰ minutes. In this test, the following parameters are evaluated and measured: ۱- Movement activity measurement index ۲- Anxiety measurement index

Results: ۳. Result The discrimination index in the ethanol ($P < ۰,۰۰۱$) and ۱۰ mg/kg astaxanthin ($P < ۰,۰۵$) groups was significantly reduced compared to the control group. While the group treated with astaxanthin ۲۰ mg/kg showed a significant increase ($P < ۰,۰۵$) compared to the ethanol group.

According to the obtained results, the duration of staying in the test center showed a significant decrease in the ethanol group (P < ٠,٠٠١) compared to the control group. Also, this index was significantly increased in ethanol groups treated with ١٠ and ٢٠ mg/kg of astaxanthin, respectively (P < ٠,٠١) and (P < ٠,٠٠١) compared to the ethanol group. According to the obtained results, motor activity in the ethanol group shows a significant increase (P < ٠,٠٠١) compared to the control group. While ethanol groups treated with doses of ١٠ and ٢٠ mg/kg of astaxanthin showed a significant decrease (P < ٠,٠٠١) compared to the ethanol group.

Conclusion: ٤. Conclusion In the present study, the protective effects of astaxanthin on behavioral indices in ethanol model mice brains were investigated. The results showed astaxanthin led to the improvement of memory and learning and anxiety-like behaviors in ethanol-induced mice.

Keywords: Ethanol, Astaxanthin, Mice, Memory, Anxiety

Effects of chronic methamphetamine abuse on the retinal nerve fiber layer, ganglion cell layer and Bruch's membrane opening minimum rim width (Research Paper)

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Introduction: Methamphetamine (Meth) is a strong psychostimulant and sympathomimetic drug with a wide-range of effects on central nervous system . It is well known that Meth could result in neurotoxicity, neurodegeneration, and psychological complication. The reported ophthalmic complications of Meth are scarce and include retinal vasculitis, panophthalmitis, scleritis, retinopathy, and transient and even permanent blindness. . Previously, in an experimental study on rats, it has been shown that treatment of retinal ischemia by antidopaminergic agents leads to increment of ERG-b wave amplitude due to the decrease in the dopamine and reactive oxygen species (ROS) levels; these results suggest that any agent that could increase dopamine, such as Meth, could affect the function of the optic nerve and retina. No previous study has investigated the effects of Meth on the peripapillary RNFL thickness, ganglion cell layer (GCL) thickness, and Minimum rim width (MRW) on human subjects. MRW is defined as the minimum space between Bruch's membrane opening and internal limiting membrane that shows the status of the neuroretinal rim tissue. In the present study, we assessed the RNFL thickness as well as MRW and GCL thickness in Meth users and com- pared them with healthy individuals.

Methods: In this case-control study, we recruited ٥٥ Meth abusers and ٤٩ healthy individuals with mean age of ٤٤,٦٣ ± ٠,٩٧ and ٤٣,٠٨ ± ٠,٩١ years, respectively. All of the participants were examined comprehensively by an ophthalmologists. Slit lamp examination, IOP measurement and examination of the retina and optic nerve with wide-field ٩٠-diopteres lens were performed. Measurement of the RNFL thickness, GCL thickness and MRW was performed using Spectral domain optical coherence topography.

Results: We found statistically significant decrease in RNFL, MRW thickness in Meth abusers (P: ٠,٠٠٢ and P: ٠,٠٠٦, respectively). We did not detect statistically significant difference regarding GCL thickness between the groups (P = ٠,٣٢٠). Our results showed a weak but statistically significant correlation of Meth dose increment and decrement of RNFL thickness ((P: ٠,٠٠٥, r = -٠,١٩٣) and

MRW (P: ٠,٠١٣, r = -٠,١٧٤). We found no correlation between duration of Meth consumption with RNFL and MRW thickness (P: ٠,٢٠٥, r= -٠,١٢٤; P: ٠,٧٧١, r= -٠,٠٢٩, respectively).

Conclusion: We found a statistically significant adverse association in meth abusers with RNFL thickness and MRW. These two parameters were also statistically associated with the meth dose as measured by daily dose of Meth. Although we found a decrease in the GCL thickness, it did not reach statistical significance.

Keywords: Ganglion cell layer; Methamphetamine; Minimumrim width; OCT; Retinal nerve fiber layer

Effects of Folate Supplementation on Inflammatory Markers in Diabetes: A Systematic Review

(Review)

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Introduction: Diabetes is a chronic metabolic disorder characterized by persistent hyperglycemia, which often leads to oxidative stress and inflammation. Chronic inflammation is a key factor in the pathogenesis and progression of diabetes and its complications such as neuropathy, nephropathy, and cardiovascular diseases. High levels of inflammatory markers, such as C-reactive protein (CRP), tumor necrosis factor-alpha (TNF-α), and interleukins like IL.٦, are commonly observed in individuals with diabetes. Folate, a naturally occurring form of vitamin B٩ that serves as an important cofactor for one-carbon (١C) transfer reactions, has been shown to modulate inflammatory pathways and reduce systemic inflammation.

Methods: We systematically searched the PubMed, Scopus, and Google Scholar databases to investigate the effect of folate supplementation on inflammatory markers between ٢٠٠٥ and ٢٠٢٤. The search terms included “folate”, “inflammation”, “diabetes”, “inflammatory markers”, and “cytokines”. Studies that investigated the effects of folate supplementation on inflammatory markers in diabetic rats, focusing on cytokines, such as TNF-α, IL-٦, IL-١β, IL-١٠, and C-reactive protein (CRP) levels, were included. Studies without a control group or those that did not present results were excluded.

Results: Of the ١٨ relevant studies reviewed, out of which ٥ were excluded due to insufficient data. ١٣ studies reported a significant reduction in inflammatory markers following folate supplementation. The results show that folate supplementation reduced the levels of important cytokines in this pathway, including TNF-α, IL-٦, IL-١β, and CRP, by suppressing the activity of the NF-κB pathway. In contrast, folate decreased the levels of homocysteine, an inflammatory marker, and increased the levels of anti-inflammatory cytokines, such as IL-١٠.

Conclusion: Our research suggests that folate supplementation is effective in reducing systemic inflammation in diabetic rats by decreasing inflammatory markers, reducing oxidative stress, and lowering homocysteine levels. Nevertheless, further investigations are required to elucidate the optimal dosage and mechanisms of action of folate in diabetic models.

Keywords: folate, diabetes, inflammation, inflammatory markers, diabetic rats

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Effects of Lactobacillus acidophilus probiotics on colorectal cancer (Review)

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Introduction: Colorectal cancer (CRC) also known as bowel cancer, colon cancer, or rectal cancer remains one of the most frequently occurring cancers worldwide. Current standard therapeutic drugs have been associated with serious side effects that can be life-threatening for some patients. Extensive efforts have been undertaken to find alternative therapies. Probiotics are useful and non-pathogenic microorganisms in the gastrointestinal tract. Probiotic bacteria are among new therapeutic options under evaluation. Lactobacilli strains are among the most used probiotics in CRC. The purpose of this study is observe how lactobacillus acidophilus effects on colorectal cancer.

Methods: for this research many groups of scientists used lots of different methods of culturing and analyzing like cell analysis , morphology analysis , real time PCR , using animal models and clinical trials on ۳۹۸ men and women with previous colorectal tumors and the data were analyzed by statistical analysis.

Results: The results showed that based on the survival rate and harness of L. acidophilus extract, it inhibits the survival and proliferation of cancer cells in a dose- and time-dependent manner. In addition, various morphological changes were observed in the treated cancer cells, which are indicators of apoptosis induction.

Conclusion: The results of the present studies suggested that based on survival rate and harness of L.acidophilus , it inhibits the survival and proliferation of cancer cells in a dose- and time-dependent manner .and various morphological changes were observed in the cancer cells.

Keywords: Colorectal cancer , Lactobacillus acidophilus , Probiotics

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Effects of Mechanical Stress on Aggregation of Zytux® (Rituximab Biosimilar): A Size Exclusion Chromatography Approach (Research Paper)

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Introduction: One popular technique for assessing the stability of therapeutic protein compositions, such as monoclonal antibodies, is mechanical stress. Many stresses are applied to proteins in this approach, including the liquid-air interface, contact with container surfaces, agitation-induced creation of vacuum bubbles, and localized temperature rise. This study aims to investigate, the phenomena of aggregation caused by mechanical stress (shaking and stirring) at different doses of Zytux monoclonal antibody (rituximab biosimilar) using size exclusion chromatography. The production of aggregate products and antibody aggregation, which can lessen therapeutic effects and enhance immunogenicity, are caused by mechanical stress increasing protein molecules' interaction with hydrophobic surfaces, air/water surfaces, and other surfaces.

Methods: Zytux monoclonal antibody samples were prepared at different concentrations and subjected to mechanical stress by being stirred and shaken at constant speeds of ۲۰۰ rpm. Throughout the experiment, samples were taken and examined regularly.

Results: The experimental findings indicated that a higher amount of aggregation occurred when mechanical stress was applied by shaking. The greater levels of mechanical stress produced during shaking instead of stirring might cause this rise. Furthermore, a positive trend associated with higher concentration levels has been seen in the aggregation level, mostly explained by Zytux's natural tendency to aggregate in high-concentration circumstances.

Conclusion: The results of this study emphasize how important it is to understand how mechanical stress affects Zytux stability and aggregation tendency. Since mechanical stress may be imposed throughout various processes, including manufacture, shipping, and product handling, this knowledge is especially important when it comes to formulation and storage conditions.

Keywords: Monoclonal antibody, Zytux, mechanical stress, stirring, shaking, aggregation

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Effects of Using Patient Portals in Patient Education: A Systematic Review (Review)

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Introduction: Patient education through portals plays a vital role in improving health outcomes of patients. Therefore, this systematic review aimed to investigate the effects of using patient portals on patient education.

Methods: This systematic review was conducted by searching keywords in the title, abstract, and keywords of the studies indexed in scientific databases including Embase, Web of Science, Scopus, and PubMed on March ٤, ٢٠٢٤, without any time limitations. The method of data analysis was qualitative. Data was extracted and the synthesized results were presented qualitatively.

Results: ١١ studies were finally included. The educational interventions focused on four aspects: self-management, self-care, knowledge improvement, and disease management. Educational approaches were classified into seven categories including text messages, video messages, image messages, e-mail, frequently asked questions, links to educational resources, and YouTube videos. Text messaging was the most common educational approach for delivering educational content through portals. Most (Four) studies dealt with the design of portals for cardiovascular diseases which indicated the effective role of portals for educating this group of patients.

Conclusion: This review showed that educational interventions through patient portals could improve the quality of life related to health, improve knowledge, and facilitate communication with healthcare providers by providing patient self-care recommendations.

Keywords: Patient portal, Patient education, Self-management, Self-care, Systematic review

Efficacy of Electromyography Biofeedback on improving motor weaknesses in Patients with Ischemic and Hemorrhagic Strokes (Review)

Negin ramezani,[١,*] Negin Ramezani ,[٦]

١.
٦.

Introduction: Stroke is the most common disabling neurological lesion in adults, i.e. the sudden onset of neurological symptoms caused by impaired blood supply of the brain. After cardiovascular diseases and cancer, stroke is the third leading cause of death in the world; according to statistics, it is the cause of more than ١٢-١٠٪ of deaths. However, more than ٥٠ percent of patients survive and suffer long-term disabilities. These sudden neurological disorders show the vascular origin of stroke. These disorders occur in several seconds, minutes, hours, or days. In general, strokes are divided into two major categories of ischemic stroke and hemorrhagic stroke (caused by bleeding). About ٧٠ percent of strokes are ischemic, ٢٠٪ bleeding, and ١٠٪ have no specific origin

Methods: In this case study (the single case), interviewing with a neurologist and studying the medical records of patients, individuals with ischemic and hemorrhagic stroke (with mild to moderate weakness intensity of movement) were identified, and then three patients were randomly selected. Participants were alert patients with a known brain stroke (mild to moderate), with a maximum of a month past the stroke.

Results: The results of data chart visual analysis revealed a significant difference between the intervention and baseline phases for the ٣ patients (PND٦٠٪ subject number ١ & ٨٠٪ subject number ٢&٦٠٪ subject number ٣). In other words, anxiety in the sample had reduced. The improving motor weaknesses remained stable in the follow up phase (١ month and ١ week after intervention).As a result, electromyography biofeedback treatment had reduced the improving motor weaknesses.

Conclusion: Using electromyography biofeedback can be an effective way in preventing or reducing improving motor weaknesses in patients with stroke.

Keywords: biofeedback - improving motor weaknesses – hemorrhagic - ischemic - stroke

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Efficacy of medicinal plants against monogenean parasites of farmed fish (Research Paper)

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Introduction: Monogenean parasites are an important part of pathogenic fish parasites that cause a lot of damage to the aquaculture industry every year.

Methods: Many clinical studies have been conducted using anti-parasitic drugs such as praziquantel and mebendazole with the aim of finding a way to treat these parasites, but their use has been costly and sometimes unsuccessful. Therefore, in recent years attempts have been paid to use medicinal herbs or plants as an alternative to the synthetic anti-parasites. In this review we obtained all available data from the scientific journals and websites and analyzed them for their antagonistic and clinical efficacies towards the fish monogeneans such as Dactylogyrus, Gyrodactylus and Neobenedenia.

Results: Rosemary (Rosmarinus officinalis), garlic (Allium sativum), ginger (Zingiber officinale), ashanti pepper (Piper guineense), peppermint (Mentha piperita), tea tree (Melaleuca alternifolia), bge seeds (Semen aesculin), and bupleurum chinense roots (Bupleuri chinensis) are the most medicinal herbs and plants that have been used against monogeneans under in vitro or in vivo conditions with promising results. In most of the studies carried out, the bath method was used to treat these parasitic diseases in fish, while in aquaculture practice, oral method is a practical method and required in the industry. In addition, unfortunately, most of the studies have no information about the bioavailability of the active ingredients of the studied medicinal plants in the organs of treated fish.

Conclusion: In most of these studies, the main focus has been on the efficacy of medicinal plants on the immunological, physiological and detoxification effects of fish, while their therapeutic properties (laboratory and clinical) have received less attention. In this study, various aspects of the effectiveness of medicinal plants against parasitic monogeneans in fish will be discussed.

Keywords: medicinal plants - monogenean parasites - farmed fish - praziquantel - mebendazole.

Elucidating the Dual Regulatory Role of microRNAs in Colorectal Cancer (Review)

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1.

Introduction: MicroRNAs (miRNAs) are small non-coding molecules, approximately 22 nucleotides in length, found in plants, animals, and viruses with DNA genomes. These miRNAs are derived from RNA transcripts organized in a hairpin structure and play a crucial role in post-transcriptional gene regulation. Colorectal cancer (CRC) poses a significant burden on global health in terms of both illness and death, demanding better approaches for prevention and treatment. Dysregulation of miRNA expression has been strongly implicated in the pathogenesis of CRC, with certain miRNAs acting as oncogenes and others functioning as tumor suppressors. This review examines the dual role of miRNAs in CRC, whereby they function both as destructive agents and as potential therapeutic interventions.

Methods: Several studies have highlighted specific miRNAs, showcasing their roles in inhibiting CRC cell proliferation, migration, and invasion through distinct mechanisms. For instance, miR-18a, miR-155, and miR-205-5p inhibit the proliferation, migration, and invasion of CRC cells, while miR-494, miR-598, and miR-17-3p enhance these abilities. Furthermore, miR-106a and miR-7 are associated with the apoptosis of CRC cells or their resistance to apoptosis. miR-221 and miR-214 have been shown to decrease the levels of autophagy in CRC cells.

Results: Numerous miRNAs have been associated with CRC, exhibiting either pro-tumorigenic or anti-tumorigenic functions. Understanding the intricate mechanisms of miRNAs in colon cancer not only sheds light on the pathogenesis of the disease but also offers avenues for novel therapeutic interventions. As a result, miRNAs have become valuable biomarkers for the diagnosis, prognosis, and potential therapeutic targeting in CRC.

Conclusion: Elucidating the complex miRNA regulatory networks in CRC holds promise for personalized therapies and advancing our understanding of the disease. Ongoing research efforts in this field continue to unveil the therapeutic potential of miRNAs as diagnostic markers and therapeutic targets in cancer treatment, offering new avenues for combating CRC and other malignancies. For further studies, elucidating the context-dependent regulation of microRNAs, such as how specific cellular or environmental factors can shift their roles from oncogenic to tumor-suppressive or vice versa, developing computational and experimental models to predict, validating the complex network of interactions between these dual-acting microRNAs and their target genes in CRC could be helpful.

Keywords: miRNA, Colorectal cancer

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Endocannabinoids reduce the expression of the alpha-۳ subunits of the GABAA receptors of the basolateral amygdala during formalin-induced inflammatory pain modulation in adult male rats (Review)

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Introduction: The basolateral amygdala (BLA) integrates cognitive and pain information and transmits it to the central nucleus of the amygdala, which is the origin of the descending pain modulatory pathway. The role of the BLA endocannabinoid system has been well shown in nociceptive processing. This system induces analgesia through its type ۱ receptors and the GABAergic system inhibition. Therefore, this study aimed to investigate the gene expression changes of α۲, α۳, and β۲-subunits of the GABAA receptors of the BLA in the antinociceptive role of the endocannabinoid system following the inflammatory pain induction.

Methods: In this study, the BLA tissue samples of male Wistar rats were used. ۲۸ Male rats (۲۲۰-۲۷۰ grams) were randomly divided into four groups of seven rats, including the control (intact animals), formalin (formalin test in intact animals), DMSO (intra-BLA injection of DMSO ۱۰ %), and AM۲۵۱ (intra-BLA injection of AM۲۵۱ ۵۰ ng/µl) groups. Following the formalin test, tissue samples were removed and stored in a -۸۰ °C freezer. Gene expression of α۲-, α۳-, and β۲-subunits of the GABAA receptors was evaluated by qRT-PCR technique.

Results: Data analysis showed that formalin injection into the left paw only decreased the gene expression of the α۳ subunit of the GABAA receptor compared to the control group (P<۰,۰۵). Also, following the inflammatory pain induction, the injection of AM۲۵۱ into the right BLA significantly decreased the gene expression of the α۳ subunit of the GABAA receptor compared to the control group (P<۰,۰۵). Still, it had no significant effect on the gene expression of the α۲ and β۲-subunits of this receptor.

Conclusion: The findings of this study suggest that the presence of the α۳ subunit in the heteropentameric structure of the GABAA receptor is probably necessary for the endocannabinoid system-induced analgesia in the basolateral amygdala.

Keywords: Endocannabinoids, inflammatory pain modulation, GABAA receptors, Formalin

Engineered Bacteria as a Versatile Platform in Cancer Therapy (Review)

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Introduction: Cancer remains one of the leading causes of death worldwide. Despite extensive research efforts and recent advancements in treatment methodologies, each approach carries specific limitations, resulting in millions of cancer-related deaths annually. Recently, bacteria have gained attention as versatile platforms that can enhance tumor detection and treatment, either as standalone agents or in combination with other therapies. Genera such as Salmonella, Escherichia, and Clostridium are known for possessing these beneficial properties. These microorganisms can be genetically engineered to deliver various therapeutic payloads locally within the tumor and its microenvironment. Furthermore, advancements in synthetic biology and genetic circuit design enable researchers to control bacterial behavior, tailoring the release of therapeutics to occur at specific times and locations. By leveraging techniques such as mutagenesis and genetic engineering, bacteria can link their growth to environmental signals from tumors, enhance their adhesion to cancer cells, and specifically amplify their growth in hypoxic areas—potentially increasing their proliferation up to ۱۰,۰۰۰-fold in these environments.

Methods: The transfer of these molecules can occur through methods such as passive diffusion, transport across microbial and mammalian membranes, or by utilizing secretion systems like the Type III secretion system (T۳SS). This system, present in Gram negative bacteria, secretes effective macromolecules into host cells using a needle-like complex. Moreover, engineered bacteria can modulate tumor metabolism, such as converting ammonia to L-arginine, which facilitates increased infiltration of lymphocytes within the tumor. Collectively, these approaches underscore the significant potential of engineered bacteria in cancer therapy by programming immune responses. Additionally, bacteria can work synergistically with external materials and technologies. External interventions, such as ultrasound and magnet-based approaches, can enhance bacterial behavior, allowing for tumor visualization and remote control, which can precisely adjust the location and timing of therapeutic release within the tumor. Integrating imaging techniques like MRI, PET, and focused ultrasound (FUS) also permits the tracking and visualization of delivered bacteria. By encoding bacteria with reporter genes or thermal switches, FUS can be utilized to trigger therapeutic release upon activation. Drugfilled nanoparticles canphysically conjugate with bacteria, enabling transportation to deep regions of tumors that may otherwise be inaccessible. The magnetic properties of certain bacteria also offer innovative approaches to cancer treatment. For example, engineered bacteria can be programmed to eliminate other bacterial strains that interfere with chemotherapy effectiveness.

Results: These challenges must be carefully addressed and managed in order to achieve higher efficacy and safety in bacterial-based cancer therapies.

Conclusion: Finally, although significant progress has been made in the development of bacterial cancer treatments, there are concerns in various areas, such as: ١. The degree of bacterial efficacy in tumor tissue at early stages. ٢. The possibility of genetic mutations in bacteria and the loss of therapeutic agents. ٣. Immune responses such as bacteremia and cytokine storms. ٤. The limited effectiveness of bacteria under environmental conditions, such as temperature and pH.

Keywords: Engineered bacteria, Cancer therapy, Tumor microenvironment, Synthetic biology

Engineered exosomes with advanced biomaterials holds great potential for synergistic effects in bone regeneration (Review)

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Introduction: Extracellular vesicles known as exosomes, which are small and enclosed by a membrane, have crucial roles in communication between cells. They range in size from ۳۰ to ۱۵۰ nanometers and are created by the inward budding of late endosomes, also called multivesicular bodies (MVBs). Upon MVBs fusing with the plasma membrane, they release exosomes, which are intraluminal vesicles, into the extracellular space. Exosomes have diverse functions in both health and disease, including intercellular communication, serving as biomarkers, delivering drugs, and modulating the immune system. The molecules serve as intermediaries in communication between cells, impacting different biological functions like immune response, transmission of signals, and presentation of antigens. Exosomes can act as biomarkers for diseases such as cancer, neurodegenerative disorders, and cardiovascular diseases by containing specific profiles of proteins and nucleic acids. They also offer information about the cellular origin and state of the donor cells. Exosomes are currently under investigation as natural carriers of drugs because they can package therapeutic substances and pinpoint particular cells or tissues while having minimal potential to provoke an immune response. They have the capability to traverse biological barriers, like the blood-brain barrier, thus improving the effectiveness of treatments. In addition, exosomes have the ability to influence immune reactions, which is advantageous in situations such as autoimmune disorders and when the body is repairing tissues.

Methods: Exosomes have become a focal point in the field of bone tissue engineering due to their ability to facilitate cell-to-cell communication and stimulate the regeneration of bone. These extremely small vesicles, produced by a variety of cell types, especially Adipose-Derived Stem Cells (ADSCs) and Bone Marrow-Derived Mesenchymal Stem Cells, contain a wide range of essential biomolecules such as proteins, lipids, and RNAs, which play a critical role in regulating cellular functions and improving the formation of bone tissue. The roles of exosomes in bone repair are diverse, with a focus on their mechanisms of action, which include stimulating the proliferation, differentiation, and recruitment of MSCs to injury sites. Additionally, there is growing interest in the modification of exosomes to improve their therapeutic effectiveness, such as altering their cargo and utilizing advanced biomaterials to optimize their delivery and sustained release at bone defect sites.

Results: Engineered exosomes have shown a significantly enhanced ability to promote osteogenesis, which is the process of bone formation. These specialized vesicles play a crucial role in facilitating both the proliferation and differentiation of osteoblasts, the cells responsible for bone formation. By promoting the growth and maturation of osteoblasts, engineered exosomes contribute to the overall development and repair of bone tissue. Engineered exosomes also improve the recruitment of MSCs to areas where there is a deficiency in bone. Methods like electroporation and transfection

are employed to introduce targeted therapeutic agents into exosomes, thereby enhancing their regenerative potential. Despite the advancements that have been achieved in recent years, a number of significant challenges continue to hinder further development and optimization in the field. One of the primary issues is irregular production, which can lead to inconsistencies in supply and affect overall efficiency. Additionally, suboptimal extraction rates remain a concern, as they can limit the yield of valuable resources and impact the economic viability of operations. Furthermore, the mechanisms of action involved in the processes are often ambiguous, leading to uncertainties that complicate efforts to improve methodologies and outcomes. Addressing these challenges is crucial for ensuring sustained progress and maximizing the potential benefits of the advancements made thus far. Current research endeavors focus on enhancing exosome engineering and the integration of biomaterials to address existing challenges and improve their utilization in clinical environments. The integration of engineered exosomes with cutting-edge biomaterials presents significant opportunities for synergistic outcomes in bone regeneration, thereby facilitating the development of novel therapeutic strategies in the field of regenerative medicine.

Conclusion: Although exosomes hold significant potential for applications in bone tissue engineering, several challenges persist in the transition of exosome-based therapies from laboratory research to clinical practice. These challenges encompass concerns regarding the consistency of production, precision in targeting, and the necessity for efficient delivery mechanisms.

Keywords: Engineered Exosomes, Regenerative Medicine, MSCs, Bone Tissue Engineering, Biomaterials

Engineering Bacillus anthracis Protective Antigen for Targeted Cancer Therapy via Urokinase Plasminogen Activator Modulation (Research Paper)

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Introduction: The challenge of cancer therapy is targeting malignant cells without harming normal tissues. The unique expression of uPA on cancer cells provides an opportunity to use bacterial proteins as precision therapeutic agents. Bacillus anthracis's protective antigen (PA) is crucial in anthrax pathogenesis, and its modifications could enhance selectivity towards these uPA-expressing cancer cells.

Methods: Bioinformatics tools were used to identify potential mutation sites within the PA gene to improve its affinity for uPA receptors. After introducing mutations via Overlap Extension PCR, plasmid construction included verification steps to ensure the accuracy of the insert. The TA-vector system was utilized for efficient cloning, and electroporation facilitated transformation into competent WB٦٠٠ cells, optimized for protein expression.

Results: Subsequent analyses, including Sanger sequencing, confirmed the successful incorporation of mutations. Advances in protein expression were monitored through SDS-PAGE and Western blotting, demonstrating increased levels of modified PA proteins. Binding assays showed the enhanced affinity of mutated PA towards uPA receptors, a significant improvement over wild-type PA.

Conclusion: The implications of these findings are profound, as the engineered PA proteins may act as vehicle-cytotoxin conjugates, selectively delivering toxic agents to cancer cells. Utilizing high-affinity binding between the modified PA and uPA could facilitate targeted therapy, reducing systemic side effects. Further preclinical studies are needed to evaluate the therapeutic efficacy and safety profile of these novel constructs in vivo. This study contributes to ongoing research in targeted cancer therapies, demonstrating the potential of bacterial proteins in clinical applications. The engineered PA proteins not only provide insight into novel treatment strategies but also pave the way for future explorations into receptor-mediated targeting mechanisms in oncology.

Keywords: Targeted cancer therapy, Bacillus anthracis, Protective antigen, Urokinase Plasminogen Activator, Ge

Engineering Bacteriophages with CRISPR-Cas۹ for Targeted Therapy (Review)

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Introduction: AMR poses a worldwide health problem, requiring options other than antibiotics. Bacterial infections such as Shigella and E. coli lead to significant death rates, particularly among children, due to diarrheal diseases. Treating multidrug-resistant bacteria is challenging due to limited availability of new antimicrobial drugs. Bacteriophages show potential because they can replicate themselves, break down biofilms, and focus on particular hosts. Nevertheless, they exhibit constraints such as limited host ranges and resistance. Genetic modification can improve their effectiveness by surpassing these restrictions. Bacteriophages can serve as carriers for administering antimicrobials, like the CRISPR-Cas۹ system, to target and eliminate specific bacterial DNA sequences. In spite of progress in synthetic biology, challenges such as contamination continue to impede their clinical application. Infection by helper phages can result in the transfer of virulence and antibiotic-resistant genes among bacterial hosts. In order to address this issue, researchers have tried deleting the DNA packaging site from different phages. In this research, a cosmid system based on bacteriophage P٤ was created to generate transducing units containing a CRISPR-Cas۹ system for targeting particular bacteria. The P٤ cosmid system, derived from a prior investigation, removes interference from the helper phage, enabling the creation of uncontaminated transducing units. The P۲ lyso mutant strain developed in this research prevents the generation of P۲ phage offspring, guaranteeing the production of transducing units that are uncontaminated. Improving the cosmid design and changing the P۲ tail fibers enhances the transduction efficiency of cosmid DNA in human gut pathogens, resulting in substantial eradication of targeted bacteria.

Methods: This research included different types of bacteria, growth environments, and techniques for altering the genetic makeup. Bacteria were grown in LB broth. Phage assays were conducted using SM buffer. Specific techniques and primers were utilized to create cosmids, CRISPR spacers, and plasmids. Gene knock-outs were achieved using Lambda-red recombineering. The process of preparing phage lysate included transformation, culture growth, and induction steps under specific conditions. The research utilizes qPCR for quantifying Cas۹ transducing units in bacteria. Chimeric tail fibers in transducing units target and infect certain bacteria, causing instability after transduction. The specific rep gene of cosmid DNA is amplified using qPCR. The measurement of transduction efficiency involves growing bacterial cells with phage lysate and enumerating CFU. Assessment of Cas۹-induced cell death involves comparing colony-forming units pre- and post-treatment.

Results: The experiments show that the P٤-derived cosmid system produces phage lysates with high titers, containing phagemid transducing units, which help in the Cas۹-mediated killing of S. flexneri strains ۲٤٥VT and ٥a M۹۰T. Moreover, adding a chimeric tail, P۲-P۱(S'), greatly improves both the transduction efficiency and the targeting effectiveness of Cas۹ on P٤ cosmids in S. flexneri M۹۰T.

Furthermore, incorporating a P۲-φV۱۰ chimeric tail enables the effective introduction of the P٤ cosmid into a different host, E. coli O۱۵۷:H۷, resulting in significant Cas۹-induced lethality in this strain. These results emphasize the capability of this system for precise manipulation and regulation of bacterial genes.

Conclusion: Utilizing genetic engineering on bacteriophages is an effective method for generating synthetic bacteriophages that possess specific characteristics to enhance therapy. Modified P٤ phages are able to transport Cas۹ constructs into intestinal bacteria such as S. flexneri and E. coli O۱۵۷:H۷. Modifications to the tail fibers increase transduction efficiency and broaden the range of hosts, which could help overcome resistance to phages. Chimeric phage tail fibers have the ability to transport Cas۹ antimicrobial systems to bacteria that are resistant to phages, showcasing the clinical promise of this technology.

Keywords: Bacteriophages, CRISPR-Cas۹, Transduction

Engineering Exosomes for Cancer Therapy (Review)

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Introduction: Abstract Exosomes are tiny vesicles that naturally transport molecules between cells and have emerged as promising systems for cancer therapy. Due to their ability to deliver drugs, proteins, and microRNAs(miRNA), they offer a selective, stable alternative to traditional cancer treatments, which often have severe side effects. Exosomes can be engineered to target cancer cells more effectively, reducing tumor growth and enhancing immune responses. However, challenges like production efficiency and standardization still need to be overcome. Artificial exosomes, which combine the benefits of natural and synthetic systems, are being developed to meet these needs. Future research could further improve exosome-based therapies, particularly for cancer treatment. Introduction Exosomes are tiny extracellular vesicles that transport biological molecules such as proteins, microRNAs, and metabolites. Despite their small size and low biomolecule expression, their biological function has only been recently understood. Nevertheless, exosomes have quickly emerged as promising systems for drug delivery, particularly in cancer therapy. Current antitumor drugs often cause severe side effects, underscoring the need for more selective and stable delivery methods(١, ٢). Exosomes, whether naturally sourced or synthetically engineered, offer a versatile platform for loading different types of molecules, including small compounds and therapeutic agents. Moreover, exosomes can be customized by selecting specific source cells or engineering them with affinity tags, allowing better adaptation to the complex tumor microenvironment(٣). Innovative cancer treatments are urgently needed to address metastatic cancer, which causes more than ٨ million deaths annually worldwide. Exosomes, which are naturally absorbed by cells, can efficiently deliver drugs, therapeutic proteins, and microRNAs. As our knowledge of exosome formation, release, and uptake grows, interest in using these vesicles as targeted delivery systems for cancer therapies has also risen(٤). Exosome engineering allows for control over their contents and migration paths, showing potential in cancer treatment. Studies using both viral and non-viral methods have engineered parent cells to produce modified exosomes or altered exosome content after secretion. The results have been promising, demonstrating reduced tumor cell migration and proliferation, improved immune responses, increased cancer cell death, and heightened sensitivity to chemotherapy. However, to fully realize the potential of exosomes in clinical applications, standards for their production, isolation, and characterization must be established(٥).

Methods: Basic Properties of Exosomes Exosomes are a subset of extracellular vesicles (EVs), which are nanosized, membrane-bound structures secreted by cells. EVs contain proteins, lipids, and nucleic acids specific to their cell of origin and can be categorized into exosomes, apoptotic bodies, and microvesicles(٦). Exosomes are produced through the endocytic pathway and are typically ٤٠–١٠٠ nm in diameter, with a lipid bilayer containing a variety of proteins, such as heat shock proteins (HSPs), tumor-related genes, and fusion proteins(٧). They also carry nucleic acids, including messenger RNA (mRNA), microRNAs (miRNA), and noncoding RNAs, which help regulate gene

expression and may play a role in cancer progression. Exosomes facilitate intercellular communication by transferring these molecules between cells, which has made them an attractive option for drug delivery (Figure ١) (٨). Exosomes are produced by various cell types and are present in numerous bodily fluids. Mesenchymal stem cell-derived exosomes, which lack certain immune markers, are especially promising for therapeutic applications due to their ability to evade immune detection(٩).

Results: Drug Delivery Vehicles for Cancer Therapy Cancer is the second leading cause of death worldwide. Conventional treatments such as chemotherapy have significant side effects, largely due to their non-selective nature, harming healthy tissues along with cancer cells. Therefore, developing drug delivery systems (DDS) that more specifically target cancer cells is crucial cancer(١٠, ١١). Nanotechnology has advanced cancer treatment by creating drug carriers that accumulate in tumors while minimizing toxicity(١٢, ١٣). However, challenges such as toxicity and poor biocompatibility remain. Exosomes, as natural DDS, provide an innovative alternative, offering advantages such as immune evasion and efficient cellular entry. Exosomes have also gained attention as drug carriers due to their role in intercellular communication(١٤-١٦). Artificial Exosomes as a Drug Delivery Vehicle To overcome the challenges of natural exosome production and standardization, artificial exosomes have been developed. These artificial vesicles, created using nanobiotechnology, combine natural and synthetic nanoparticles' benefits and show potential for drug delivery applications. Despite these advancements, hurdles such as large-scale production and drug loading remain(١٧-١٩). Engineering Exosomes for Drug Delivery Exosomes have advantages over synthetic systems, including their ability to fuse with cell membranes, improving drug delivery. Strategies to target exosomes to tumors include using peptides or antibodies to bind specific receptors on cancer cells. However, avoiding rapid clearance by the immune system remains a challenge. Modifying exosomes to bypass immune detection or using metalloproteinases to alter exosome contents are potential solutions(٢٠-٢٢).

Conclusion: Summary and Future Perspective Exosomes offer significant advantages as drug delivery systems, with low immunogenicity, high safety, and minimal cytotoxicity. However, challenges such as standardization, drug loading, and large-scale production need to be addressed for their full potential to be realized. Artificial exosomes could offer scalable solutions, and future developments in this area could revolutionize cancer treatment(٢٣-٢٥).

Keywords: Exosome, drug delivery, cancer therapy.

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Estimation of Bladder Pressure from Pudendal Electrical Activity of Rabbit Based on the Self-Organized Recurrent Neural Network (Research Paper)

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٤.

Introduction: Hyper-reflexive and loss of voluntary control is a common result of neurological diseases such as spinal cord injury. Electrical stimulation is an alternative treatment for hyperreflexia. To inhibit the bladder, we need to detect nascent bladder contraction. Previous studies reported that electrical activity of the pudendal nerve is correlated with bladder pressure. The aim of this study is developing a neural network model for estimating bladder pressure during bladder contraction based on the electrical activity of the pudendal nerve.

Methods: Three models of neural networks were used to identify the relationship between bladder pressure and pudendal nerve activity: NARX, GRNN, and SRBFNN. Ten adult male rabbits were used in this study. Five experiments were performed to record bladder pressure at different conditions. Finally, to evaluate the performance of the ENG -pressure neural network model, the normalized root-mean-square (NRMS) index was calculated.

Results: NRMS for NARX, GRNN, and SRBFNN were obtained ١٢,١٦, ١٠,٤٩, and ٩,٤٢, respectively. Results indicate that the SRBFNN network has less NRMS error than the other networks. Results shows proposed research is a promising approach to detect nascent bladder contraction.

Conclusion: Using recurrent neural network can characterize nascent bladder contraction

Keywords: Hyperreflexia, Spinal cord injury, Neural network, Bladder

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Estimation of DNA methylation correlated Rheumatoid Arthritis in Iraqi patients (Research Paper)

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Introduction: Background: Rheumatoid arthritis (RA) is considered one of the most important autoimmune diseases that cause different health problems. This study was conducted to estimate DNA methylation correlated with patients treated with Methotrexate drugs.

Methods: Methods: Blood samples were collected from ٧٥ patients with RA treated with MTX and ٧٥ healthy individuals in Iraq. DNA was extracted from blood samples. ELISA method was used to detect DNA methylation in all samples. DNA denaturation was performed using High-temperature in thermocycle PCR.

Results: Results: ELISA results were as follows: a significant difference in DNA methylation was witnessed between the control and RA patients, where the DNA methylations decreased in patients at level ٠,٠٥. Statistically, a significant difference was witnessed in DNA methylation in patient groups and the duration of the disease. The results of DNA methylation were not significant in relation to the duration of MTX and RA disease. Significantly, the outcomes of DNA methylation among urban and rural individuals indicated that ٨٥٪ of them were urban and ١٥٪ were rural. Family history in relation to DNA methylation revealed that there is not a statistically significant difference between the groups. Results of urban and rural DNA methylation in relation to residence were high in rural and non-significant. DNA methylation in RA patients related to the route of MTX treatment was non-significant.

Conclusion: Conclusion: Low DNA methylation in patients with RA in comparison to healthy individuals suggests that DNA methylation plays a significant role in RA.

Keywords: Keywords: DNA methylation, Methotrexate drug, Rheumatoid arthritis.

Evaluating the Efficacy of Chemotherapeutic Regimens in Acute Myeloid Leukemia: A Comparative Analysis (Review)

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Introduction: Acute Myeloid Leukemia (AML) stands as a formidable challenge in the realm of oncology, with its aggressive nature and complex treatment requirements. The cornerstone of AML management has traditionally been chemotherapy, with a myriad of agents employed to combat this malignancy. This study delves into the comparative efficacy of various chemotherapy drugs, aiming to elucidate the most effective treatment modalities for AML patients.

Methods: This study embraced a comprehensive retrospective analysis, encompassing a diverse cohort of ١٥٠ AML patients. The demographic distribution included ٩٠ male and ٦٠ female participants, with an overarching mean age of ٥٥ years. The therapeutic interventions scrutinized comprised standard chemotherapy protocols juxtaposed with novel treatment regimens. The standard protocol entailed a combination of cytarabine and anthracycline-based therapies, while the novel regimen incorporated FLT٣ inhibitors. The evaluation metrics centered on overall survival (OS), complete remission (CR) rates, and event-free survival (EFS), providing a multifaceted perspective on treatment outcomes.

Results: The empirical evidence gleaned from the study presented a compelling narrative. Patients who were administered FLT٣ inhibitors alongside the standard chemotherapy regimen exhibited a CR rate of ٥٣,٣٣٪, with ٨٠ individuals achieving complete remission out of the ١٥٠ treated. In stark contrast, the standard therapy cohort, devoid of FLT٣ inhibitors, manifested a CR rate of ٤٣,٣٣٪, with ٦٥ patients reaching complete remission. The mean OS for the cohort receiving the combination therapy was a notable ١٨ months, surpassing the ١٢-month mean OS observed in the standard therapy group. Furthermore, the EFS metric underscored the efficacy of the combination therapy, with a mean duration of ١٤ months, in comparison to a ٩-month mean EFS for those subjected solely to standard therapy.

Conclusion: The study's findings illuminate the enhanced efficacy of incorporating FLT٣ inhibitors into the chemotherapy regimen for AML patients. The superior CR rates, augmented OS, and prolonged EFS associated with the combination therapy underscore the potential benefits of integrating targeted agents into the treatment paradigm. These insights pave the way for a more tailored approach to AML therapy, advocating for the customization of treatment plans to optimize patient outcomes.

Keywords: Acute Myeloid Leukemia,Chemotherapy Efficacy,FLT٣ Inhibitors,Treatment Outcomes,Comparative Analysis

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Evaluating the Role of the Gut Microbiome in Cancer Immunotherapy Response: Mechanisms and Clinical Applications (Research Paper)

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۲.

Introduction: The gut microbiome has emerged as a crucial player in modulating the host's immune system, with growing evidence linking its composition and function to the efficacy of cancer immunotherapies. Understanding the intricate interactions between the gut microbiota and immune responses can pave the way for novel therapeutic strategies to enhance cancer treatment outcomes.

Methods: This study systematically reviews and synthesizes findings from preclinical and clinical studies investigating the impact of gut microbiota on the efficacy of immune checkpoint inhibitors (ICIs) and other cancer immunotherapies. Advanced bioinformatics tools were utilized to analyze microbiome composition in patients undergoing treatment, while experimental models were employed to validate causal relationships and elucidate underlying mechanisms. Additionally, interventions such as probiotics, prebiotics, and fecal microbiota transplantation (FMT) were evaluated for their potential to modulate treatment responses.

Results: Findings highlight a significant correlation between gut microbiota diversity and treatment efficacy, with specific bacterial strains such as Akkermansia muciniphila and Bifidobacterium longum emerging as key modulators of immune responses. Mechanistically, these microbes influence the tumor microenvironment by enhancing antigen presentation, promoting T-cell infiltration, and reducing immunosuppressive factors. Clinical trials investigating microbiome-based interventions demonstrated promising results, with improved response rates in patients receiving FMT or microbiome-targeted therapies.

Conclusion: The gut microbiome plays a pivotal role in shaping the host's immune landscape and determining the success of cancer immunotherapies. Future research should focus on integrating microbiome profiling into routine clinical practice to identify biomarkers for treatment stratification and develop personalized therapeutic approaches. Leveraging microbiome-targeted strategies offers a transformative opportunity to enhance the efficacy and safety of cancer immunotherapies.

Keywords: gut microbiome, cancer, FMT

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Evaluation and bioinformatic analysis of the genetic origin in patients with colon cancer and response to chemical drugs in the new generation (Research Paper)

Majid Mesgartehrani,[۱,*] Elham SangariKojour,[۲] Mohammad Mahdi Eslami,[۳]

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Introduction: Colon cancer is one of the leading causes of cancer-related deaths worldwide, primarily driven by a complex interplay of genetic, environmental, and lifestyle factors. Recent advancements in bioinformatics have enabled the identification of genetic mutations and molecular pathways associated with colon cancer. Furthermore, understanding how these genetic variations influence the response to chemical drugs in new-generation therapies is critical for improving patient outcomes. This study aims to evaluate the genetic origins of colon cancer through bioinformatic tools and analyze the relationship between genetic variations and drug response.

Methods: A cohort of patients diagnosed with colon cancer was recruited, and their genetic profiles were analyzed using next-generation sequencing (NGS) techniques. The raw sequencing data were processed using advanced bioinformatic pipelines to identify key mutations and genetic variations. To evaluate drug responses, in vitro experiments were conducted on patient-derived cells treated with a panel of new-generation chemotherapeutic agents. Statistical models and bioinformatic algorithms were applied to correlate genetic mutations with drug efficacy and resistance patterns.

Results: The bioinformatic analysis revealed recurrent mutations in genes such as APC, TP۵۳, KRAS, and PIK۳CA, which were significantly associated with colon cancer pathogenesis. Drug sensitivity assays demonstrated varied responses to chemotherapeutic agents based on the identified genetic profiles. For instance, patients with KRAS mutations showed limited response to EGFR inhibitors, whereas those with PIK۳CA mutations exhibited enhanced sensitivity to PI۳K/mTOR inhibitors. Integrative bioinformatic analysis further identified novel biomarkers predictive of drug response, providing insights into personalized therapeutic strategies.

Conclusion: This study highlights the critical role of genetic profiling and bioinformatics in understanding colon cancer and optimizing drug response. The findings emphasize the potential of integrating genetic data into clinical decision-making to develop personalized treatment plans, improve therapeutic efficacy, and minimize adverse effects. Further research is warranted to validate these biomarkers in larger cohorts and explore their application in real-world clinical settings.

Keywords: APC, TP۵۳, KRAS, PIK۳CA

Evaluation and bioinformatic analysis of the genetic origin of acute lymphoblastic leukemia cancer patients and their response to novel chemotherapy drugs (Research Paper)

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Introduction: Acute lymphoblastic leukemia (ALL) is a relatively rare heterogeneous blood malignancy in adults, but it is one of the most common types of cancer in children, which is characterized by the uncontrolled proliferation of lymphoid progenitor cells in the bone marrow and peripheral blood. ALL is characterized by the rapid development of white blood cell precursors called lymphoblasts, which divide inappropriately and disrupt the production of healthy blood cells, resulting in the production of very low amounts of red blood cells, white blood cells and platelets, which cause anemia, neutropenia and thrombocytopenia respectively. The two main subtypes of ALL, which are classified according to immunophenotype, are B cell ALL (in ٨٥ to ٩٠٪ of cases) and T cell ALL (in ١٠ to ١٥٪ of cases) are ALL. This disease is very common in children but also occurs in adults, but the probability of treatment in adults is very low, but in children, treatments are a good opportunity for their recovery. Chemotherapy and radiation exposure may increase the risk of developing ALL. Leukemia treatment means that the cancer is gone, does not recur and no further treatment is needed.

Methods: To conduct this research, prominent sources in the field of bioinformatics and molecular biology were used, including the NCBI database and using Mega-gene pharmacogenetic software. With the help of this program, we categorized and analyzed the data related to the data management of each gene, the data related to the polymorphism of a gene, and the drug information related to the disease, In order to be able to analyze the polymorphism information of the genes involved in this disease and to diagnose the side effects of medicinal uses with genetic origin of people.

Results: With the investigations entered in Mega-gene, we have reached the processing of common polymorphisms in the occurrence of this disease, which includes, among the ٤٧ genes that are involved in the occurrence of the disease, three genes have the highest percentage. the Effect of a gene is based on its occurrence rate in the statistical population and also the highest number of reports of that gene. Polymorphism refers to the presence of two or more different forms of a particular DNA sequence that can occur in different individuals or populations. The most common type of polymorphism involves changes in SNPs, so each SNP represents a difference in a DNA building block called a nucleotide. As mentioned, among all the genes that are effective in the occurrence of this disease, despite the presence of polymorphism in each of them, these three genes have the highest polymorphism statistics, which include: ١- JAK٢ with ٤٨ SNPs and ٦,٠٤٪

influence in the community. ٢- RUNX١ with ٢٥ SNPs and ٣,١٤٪ influence in society. ٣- RB١ with ٢٣ SNPs and ٢,٨٩٪ influence in society. Also, by examining the effects of drug treatment in affected people, despite the existence of polymorphisms in the genes involved in this disease, by examining ٢٤ different drugs in the treatment of ALL, affected patients should not use a number of drugs to treat their symptoms. These six items include: ١- People with MLH١ genetic background, taking the drugs Adriamycin, Thioguanine, Erwinase, Dasatinib and Azacitidine causes side effect of nausea in patients. ٢- People with JAK٢ genetic background by using Methotrexate, L-Asparaginase and Azacitidine drugs cause side effect of Crohn, Inflammation, Platelet Hyperaggregability and Psoriasis in patients. ٣- People with RB١ genetic background by using Etoposide drugs causes side effect of Mucositis in patients. ٤- People with TP٥٣ genetic background by using Nelarabine drugs causes side effect of Anorexia in patients. ٥- People with BCR genetic background by using Dasatinib drugs causes side effect of Tinnitus in patients. ٦- People with IKZF١ genetic background by using Thioguanine drugs causes side effect of Decreased cell growth in patients.

Conclusion: To use drugs to treat the ALL disease Before prescribing medicine and therapy, it is necessary to carry out genetic tests to check the presence of polymorphisms in common genes, including MLH١, JAK٢ and RB١ then It should be done on patients so that in case of polymorphism, drugs with less side effects can be prescribed for the patient.

Keywords: acute lymphoblastic leukemia, Bioinformatic database, chemotherapy drugs, Cell lines, polymorphisms

Evaluation of a Probiotic Gel for the Treatment of Diabetic Foot Ulcers and Infections Introduction:

(Research Paper)

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Introduction: Diabetic foot ulcers (DFUs) are a common and severe complication of diabetes, often leading to infection, prolonged hospitalization, and even amputation. The increasing prevalence of antibiotic-resistant bacteria poses a significant challenge in managing DFUs. Probiotics, known for their antimicrobial and anti-inflammatory properties, offer a potential alternative therapeutic approach to enhance wound healing and prevent infections. This study investigates the effectiveness of a topical probiotic and aloe vera gel in treating DFUs and related infections in laboratory animals.

Methods: Thirty Albino Wistar rats were purchased from the animal shelter of the Pasteur Institute of Iran, weighing ٢٥٠-٣٠٠ grams. In this study, the mice were divided into five groups of six and were identified based on the painted area: ١. Control group; in this group, no medicinal substance was used. ٢. In this group, the supernatant mix of Lactobacillus casei bacteria and the Aloe Vera plant was used for treatment. ٣. L. casei supernatant was used for treatment in this group. ٤. In this group, the supernatant of the aloe vera plant was used for treatment. During the four-week treatment period, the supernatant of L. casei and Aloe vera was inoculated into the wounds caused by diabetes and Staphylococcus aureus infection in the form of a gel every day, and the healing of diabetic wounds was observed qualitatively and finally. Histological examinations were evaluated.

Results: The effect of treatment on fibroblast cells showed that the group treated with probiotic gel and aloe vera had more fibroblast cells than the untreated group. In addition, this supernatant increased the rate of fibroblast cells, re-epithelialization in the wound area, and increased the thickness of the epidermis and dermis layers.

Conclusion: The study findings suggest that a topical probiotic and aloe vera gel is effective in promoting the healing of diabetic foot ulcers and reducing the risk of bacterial infections. The probiotic and aloe vera formulation demonstrated both antimicrobial and anti-inflammatory effects, contributing to improved wound healing outcomes. The probiotic and aloe vera gel was safe and well tolerated, highlighting its potential as a promising adjunct therapy for managing diabetic foot ulcers. To confirm these results and discover the therapeutic benefits of this type of probiotic-plant gel in diabetic wound management, research on patients and longer follow-up periods are recommended.

Keywords: Diabetic Foot Ulcers (DFUs), Probiotic Gel, Aloe Vera, Antimicrobial Properties, Wound Healing

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Evaluation of anticancer effects of postbiotics derived from Enterococcus faecium strain KCH-۱ on HT۲۹ colon cancer cell line (Research Paper)

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Introduction: Colorectal cancer (CRC) is a prevalent and life-threatening malignancy closely linked to the intestinal epithelium and gut microbiome. Recent advancements in research have highlighted postbiotics—defined as non-viable microbial cells or their components that confer health benefits—as a safer and more stable alternative to probiotics. This study aims to investigate the anti-cancer potential of postbiotics derived from Enterococcus faecium strain KCH-۱, specifically focusing on their effects on HT۲۹ human colon cancer cell lines. The findings demonstrate that postbiotic components, including cell-free supernatants and exopolysaccharides, significantly inhibit cancer cell proliferation, induce apoptosis, and enhance oxidative stress. These results suggest that postbiotics could serve as effective agents in CRC treatment by modulating immune responses and interfering with tumor cell growth. This research contributes to the growing body of evidence supporting postbiotics as a novel therapeutic strategy in oncology, offering a promising approach to complement traditional cancer therapies.

Methods: This study details the methodologies employed to evaluate the anti-cancer effects of postbiotics derived from Enterococcus faecium strain KCH-۱ on HT۲۹ colon cancer cells. Microbial cultures were initiated by preparing solid and liquid MRS media, followed by inoculation with bacterial strains revived from frozen storage. A microbial suspension was cultivated at ۳۷°C, with subsequent centrifugation to separate bacterial cells from the supernatant, which was then processed for lyophilization to produce postbiotics. The HT۲۹ colon cancer cell line was acquired and cultured in DMEM supplemented with ۱۰٪ FBS and antibiotics For experimental assays, cell viability and cytotoxicity were assessed using the MTT assay, while the effects of postbiotics on cell apoptosis and cell cycle progression were analyzed through flow cytometry, utilizing staining methods with Annexin V-FITC/PI and propidium iodide (PI). Additionally, reactive oxygen species (ROS) levels were evaluated to determine oxidative stress effects. This comprehensive methodological approach facilitates the exploration of postbiotic applications in cancer therapy, providing insights into their potential mechanisms of action.

Results: The results of this study demonstrate the significant anti-cancer effects of postbiotics derived from Enterococcus faecium strain KCH-۱ on HT۲۹ colon cancer cells. The MTT assay revealed that varying concentrations of postbiotics (۱۰۰۰, ۵۰۰, ۲۵۰, ۱۲۵, and ٦۲,۵ µg/ml) resulted in a marked reduction in cell viability over ۲٤, ٤۸, and ۷۲ hours, with an IC۵۰ value of ۱۰۰۰ µg/ml

corresponding to ٥١,٤٢٪ cell survival at ٤٨ hours. Flow cytometric analysis indicated a notable increase in early apoptosis (٢١,٦٪) in treated cells compared to the control, where the proportion of viable cells decreased to ٧٦,٤٪. Furthermore, treatment with postbiotics significantly affected cell cycle progression, leading to an increase in cells arrested in the S phase (٤٠,٩٢٪), indicating that postbiotics promote apoptosis and disrupt normal cell division. Additionally, the assessment of reactive oxygen species (ROS) levels showed that postbiotic treatment led to a substantial reduction in macrophage migration inhibitory factor (MIF) levels, suggesting an increase in oxidative stress and contributing to the observed cytotoxic effects. Overall, these findings underscore the potential of Enterococcus faecium derived postbiotics as effective agents in the treatment of colorectal cancer by inducing apoptosis and enhancing oxidative stress within cancer cells.

Conclusion: The study highlights the promising anti-cancer effects of postbiotics derived from Enterococcus faecium on HT٢٩ colon cancer cells. Findings demonstrate that these postbiotics significantly inhibit cell viability and promote apoptosis in a dose-dependent manner. The MTT assay confirmed that increasing concentrations of postbiotics lead to decreased cell survival, with a notable $IC_{٥٠}$ value of ١٠٠٠ µg/ml resulting in ٥٢,٢٤٪ cell viability at ٤٨ hours. Flow cytometric analysis revealed increased early apoptosis and cell cycle arrest, particularly in the S phase, indicating a disruption in cellular proliferation. Furthermore, elevated levels of reactive oxygen species (ROS) were observed, suggesting that postbiotics induce oxidative stress, which may contribute to their cytotoxic effects. Overall, these results underscore the potential of Enterococcus faecium-derived postbiotics as a novel therapeutic strategy for colorectal cancer treatment, emphasizing their ability to enhance apoptotic pathways and generate oxidative stress in cancer cells. This research supports the exploration of postbiotics as adjunctive therapies in oncology, offering a safe and effective alternative to conventional cancer treatments.

Keywords: Probiotic , postbiotic , colon cancer

Evaluation of antimicrobial and cytotoxicity of the combination of honey and Zataria multiflora and Black cardamom plants on Staphylococcus aureus, Pseudomonas aeruginosa and Escherichia coli bacteria **(Research Paper)**

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Introduction: Considering the high rates of global antimicrobial resistance, researchers are looking for new ways to deal with the resistance. Therefore, this study aims to analyze the bioactive compounds and antimicrobial effects of honey and alcoholic extracts of Zataria multiflora and Black cardamom.

Methods: The bioactive compounds of alcoholic extracts of Zataria multiflora and Black cardamom plants were analyzed by GC-MS. The effect of cytotoxicity of honey and alcoholic extracts of the mentioned plants on the HEK٢٩٣ epithelial cell line and human erythrocytes was performed by MTT and hemolytic methods, respectively. We evaluated the antimicrobial effects of honey and alcoholic extracts of both plants, first individually and then in combination with different ratios on some bacteria, to determine the minimum inhibitory concentration (MIC) based on the latest CLSI٢٠٢٣.

Results: Studying the use of the composition of honey (٣٠٪) and alcoholic extracts of Zataria multiflora (٣٥٪) and Black cardamom (٣٥٪) against three tested bacteria revealed MIC=١٠٠٠ µg/ml on Staphylococcus aureus and Pseudomonas aeroginosa and also minimum bactericidal concentration (MBC)=١٠٠٠µg/ml against Escherichia coli. Thymol, Resorcinol, Phenol, ٢-methyl-٥-(١-methyl ethyl, ٣,٧-Octadiene-٢,٦-diol, ٢,٦-dimethyl) were identified and analyzed as possible compounds using GC-MS. The toxicity combination of F٦ against human blood cells and human kidney epithelial cells (HEK٢٩٣) was ١١,١٣٪, and ١٣,٨٤٪ less against triton X-١٠٠ toxicity (٩٥٪) respectively.

Conclusion: Compound F٦ honey (٣٠٪) and alcoholic extracts of Zataria multiflora (٣٥٪) and Black cardamom (٣٥٪) due to better antibacterial properties against Escherichia coli bacteria, and less toxicity against eukaryotic cells due to the presence of chemicals such as hydrogen peroxide, thymol and resorcinol, is a suitable candidate for further studies, including the relationship between the components of the composition and animal studies.

Keywords: Honey, Black cardamom, Zataria multiflora, Cytotoxicity, Antibacterial.

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Evaluation of Benzalkonium Chloride Effects on Apoptosis Gene Expression in the Chick Embryo Chorioallantoic Membrane (CAM) Model (Research Paper)

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Introduction: Apoptosis, or programmed cell death, is a crucial process for maintaining tissue homeostasis and regulating cell growth. This process is controlled by the balance between pro-apoptotic genes like BAX and anti-apoptotic genes like BCL-٢. Disruption in this balance can lead to various diseases, including cancer and developmental abnormalities. Benzalkonium chloride (BAC) is a widely used biocide in the poultry and pharmaceutical industries. Given the extensive use of this compound, it is essential to investigate its effects on key biological processes such as apoptosis and angiogenesis. The chick embryo chorioallantoic membrane (CAM) is a well-established model for studying angiogenesis and apoptosis due to its simple structure and the ability to directly observe these processes. This study aims to investigate the effects of BAC on the expression of BAX and BCL-٢ genes in the CAM vasculature, marking the first study on BAC's influence on apoptosis in this model.

Methods: This study utilized ١٤ fertilized eggs obtained from Mahan Kerman Poultry Hatchery. The eggs were randomly divided into two groups of ٧ eggs each. The first group was treated with ٠,٢٪ BAC, while the second group received PBS (phosphate-buffered saline) as a control. The treatments were administered intra-egg at ٢٤, ٤٨, and ٧٢ hours post-incubation. The CAMs were harvested ٢٤ hours after the final treatment for gene expression analysis. RNA extraction from the CAM tissues was performed using commercial RNA extraction kits, followed by cDNA synthesis. Gene expression of BAX and BCL-٢ was analyzed using Real-Time PCR, with GAPDH serving as the reference gene for normalization. All PCR reactions were conducted in triplicates using specific primers and a Real-Time PCR system. Statistical analysis of the results was performed using SPSS version ٢٥, and a T-test was applied to determine the significance of the data, with a significance threshold set at $P<٠,٠٥$.

Results: Real-Time PCR results demonstrated that BAC significantly increased the expression of the BAX gene in the treated group ($P<٠,٠٥$). Conversely, the expression of BCL-٢ was significantly reduced in this group compared to the control ($P<٠,٠٥$). These findings indicate an increase in apoptosis within the CAM vasculature as a result of BAC treatment. The analysis of the BAX/BCL-٢ expression ratio revealed a marked increase in the BAC-treated group, strongly suggesting the activation of pro-apoptotic pathways and the suppression of anti-apoptotic activity.

Conclusion: The findings of this study clearly indicate that BAC has a direct impact on apoptosis in the chick embryo chorioallantoic membrane. The increase in BAX expression and decrease in BCL-٢ expression provide strong evidence of BAC-induced apoptosis. These results offer valuable insights into the potential biological impacts of BAC in both biomedical and industrial contexts. In mammals, angiogenesis plays a crucial role in the formation and growth of the placenta and the fetus. The use

of BAC could potentially induce apoptosis, leading to adverse effects on fetal development. However, further research is needed to confirm these effects in mammalian models. Given the widespread use of BAC as a preservative in the pharmaceutical industry and its demonstrated negative effects on fetal development, caution is advised when administering medications containing BAC during pregnancy. On the other hand, the pro-apoptotic and anti-angiogenic properties of BAC suggest its potential utility in the treatment of angiogenesis- and apoptosis-related diseases, such as controlling tumor growth. Inducing apoptosis in vascular cells could offer a promising strategy for inhibiting tumor angiogenesis and growth, positioning BAC as a potential agent in cancer treatment.

Keywords: Benzalkonium Chloride (BAC), Apoptosis, Chick Embryo Chorioallantoic Membrane (CAM), Angiogenesis

Evaluation of common COL٢A١ gene variants in Iranian patients suspected with Stickler syndrome type I (Research Paper)

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Introduction: Stickler syndrome, also known as hereditary progressive arthro-ophthalmopathy, is a connective tissue disorder caused by mutation in several genes with distinct hereditary patterns. Stickler syndrome type I is an autosomal dominant inherited syndrome caused by mutations in COL٢A١ gene (Stickler syndrome type I. The present study aims to investigate the common variants of the COL٢A١ gene in patients suspected to be affected by Stickler syndrome type I.

Methods: The peripheral blood samples from ٢٦ Iranian patients suspected to Stickler syndrome type I were collected in genetic lab at Alzahra university hospital (affiliated with Isfahan University of Medical Sciences) after Fillings Consent Form by these patients. Following DNA extraction, the PCR amplification was performed on selected exons and purified amplicons considered for Sanger sequenced. The common variants of the COL٢A١ gene were studied on the relevant exons.

Results: Overall, two DNA variants and six polymorphisms were observed in the patients consist of: A heterozygous synonymous mutation (c.٢١٣C>T) in exon ٢ and a heterozygous hot spot mutation (c.١٠٣٠C>T) in exon ١٧

Conclusion: In this project a total of ٢٦ patients suspected to Stickler syndrome type I were examined by DNA sanger sequencing which identified a pathogenic point mutation variant (c.١٠٣٠C>T) in a single individual. Accurate genetic counseling is of paramount importance to reduce the chance of recurrence by guiding family planning decisions and encouraging prenatal testing. The diagnosis of a COL٢A١ gene mutation can also significantly enhance disease management for affected individuals.

Keywords: Stickler syndrome type I, Hereditary Arthro-Ophthalmopathy, Stickler Syndrome vitreous type I

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Evaluation of culture parameters on the rituximab glycan profile in recombinant chines hamster ovary cells using a ٢٠٠-liter bioreactor (Research Paper)

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Introduction: The biopharmaceutical industry has witnessed substantial advancements in the production of therapeutic antibodies, particularly those targeting immune-related diseases such as autoimmunity and cancers. Key to the efficacy and specificity of these monoclonal antibodies is their glycosylation profile, which is influenced by various biosynthetic mechanisms. This study specifically examines the impact of culture duration and manganese chloride (Mn٢+) concentration on the glycan profile of rituximab, a widely used therapeutic antibody produced in Chinese Hamster Ovary (CHO) cells.

Methods: Both upstream and downstream processes were methodically designed to assess the glycosylation changes in relation to these process parameters. CHO (DG٤٤) cells were cultured in a defined protein-free medium (MAMPFVV) under controlled conditions. The cultures were categorized based on varying Mn٢+ concentrations (١٥ mM and ٣٥ mM) and cultivation durations (٣٠٠ hours vs. ٢٦٤ hours). Our results indicated that optimized culture conditions can significantly enhance galactosylation of rituximab, achieving increases of up to ٨٪ in the glycan profile. Harvesting was performed through depth filtration, followed by chromatographic purification techniques, including affinity chromatography, which retained high selectivity and resolution. Subsequent viral inactivation and a series of analytical tests confirmed the integrity and purity of the final product, with impurity levels remaining within acceptable ranges as determined by size exclusion chromatography (SE-HPLC) and SDS-PAGE analyses.

Results: The findings highlight a complex interaction between cultivation duration and manganese chloride concentration. While extended cultivation periods increased protein yields, they inversely impacted the extent of galactosylation; reducing the cultivation duration enabled optimal enzyme activity for the maturation of glycosylation pathways. Moreover, the study demonstrates that Mn٢+ concentration plays a critical role as a cofactor in enhancing galactosyltransferase activity, thereby promoting higher levels of galactosylated antibody production.

Conclusion: In conclusion, optimizing upstream parameters such as culture conditions effectively influences the therapeutic glycoprotein's glycan profile, ultimately enhancing its clinical efficacy in immunotherapy. This research provides valuable insights into the biotechnological production strategies that can be employed to maximize the therapeutic potential of monoclonal antibodies, setting a foundation for future developments in antibody engineering and production.

Keywords: Rituximab, Glycosylation, PTM, Complement Dependent Cytotoxicity, Culture duration

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Evaluation of frequency and relationship between underlying diseases and the rate of SARS-CoV-۲ infection (Research Paper)

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Introduction: Introduction In late December ۲۰۱۹, an unknown pneumonia case was reported in Wuhan, Hubei Province, China, with clinical characteristics very similar to viral pneumonia. COVID-۱۹, as a global respiratory infectious disease, has led to a focus on the impact of underlying diseases on its severity and side effects. This study was designed and conducted to determine the relationship between the incidence of COVID-۱۹ and underlying diseases in patients.

Methods: Materials and Methods In the first stage, the study objectives were explained to the patients, and written informed consent was obtained from them. In the next stage, a total of ۳٤۲ nasopharyngeal samples were taken from suspected patients using sterile swabs. RNA extraction was performed using a kit approved by health authorities. LAMP primers for the N gene were designed using Primer Explorer V٥ software, resulting in a total of ۳ primer pairs. The one-step LAMP assay was performed in a ۲٥ microliter reaction mixture. To confirm the results of LAMP products, ۱,٥٪ agarose gel was used with DNA-Safe staining.

Results: Results Data was recorded in SPSS version ۲۲ statistical software and analyzed using chi-square and logistic regression tests at the significance level. Of the ۳٤۲ participants in this study, ۷٤ (۲۱,٦٪) were women and ۲٦۸ (۷۸,٤٪) were men. The age range was ۱ to ۹۰ years, and the mean age of the study participants was ٤۳,۲٤±۱۷,۲۱ years. There was no significant difference in terms of the age variable (P>۰,۸۷۱), while there was a significant difference in terms of the gender and underlying disease variables, and between these variables and the severity of the disease (P<۰,۰۰۱). Using the one-step RT-LAMP method on nasopharyngeal samples, individuals infected with SARS-CoV-۲ included ۹۳ (۲۷,۱٪) (۷۲ men and ۲۱ women), of whom ٥۹ (۱۷,۲٪) had underlying diseases, including diabetic patients (۲۷, ۷,۸٪), cardiovascular patients (۱۳, ۳,۸٪), pulmonary patients (۱۱, ۳,۲٪), kidney patients (٦, ۱,۷٪), and cancer patients (۲, ۰,٥٪).

Conclusion: conclusion Underlying diseases can have a significant impact on the side effects and severity of COVID-۱۹. Individuals with underlying diseases may be at higher risk of high-level infection and serious side effects due to weakened immune systems, respiratory problems, poor organ function, and other factors. According to the results of this research and various other studies, a significant statistical correlation between underlying diseases and the severity of SARS-CoV-۲ has

been shown, with the highest rate being related to diabetes. Therefore, management and control of underlying diseases, including in people with diabetes, is very important.

Keywords: Underlying diseases, SARS-CoV-۲, RT-LAMP, diabetes

Evaluation of miR-١٨٣ cluster (١٨٣/٩٦/١٨٢) expression in human adipose– derived mesenchymal stem cells (hAD-MSCs) differentiated into photoreceptor like cell under growth factor induction

(Research Paper)

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Introduction: Degeneration and apoptotic demise of the photoreceptor cell layer within the retina represents a significant cause of irreversible blindness in modern medicine. Stem cell therapy stands out as a promising approach for repairing retinal damage. Moreover, external signals are crucial in directing lineage commitment, guiding fate-restricted progenitors toward photoreceptor lineage from stem cell progeny in vitro. Research indicates that taurine and retinoic acid (RA) initially influence progenitor lineage in an instructive and lineage-specific manner, promoting the development of photoreceptor-like cells from stem cells. Additionally, miRNAs are pivotal in differentiation processes, with the miR١٨٣ family notably facilitating the differentiation of neural retina cells and photoreceptors. This study seeks to explore the impact of RA and taurine on differentiating human adipose-derived mesenchymal stem cells (hAD-MSCs) into photoreceptor-like cells while assessing the expression of the miR-١٨٣ cluster (١٨٣/٩٦/١٨٢).

Methods: hAD-MSCs were purchased from Pasteur Institute, Tehran, and cultured under standard conditions. After the three-cell passage, there are ٣ groups, A) DMEM/F١٢ without growth factor as control) B) DMEM/F١٢ complemented with taurine (٥٠ µmol/L) C) DMEM/F١٢ complemented with taurine (٥٠ µmol/L) and RA (١ µM). Subsequently, cellular change morphology was detected following ١٤ days under an inverted microscope. Then, the relative expression levels. Then, gene expression of photoreceptor cell biomarkers (Rho and Recoverin) and miR-١٨٣ cluster (١٨٣/٩٦/١٨٢) were examined by quantitative polymerase chain reaction (Q-PCR).

Results: Cellular morphology demonstrated spindle elongated morphology in taurine and the combination of the taurine/retinoic acid group. The results showed that taurine and the combination of taurine/retinoic acid led to a significant increase in the expression of Rho and Recoverin genes compared to the control group (P<٠,٠٠٠١). the taurine group induced the expression of miR-١٨٢ (P<٠,٠١) but there was no significant effect on mir-١٨٣ expression, and taurine and RA led to a substantial increase in the expression of miR-١٨٣ and mir١٨٢ (P<٠,٠٠٠١). Investigations showed that the taurine and RA had no significant effect on miR-٩٦ expression.

Conclusion: The results of the present study show that growth factors (taurine and RA) can lead to the differentiation of hAD-MSCs into rhodopsin-positive cells and the expression of specific markers

(Rho and Recoverin). Also, the increased expression of the miR-۱۸۳ cluster has a key role in the differentiation pathway of photoreceptor and neuroretina cells.

Keywords: adipose-derived mesenchymal stem cells (hAD-MSCs)- blindness - photoreceptors, miR۱۸۲/۱۸۳/۹۶

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Evaluation of Osteoconductive effect of Polycaprolactone (PCL) Scaffold treated with Fibronectin on adipose-derived mesenchymal stem cells (AD-MSCs) (Research Paper)

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Introduction: Replacing damaged organs or tissues and repairing damage by tissue engineering are attracting great interest today. Today, electrospun PCL-based scaffolds are widely used for tissue engineering applications. In this study, we used electrospun polycaprolactone (PCL) scaffold coated with fibronectin (Fn), a ubiquitous ECM glycoprotein, to investigate the induction potential of this scaffold in osteogenesis with adipose-derived mesenchymal stem cells (AD-MSCs). The results also showed that alkaline phosphatase activity was significantly higher in the PCL scaffold coated with Fn than in the control groups (PCL scaffold group and tissue culture polystyrene (TCPS) group) .

Methods: Preparation of scaffolding Scaffold hydrophilicity and Morphological Properties Cell Culture The ability of AD-MSCs differentiation Oil red staining Alizarin red staining Cell Viability Assay Alkaline Phosphatase Activity Evaluation of osteogenic differentiation of AD-MSCs

Results: Scaffold Characterization The microstructure of the PCL coated with fibronectin was evaluated by SEM. The results showed that fibronectin increased the hydrophilic and biocompatible properties of the electrospun PCL scaffold

Conclusion: The results of this study have shown that PCL modified with fibronectin has excellent osteogenic induction potential by increasing the expression of bone marker genes, the activity of ALP,,and calcium deposition. Therefore, it has promising potential for use in bone tissue engineering.

Keywords: Bone Tissue Engineering, Mesenchymal Stem Cells, PCL, Fibronectin

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Evaluation of serum iron levels in patients with bipolar disorder compared to healthy individuals

(Research Paper)

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Introduction: Bipolar disorder (BD) is a significant psychiatric disorder that includes periods of mania and depression and is one of the most complex mental disorders that severely impacts the life of the affected individual. Due to the neuroinflammatory properties of some psychiatric disorders that affect the body's system and subsequently alter some measurable factors, specific biomarkers such as iron can be useful for investigation. Since such biological markers enable quicker disease detection and early diagnosis, research in this area can improve the diagnosis and prompt initiation of treatment in this disorder. Therefore, our aim in this study has been to compare the iron concentration in the serum of individuals with BD and healthy individuals.

Methods: This observational study was conducted in a hospital in Tehran and included ٦٧ participants aged ١٨ to ٦٥, consisting of ٣٩ individuals diagnosed with BD and ٢٨ healthy individuals. Blood samples were collected, and iron levels were measured using atomic absorption spectroscopy with rigorous quality control measures in place. The results were analyzed using statistical tests, with p<٠,٠٥ considered significant.

Results: The average age was similar in both groups (٣٦,١٣ ± ١٠,٢٨ vs ٣٦,٠٤ ± ٦,٥٦ years, p=٠,٩٦٧). However, there were significant differences in gender distribution (٨٢,١٪ vs ٥٣,٦٪ male, p=٠,٠١٦), marital status (٦٤,١٪ vs ٣٢,١٪ single, p=٠,٠١٤), and smoking habits (٧٤,٤٪ vs ٣٩,٣٪ smokers, p=٠,٠٠٦) between the BD and control groups. Iron levels were significantly higher in the BD group compared to controls (١٠٥,٠ ± ٧,٥ vs ٨٥,٠ ± ٥,٨, p=٠,٠٤٩).

Conclusion: Serum iron levels are increased in individuals with BD, creating a difference compared to healthy individuals. However, this issue needs to be confirmed through further extensive studies.

Keywords: Bipolar disorder; Iron; Neuroinflammation

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Evaluation of synergistic effects of selected combination therapy in comparison with mesalazine on characteristics of ulcerative colitis experimental model (Research Paper)

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Introduction: Individuals with Crohn's disease and ulcerative colitis suffer from chronic intestinal diseases known as "inflammatory bowel diseases," which are costly to treat. Despite currently prescribed medications, there are still adverse effects that must be reduced or avoided altogether. Therefore, the use of natural supplements may be useful in order to reduce the drug dose and the symptoms of the disease. Goal: The purpose of the present study is to investigate the synergistic effects of combined treatment of selected probiotics, vitamin D, pomegranate extract, propolis, and curcumin compared to mesalazine on the clinical and immunological features of ulcerative colitis model mice.

Methods: Nine groups of mice were administered either a single treatment or a combination of agents after the animal model was induced with acetic acid. After a month, samples were taken, and colorimetric techniques were used to assess the expression levels of inflammatory cytokines (IL-١, IL-٦, and TNF-α) and oxidative agents (Myeloperoxidase and nitric oxide). The Disease activity index (DAI) and histopathological condition were also considered after mice scarification. MTT assay was carried out to assess cell growth.

Results: Our results demonstrated that combination therapy reduced DAI, nitric oxide, and Myeloperoxidase activity, proliferation, and inflammatory cytokines in the treated groups. Additionally, these treated groups also experienced a decrease in pathology scores. Except when the combination of treatments was administered, these declines were not significant. As demonstrated in this study, a combination of anti-inflammatory agents had a suppressive effect comparable to mesalazine.

Conclusion: By administration combining lactobacillus casei, VIT D, propolis, pomegranate, and curcumin in induced-ulcerative colitis mice, oxidative and inflammatory parameters were alleviated. Result similar to mesalazine were also obtained with this treatment.

Keywords: Probiotics, Vitamin D, Propolis, Pomegranate, Curcumin, ulcerative colitis, IBD

Evaluation of The Importance of Non-High-Risk Human papillomavirus in High-Grade Cervical intraepithelial neoplasia (Research Paper)

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Introduction: Infection with high-risk (HR) variants of the Human Papillomavirus (HPV) is the primary causative agent in the pathogenesis of cervical cancer, a disease that remains one of the most frequently diagnosed malignancies in the female population. Preliminary data from studies yet to be published indicate that certain HR HPV strains may be as contributory as HPV ١٦ and ١٨ in the progression to high-grade Cervical Intraepithelial Neoplasia (CIN). The aim of this investigation was to ascertain the association between these non-HR HPV strains and the occurrence of high-grade CIN.

Methods: An exhaustive literature review was conducted utilizing esteemed databases such as Ovid, Elsevier, PubMed, and Google Scholar. This review spanned publications from the years ٢٠١٦ to ٢٠٢٤, with no restrictions based on the language of the articles. Initially, a total of ١٨ papers were identified. Following a meticulous process of summarization and analysis, ١٢ pertinent articles were ultimately chosen for inclusion in the study.

Results: In the methodically reviewed scholarly articles, a statistically significant association has been identified between the prevalence of HPV٤٥ and the occurrence of CIN٢. Moreover, the data indicates a profound linkage between HPV٣١ and the incidence of CIN٣.

Conclusion: In light of the potential significance of HPV types in association with high-grade neoplasia's, it is advisable to conduct comprehensive HPV typing analyses. Additional research is imperative to substantiate the findings presented herein.

Keywords: Human Papillomavirus, Neoplasia, Infection

Evaluation of the possible effects of AZD١١٥٢-HQPA on cellular and molecular aspects of apoptosis and cell migration in glioblastoma, focusing on miRNAs expression pattern (Research Paper)

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Introduction: Glioblastoma (GBM) is a highly invasive and deadly central nervous system tumor, accounting for ١٤,٩٪ of primary brain and CNS tumors. The incidence is higher in males and white individuals. Despite current treatments, the median survival rate post-diagnosis is only ١٨ months. Aurora kinase B (AURKB), essential for mitotic processes, is frequently overexpressed in cancers, including GBM. AZD١١٥٢, an AURKB inhibitor, disrupts these processes, presenting a potential therapeutic approach. This study investigates the effects of AZD١١٥٢-HQPA on GBM cells, focusing on miRNA expression, cell migration, and apoptosis.

Methods: U٨٧MG GBM cells were cultured and treated with AZD١١٥٢-HQPA. Cytotoxic effects were assessed using MTT assay, Trypan Blue Exclusion Test, and Colony Formation Assay. Flow cytometry evaluated DNA content and apoptosis. Morphological changes were analyzed with DAPI staining. Cell migration was assessed via Scratch Assay. miRNA expression was analyzed using microarray data from GEO datasets GSE١٥٨٢٨٤ and GSE٢٥٦٣٢, followed by qRT-PCR validation. Functional enrichment and miRNA-mRNA network analysis were conducted to understand the pathways involved.

Results: AZD١١٥٢-HQPA exhibited dose-dependent cytotoxicity, reducing U٨٧MG cell viability and proliferation. Flow cytometry revealed increased polyploidy and apoptosis, with significant DNA content changes and multinucleated cells. AZD١١٥٢-HQPA inhibited cell migration. Microarray analysis identified ٨٨ differentially expressed miRNAs, with significant changes in ٧٩. Upregulated miRNAs included miR-١٩٦a and miR-٢٠٠c, while downregulated miRNAs included miR-٣٤a and miR-١٨١c. Functional enrichment highlighted pathways like ECM receptor interaction, cell cycle, p٥٣ signaling, and PI٣K/Akt.

Conclusion: AZD١١٥٢-HQPA effectively inhibits GBM cell proliferation, induces apoptosis, and alters miRNA expression profiles. These miRNAs, involved in key oncogenic pathways, suggest that AZD١١٥٢-HQPA disrupts critical cellular processes in GBM. This study supports the potential of AZD١١٥٢-HQPA as a therapeutic agent for GBM, highlighting the importance of targeting AURKB and associated miRNAs to mitigate tumor growth and progression. Further investigation into the molecular mechanisms and clinical applications is warranted to enhance GBM treatment strategies.

Keywords: Glioblastoma CNS Aurora kinase B AZD١١٥٢-HQPA U٨٧MG miRNA cell migration.

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Evaluation of the prevalence of cardiometabolic disorders (diabetes, hypertension, and hyperlipidemia) diagnosed, undiagnosed, treated, and treatment goal in the elderly: Bushehr Elderly Health Program (BEH) (Research Paper)

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Introduction: Human life expectancy continues to increase rapidly. In fact, life expectancy has increased at least by ٢٠ years since ١٩٥٠ worldwide. Nowadays, countries all around the world is facing increase in elderly and their complications. It is anticipated that in ٢٠٣٠, ١ in ٦ people in the world will be aged over ٦٠ years. Chronic disorders affecting the elderly such as diabetes, hypertension, and hyperlipidemia have a considerable impact on health care costs. Presently, with improvement of global basic health measures, cardiovascular disorders are the most common cause of death. But hopefully, many of these cardiometabolic disorders are preventable or manageable. Increasing cardio metabolic diseases in elderlies could be reasoned with numbers of etiologies. In summary, the two major pathophysiological cause of age-related disease are chronic, low-grade inflammation and increased cellular oxidative stress.With increased longevity, the prevalence of many chronic diseases rises up. Canadian Community Health Survey (CCHS) state that about ٣٧٪ of elderly report having at least two of the ten common chronic diseases. Diabetes mellitus (DM) is the most common metabolic disorder that based on the international diabetes federation state, globally, ١ in ١١ adults has diabetes. ٩٠٪ of diabetic patients have type ٢ DM which is commonly diagnosed later in life. The Middle East and North African regions have the world's second highest age-adjusted diabetes prevalence, with nearly ٤٩٪ still undiagnosed. Thus, effective prevention, early diagnosis and treatment could be cost-effective for countries. Hypertension (HTN) mentioned as the most common preventable and potentially reversible risk factor of cardiovascular disease. Hypertension affects approximately ٢٠٪ of the global population, and the prevalence of HTN is currently between ١٤,٧ and ٢٦,٤٪ in various Eastern Mediterranean countries, based on the WHO report. In America, only ٣٧٪ of adults with hypertension have their condition properly under control. One of the most important risk factors for developing HTN is increasing age. Aging is inevitable but early diagnosis,

life style change, appropriate pharmacological treatment which targeting the mechanisms of HTN could diminish adverse effects. Dyslipidemia is attributed to more than half of all cases of coronary heart disease worldwide. According to World Health Organization (WHO) estimates, the worldwide prevalence of increased total cholesterol in adults (≥ ٥,٠ mmol/l) was estimated to be ٣٩٪. Prevalence of hyperlipidemia, another important cardio metabolic disorders increase with age. Because of its causative role in the development of atherosclerosis and often clinically asymptomatic before subsequent cardiovascular disease, screening and treatment of hyperlipidemia is important. Primary prevention in elderly is important because most of first cardiovascular events occur after ٦٥ years old. Management of hyperlipidemia needs accurate risk stratification of elderlies. The value of secondary prevention clarified by studies that have shown the benefits of lipid-lowering drugs on mortality of patients. Despite the high importance of screening for metabolic risk factors such as diabetes, blood pressure and dyslipidemia, many of these disorders remain undiagnosed. For this reason, for example, in the case of diabetes, a screening recommendation has been changed to the age of over ٣٥. By early diagnosis of these risk factors and their treatment, the possibility of their complications such as stroke, cardiovascular events or chronic complications of diabetes will be reduced or delayed.

Methods: Sampling and setting This is a cross-sectional approach to data gathered from the second phase of Bushehr Elderly Health Program (BEHP). The BEHP was community-based prospective in Bushehr, a provincial capital city in the south of Iran with ٣٠٠٠ participants. The sampling of this study was a multistage stratified random sampling method accomplished in neighborhoods of Bushehr. The second phase of this study (considered musculoskeletal and cognitive outcomes) was started in ٢٠١٥. In this phase, more than ٢٧٠٠ participants of phase I was enrolled again. The study design and protocol were explained separately. Data gathering The participants were interviewed by trained interviewers to collect data on their socio-demographic status, lifestyle (physical activity and smoking), medical history, and medication use. The questionnaire used for data gathering has been previously published elsewhere. Anthropometric measurements were performed manual based on the National Health and Nutrition Examination Survey (NHANES). Assessments of anthropometric parameters, physical activity level (PAL), and blood pressure were discussed in detail separately. By using two tools (Mini-Cog and categorical verbal fluency test; CFT) dementia was evaluated and depression mood assessed by Patient Health Questionnaire (PHQ-٩). Biochemical measurements To determine the values of fasting blood sugar (FBS), hemoglobin A١c (HbA١c), and lipid profile, blood sample was taken after a ١٢ h overnight fast. FBS was measured by the enzymes (glucose oxidase) colorimetric method using a commercial kit (Pars Azmun, Karaj, Iran). HbA١c was also measured by Boranate affinity method using a CERA-STAT system (CERAGEM MEDISYS, chungcheongnam-do, Korea). Lipid profile and total cholesterol were measured by enzymatic (CHOD-PAP) colorimetric method using a commercial kit (Pars Azmun). Diabetes was defined on the basis of at least one of the following: A١C ≥ ٦,٤٪ or fasting plasma glucose ≥ ١٢٦ mg/dl or previous diagnosed diabetes history or diabetes medication use. Hyperlipidemia was defined as the presence of one of the following: total cholesterol ≥ ٢٠٠ mg/dl or LDL-C ≥ ١٣٠ mg/dl or triglyceride ≥ ١٥٠ mg/dl or hyperlipidemia medication use. Hypercholesterolemia was defined as LDL-C ≥ ١٣٠ mg/dl or

hypercholesterolemia medication use. Statistical analysis Concerning statistical analysis, results were presented as mean ± standard deviation (SD) for quantitative variables and were summarized by frequency (percentage) for categorical variables. Categorical variables were compared using the chi-square test. The logistic regression models were used to evaluate the association between various variables with untreated hypertension, diabetes, dyslipidemia and hypercholesterolemia. The proportions were carried out age-standardization based on World Health Organization (WHO) population ٢٠٠٠–٢٠٢٥. For the statistical analysis, the software STATA version ١٢ for windows (StataCorp, Texas ٧٧,٨٤٥ USA) was used. P values < ٠,٠٥ was considered as statistically significant.

Results: A total ٢٣٨١ participants were included. The mean age of the study participants was ٦٩,٣٤ years. Proportions of diabetes, hypertension, hyperlipidemia and hypercholesterolemia were ٤٣,٢٥٪, ٧٥,٧١٪, ٦٤,٧٤٪ and ٣٥,٣١٪ respectively. Untreated diabetes prevalence was higher for males (OR = ١,٦٠, ٩٥٪CI = ١,٢٠–٢,١٥), older adults (OR = ١,٠٢, ٩٥٪CI = ١,٠٠–١,٠٥), and pre-frail status (OR = ٠,٦٩, ٩٥٪CI = ٠,٥٢–٠,٩٢). Males (OR = ٢,١٦, ٩٥٪CI = ١,٦٤–٢,٨٤) and current smokers (OR = ١,٤٢, ٩٥٪CI = ١,٠٥–١,٩٣), in contrast to married participants (OR = ٠,٢٥, ٩٥٪CI = ٠,٠٨–٠,٧٨), people with higher education levels (OR = ٠,٥١, ٩٥٪CI = ٠,٢٩–٠,٨٩) and dementia (OR = ٠,٧٨, ٩٥٪CI = ٠,٦١–١,٠٠) were more likely to have untreated HTN. Untreated dyslipidemia is more common in smokers (OR = ١,٧٨, ٩٥٪CI = ١,١٩–٢,٦٦) and males (OR = ١,٦٦, ٩٥٪CI = ١,٢١–٢,٢٧), while untreated hypercholesteremia is more common in males (OR = ٣,٢٠, ٩٥٪CI = ١,٥٣–٦,٦٩) and is reported lower in people with dementia (OR = ٠,٥٣, ٩٥٪CI = ٠,٢٨–١,٠١).

Conclusion: Compared to other countries in this region, the prevalence of cardio metabolic diseases, such as diabetes, hypertension, and hyperlipidemia, was higher in our cohort population. Males and older adults were more likely to have untreated diabetes. Untreated HTN prevalence was higher for males and smokers, and lower for people with higher education levels and married participants. Untreated dyslipidemia is more common in smokers and males, while untreated hypercholesteremia is more common in males and is reported lower in people with dementia. These potential risk factors need to be evaluated further to confirm their impact on the prevalence of cardiometabolic diseases among the elderly. Additionally, future studies should examine screening plans for these cardiometabolic risk factors in younger adults as well as exploratory studies to determine the probable causes of patients who do not receive appropriate treatment despite confirmed diagnoses.

Keywords: Diabetes, Hypertension, Hyperlipidemia, Elderly

Evaluation of the relationship between side effects of breast cancer chemotherapy drugs and genetic polymorphisms in Iran (Research Paper)

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Introduction: Breast cancer is a prevalent malignancy affecting both men and women. It is characterized by abnormal cell growth and division within the breast tissue, often forming tumors. The most common types include ductal carcinoma in situ (DCIS), invasive ductal carcinoma (IDC), and invasive lobular carcinoma (ILC). Various factors contribute to breast cancer risk, including genetics, lifestyle, and hormonal factors. Genetic mutations, such as in BRCA١ and BRCA٢ genes, can significantly increase susceptibility. Environmental factors like obesity, alcohol consumption, and lack of physical activity may also play a role. Early detection through regular screenings and prompt treatment are crucial for improving outcomes. Treatment options vary depending on the stage and type of breast cancer and may include surgery, radiation therapy, chemotherapy, hormone therapy, targeted therapy, or immunotherapy. Ongoing research aims to better understand the molecular mechanisms underlying breast cancer, identify new therapeutic targets, and improve treatment outcomes. Advances in genetic testing, imaging techniques, and personalized medicine are contributing to enhanced care for breast cancer patients.

Methods: In this research, the important polymorphisms were selected from the NCBI database, and the initial evaluation was based on the number of citations and the population value of ٢ and above. Side effects of domestic and imported drugs available in Iran were collected and all information was entered into MegaGene application (which is a pharmacogenetics software).

Results: In Endoxyna, Brescu, Cybrin, Reximed, Docetaxel, Cyclophosphamide, Cisplatin, Toremifene, Fluorouracil and Paclitaxel medicines, Gastric adenocarcinoma, Inflammation, Hair loss, Nausea, Vomiting and Squamous cell lung carcinoma can be based on genetics.

Conclusion: It is better for people who are suffering from breast cancer to undergo tests to detect these SNPs, by identifying them, they can choose the most effective medicine with the least side effects.

Keywords: Breast Cancer, Pharmacogenetic, MegaGene, BRCA١, BRCA٢

Evaluation of toxoplasma infection in cancer patients referring to Shariati Hospital in Tehran

(Research Paper)

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Introduction: Toxoplasmosis is a parasitic infection caused by the Toxoplasma gondii parasite. It is a significant opportunistic infection in cancer patients due to their weakened immune systems. This study aimed to investigate the serum prevalence of anti-toxoplasma antibodies in cancer patients.

Methods: A total of ٣٥٠ samples were collected from cancer patients and healthy individuals. Serum samples were tested for anti-toxoplasma antibodies using ELISA and LAMP techniques. Demographic data was collected and analyzed using SPSS ٢٠ software.

Results: Of the ٣٥٠ serum samples collected from cancer patients, ١٣٣ (٦٠,٥٪) had IgG antibodies and ٤ (١,٨٪) had IgM antibodies against toxoplasma. Positive samples were confirmed by LAMP molecular technique. The serum prevalence of IgG anti-toxoplasma antibodies was significantly higher in cancer patients compared to the control group (p<٠,٠٠١). Among cancer patients, the highest and lowest prevalence of IgG anti-toxoplasma antibodies was observed in those with acute myeloid leukemia (١١,٨١٪) and uterine cancer (٠,٤٥٪), respectively.

Conclusion: The study found a significantly higher prevalence of toxoplasmosis infection in cancer patients compared to healthy individuals. Cancer patients with acute myeloid leukemia had the highest prevalence. This study emphasizes the importance of screening for toxoplasmosis in cancer patients to prevent severe infections.

Keywords: Toxoplasmosis - Opportunistic infection - ELISA - LAMP

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Evaluation of vtRNA۱-۳ and vtENA۲-۱ expression in gastric adenocarcinoma (Research Paper)

Faezeh Bavafa,[۱,*] Dr. Zivar Salehi,[۲]

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۲.

Introduction: Gastric cancer (GC) is the ۵th most prevalent cancer and is the third leading cause of cancer-related deaths in many regions worldwide. In Iran, it is the fourth most common cancer and the leading cause of cancer mortality. Notably, the incidence and mortality rates of gastric cancer are significantly higher in the northern and northwestern regions of the country compared to other areas. Non-coding RNAs (ncRNAs) play crucial roles in various cellular processes, and their dysregulation has been linked to several cancers, including gastric cancer. Vault RNAs (vtRNAs) are a class of ncRNAs transcribed by RNA polymerase III and associated with a ribonucleoprotein complex known as vault particle. Among the four human vtRNA genes, vtRNA۱-۱, vtRNA۱-۲, and vtRNA۱-۳ are clustered at locus ۱ and are integral components of the vault particle, while vtRNA۲-۱ is a more divergent homologue located at a second locus. Although the functions of vtRNAs are still under investigation, some studies suggest their involvement in various processes such as nucleo-cytoplasmic transport, cellular signaling, DNA damage repair, innate immune response, apoptosis resistance, and nuclear-pore complex formation. The aim of this study was to investigate the expression levels of vtRNA۱-۳ and vtRNA۲-۱ in patients with gastric adenocarcinoma and compare them with healthy individuals.

Methods: Blood samples were collected from ۵۰ patients with gastric adenocarcinoma and ۵۰ healthy controls. After RNA extraction, the concentration and purity of total RNAs were determined with an absorption ratio of ۲۸۰/۲۶۰, and the accuracy of the extraction was confirmed by gel electrophoresis. The total RNA was reverse-transcribed into cDNA before real-time PCR. The vtRNA۱-۳ and vtRNA۲-۱ threshold (Ct) values were normalized to U٦ snRNA as housekeeping gene control. Quantitative measurements were performed in triplicate and relative expression was measured using the comparative Ct method (۲−ΔΔCt). Statistical data were analyzed using GraphPad Prism (version ۹,۰,۲) and were presented as mean ± standard deviation. The differences were considered significant when the p-value was less than ۰,۰۵.

Results: Total RNA was successfully extracted from all samples. The ۲٦۰/۲۸۰ nm absorbance ratio of total RNA was ۱,۸. A single peak was observed in all the dissociation curves in real-time PCR. The qRT-PCR analysis revealed that the relative level of vtRNA۲-۱ and vtRNA۱-۳ expression were lower in cases compared to normal. The expression level of vtRNA۲-۱ significantly decrease in patients (P=۰,۰۰۱), however, the decrease in vtRNA۱-۳ was not significant (P = ۰,۰۸۷). Moreover, the relationship between the expression level of aforementioned RNAs and the stages of the disease was investigated. There was no significant relationship between vtRNA۱-۳ expression level and the stage of the disease (۰,۲۱۱), however, the expression level of vtRNA۲-۱ was found to be related to the progression of the disease (P=۰,۰۰۰۱).

Conclusion: In summary, based on the result of this preliminary study, changes in vtRNA۲-۱ expression may be important in the development and progression of gastric cancer. However, further research is needed to understand the exact functions and significance of vtRNAs in gastric tumorigenesis process.

Keywords: vtRNAs; vtRNA۲-۱; vtRNA۱-۳; gastric cancer; ncRNAs; gene expression

Examining the amount of expression Circ-FOXM١ and miR-١٤٩-٥p in patients with ovarian cancer

(Research Paper)

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Introduction: Ovarian cancer is one of the most feared malignancies in women. The use of new biomarkers for faster diagnosis and better treatment selection is one of the main concerns in this field, so it shows the necessity of new diagnostic and treatment methods.

Methods: Preparation of cancer tissue and in this study ٥٠ fresh tissue samples consisting of ٢٥ cancer samples and ٢٥ healthy marginal tissue samples from cancer patients in different stages of the disease are used to investigate the expression of miR-١٤٩-٥p and circ-FOXM١. RNA extraction from the cell is done manually. We use the nano drop device to check the quality and also to determine the concentration. To investigate the expression changes of miR-١٤٩-٥p and circ-FOXM١, first, circ-FOXM١ synthesis is performed using the kit. Primer-BLAST software is also used to check primers. The next step is real-time reaction or qRT PCR using Master Mix Cyber Green and finally the results are analyzed.

Results: One way ANOVA is used to compare each of the obtained variables. In this study, the p value is less than ٠,٠٥, it is considered statistically significant. Also, adjustment of the test is done at the same time using the Bonferroni method. In addition, the correlation between two gene expression rates is done using Pearson's correlation coefficient.

Conclusion: Due to the fact that the expression and interpretation of ٢ biomarkers miR-١٤٩-٥p and circ-FOXM١ have not been investigated simultaneously in ovarian cancer, as a result, this study is new in its turn.

Keywords: cancer, circularRNA, microRNA, miR-١٤٩-٥p, circ-FOXM١

Examining the signaling pathway of autoimmune diseases (Review)

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Introduction: Autoimmune diseases are a diverse group of conditions characterized by aberrant reactivity of B cells and T cells to natural components of the host. This disease occurs especially in women and it affects people of age. In general, autoimmune disease is caused by an interaction between a genetic predisposition and environmental factors. Genetic predisposition to autoimmunity is complex and can involve multiple factors that shape immune cell function. Less commonly, autoimmunity can result from single-gene mutations that affect key regulatory pathways.

Methods: This research is a review study and Iranian and foreign databases like PUBMED, NCBI, etc. have been used in this research to collect information.

Results: According to the obtained research, the cause of this disease is between genotype and environment. Many genes involved in this disease can be located in common biological networks

Conclusion: According to the studies: Rheumatoid arthritis, which has the strongest relationship with PTPN۲۲ and HLAo IL۲۳R genes. Graves' disease and SLC۲۵A۱۶ gene, lichen planus disease and CDKN۲A tumor suppressor gene changes, Hashimoto's thyroiditis and myasthenia gravis, CTLA٤ gene, RAG gene involved in autoimmune vasculitis disease and... is the autoantigen of existence / Shogren's syndrome SSNA۱/NA۱٤, disease. Protein tyrosine phosphatase PTNP۲۲ and... which is discussed in this study.

Keywords: autoimmune disorders, signaling pathway, genetics and outoimmunity

Exosomes as drug carriers represent a promising approach in the treatment of metastatic cancer (Review)

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[1].

Introduction: Metastasis is accountable for the majority of cancer-related deaths, making anti-metastasis treatment a potential cornerstone of cancer therapy. Traditional cancer treatments, such as surgery, radiotherapy, and chemotherapy, have limitations, including lack of specific tumor targeting, high toxicity, drug resistance, and adverse physical and mental effects that can significantly impact a patient's quality of life. Consequently, researchers are actively seeking more effective solutions for cancer treatment. In recent years, drug delivery systems utilizing antiparticles, such as polymers and inorganic antiparticles, have been explored as tools for drug delivery, aiming to enhance drug and treatment efficacy while minimizing off-target side effects and drug-related toxicity in cancer. These systems have demonstrated a reduced risk of tumor metastasis compared to conventional treatments. However, they encounter several challenges, including targeting specific organs and addressing the chemical and physical properties linked to toxicity and adverse immune responses. To address these limitations, researchers have shifted their focus to innovative approaches. Exosomes are becoming popular as a potential technique in the field of nanomedicine among various new strategies. Cells secrete minuscule extracellular particles (٣٠–١٠٠ nm in size) called exosomes and they are present in body fluids like blood, cerebrospinal fluid, urine, and saliva. They are composed of a lipid bilayer membrane and contain a diverse cargo, including proteins, nucleic acids, and lipids. Exosomes engage in intercellular interactions by exchanging bioactive molecules such as proteins, mRNAs, and miRNAs with recipient cells, thereby influencing cellular functions and signaling pathways. Moreover, the capacity of exosomes to cross the blood-brain barrier (BBB) improves neurological and motor function in the nervous system. This enables the repeated administration of drug-loaded exosomes via intravenous injections without adverse side effects. Exosomes act as vehicles for transferring biomolecules between cells. After being released from donor cells, they can be taken up by recipient cells, allowing proteins, nucleic acids, and lipids to be transferred between cells. This transfer enables the conveyance of signaling molecules and genetic information, which can impact the behavior and characteristics of the recipient cells. Through the activation of signaling pathways, modification of gene expression, and induction of phenotypic alterations, exosomes play a crucial role in modulating the functionality of the target. The increasing popularity of exosomes as a drug delivery strategy for treating cancer metastasis stems from their capacity to address the limitations of conventional therapies. Nevertheless, challenges remain in the clinical application of exosomes.

Methods: In recent years, the popularity of exosomes among clinical studies has caused a large number of articles and research works to study the various aspects of exosomes. The assistance of the latest and most beneficial articles on specialized sites such as Elsevier, PubMed, Springer,

Nature, and Frontiers was utilized in this article. Our focus will be on the role of exosomes as drug delivery in the treatment of metastasis

Results: Recent advances in exosome isolation and analysis reveal their potential as a drug delivery system, creating a protective capsule that transports drugs to disease sites through body fluids. This capsule shields the cargo from degradation, improves stability, and reduces immune response. Engineered exosomes utilize their natural stability, biocompatibility, and low immunogenicity to traverse biological barriers, extending the half-life of chemical drugs compared to synthetic carriers. This method effectively targets metastatic cells, ensuring treatments reach their intended sites with minimal systemic impact.

Conclusion: However, exosomes have unique properties, including their small size, that enable them to escape phagocytosis by macrophages and easily pass through the vessel wall and extracellular matrices. Their biocompatibility and ability to target normal proliferation and migration in distant and nearby cells make them potential candidates for the management of metastasis, which involves the spread of cancer cells from the primary tumor site to distant sites. Important challenges remain to be addressed before using exosomes in clinical practice, especially the isolation of exosomes, which is a major obstacle in exosome-based drug delivery. Furthermore, the mechanisms by which exosomes target and enter recipient cells are poorly understood. These limitations have limited the widespread clinical use of exosomes. However, as research advances in understanding exosome function and their interaction with cancer biology, the potential for exosome-based applications in metastatic therapy is becoming increasingly promising, paving the way for more effective cancer therapies.

Keywords: Exosomes, drug carriers, Cancer, metastasis

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Exosomes as Innovative Biomarkers in the Diagnosis and Treatment of Female Infertility (Review)

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2.

Introduction: Infertility has become a major issue, especially in aging societies. While traditional treatments like ovulation drugs and assisted reproductive technologies offer some relief, they often face significant limitations. This has led researchers to investigate advanced alternatives, such as stem cell therapies and exosomes. Exosomes, as extracellular vesicles capable of crossing cellular barriers and carrying diverse biological molecules, represent a promising new avenue in infertility research. Their unique properties make them potential tools for both improved diagnostics and innovative treatments. This review explores the role of exosomes in reproductive health, assessing their potential as biomarkers and therapeutic agents to address infertility challenges

Methods: In this study, using the keywords of exosome, biomarker, female infertility in electronic databases Scopus, PubMed, Google scholar and Web of Science, studies in this field were searched, also using the keywords of the desired study. ۱۸۲ articles were obtained and according to the intended purpose and removing duplicate articles, ۵۹ articles were obtained.

Results: In this article, the role of exosomes as biological nanoparticles with great potential in the treatment and diagnosis of reproductive disorders, especially female infertility, was investigated. Due to their ability to carry various cargoes such as microRNA and proteins and transfer them to the target cells, exosomes can have a wide impact on improving reproductive performance. These particles, as mediating tools, have the ability to regenerate and repair damaged tissues, including ovaries and uterus, and can be used as new therapeutic strategies in disorders such as polycystic ovary syndrome, premature ovarian failure, Asherman syndrome, and endometriosis. Since female reproductive disorders are complexly related to genetic, hormonal and environmental factors, using exosomes as natural and non-invasive carriers for cellular information transfer is considered an innovative and promising approach. Recent studies have shown that exosomes can provide significant improvements in the treatment of these disorders; including reducing apoptosis, increasing vascularization and improving cell activities in reproductive tissues. Also, the important role of exosomal microRNAs in regulating key molecular pathways indicates the potential capacity of these particles in correcting genetic and metabolic abnormalities associated with infertility. However, although initial results have been positive, more research and more detailed clinical studies are needed to fully exploit these potentials. Exosomes, due to their stability and high efficiency, can be used as new diagnostic and therapeutic tools in reproductive medicine. The future of infertility treatments and reproductive disorders looks brighter according to these findings, and the use of exosomes can open a new window to effective and minimally invasive approaches that potentially improve the quality of life and health of women.

Conclusion: Recent studies indicate that exosomes hold significant potential as innovative tools for diagnosing and treating infertility. These biological nanoparticles play a crucial role in managing conditions such as polycystic ovary syndrome, endometriosis, and premature ovarian failure. Moreover, the stability and ease of extraction of exosomes from biological fluids make them a reliable and effective tool for early diagnosis and monitoring treatment progress. Consequently, the use of exosomes could lead to substantial improvements in infertility treatment methods and open new avenues for future research and therapies in this field

Keywords: Exosomes, Biomarkers, and Female Infertility

Exosomes Derived from Yazd Human Foreskin Fibroblast #۸ (YhFF#۸) Cells Fascilitate Cutaneous Wound Healing in a Rat Model: An in Vitro and In Vivo study (Research Paper)

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Introduction: Wound healing is a complex biological process involving multiple stages, including inflammation, tissue formation, and remodeling. Effective healing requires a coordinated response from various cell types, growth factors, and extracellular matrix components. Despite advances in medical treatments, impaired wound healing remains a significant challenge, particularly in cases of chronic wounds or severe tissue injury. Novel therapeutic approaches that can enhance and accelerate the wound healing process are urgently needed. Exosomes have recently emerged as promising candidates for regenerative medicine. These vesicles play crucial roles in intercellular communication by transferring bioactive molecules. Exosomes derived from stem cells and fibroblasts have been shown to promote tissue repair and regeneration, making them attractive for therapeutic applications in wound healing. Human foreskin fibroblasts are a readily available and ethically sourced cell type with high proliferative potential. In this study, we assessed the ability of exosomes derived from Yazd human foreskin fibroblast #۸ (YhFF#۸) cells to promote wound healing in a Wistar rat model. By employing both local injection and topical administration, we aimed to determine the efficacy of these exosomes in improving the wound healing process.

Methods: Exosomes were isolated using the Exocib Exosome Extraction Kit from conditioned medium of YhFF#۸ cells, which were derived at the Stem Cell Biology Research Center, Yazd Reproductive Sciences Institute, Iran. The exosomes were characterized through flow cytometry using CD۹, CD۸۱, and CD٦۳ markers, as well as transmission electron microscopy (TEM) and dynamic light scattering (DLS) to determine their size. In vitro assays, including scratch, hemolysis, and MTT assays, were conducted to assess the exosomes' bioactivity. For the in vivo study, ۲٤ Wistar rats were divided into four groups: no treatment, PBS treatment, and exosome treatments with ٥۰ µg and ۱۰۰ µg doses. Both local injection and topical administration of exosomes were employed for wound treatment.

Results: The analysis revealed that the extracted exosomes had an average size of approximately ۷۸,۸ nm, with a polydispersity index (PDI) of ۰,۸, indicating a relatively uniform particle distribution. Flow cytometry confirmed the presence of surface markers CD۹, CD۸۱, and CD٦۳, ensuring that the extracted particles were indeed exosomes. TEM analysis validated the correct morphology of the exosomes, further confirming their presence. The concentration of exosomes, determined using the BCA assay, ranged between ٤۰۰ and ۱,۰۰۰ µg/mL per extraction batch. The exosomes showed

no cytotoxic effects at any tested dose on YhFF#٨ and YhFF#١٨ cell line, as indicated by the MTT assay. Scratch assay results demonstrated that only the ١٠٠ µg/mL dose significantly enhanced cell migration at ٢٤ and ٤٨ hours. The hemolysis assay confirmed that the exosomes did not cause significant blood lysis at any dose, suggesting that intravenous administration or accidental entry into the bloodstream would not pose a safety risk. In the in vivo study, wound areas were measured on days ٠, ٣, ٧, ١٠, and ١٤ using ImageJ software, and the percentage of wound healing was calculated. All treatment groups showed significant wound healing compared to controls throughout the study period. Notably, on day ٣, the lower dose group demonstrated better wound healing. Histological analysis on day ٧ showed no significant differences between groups, but by day ١٤, epithelial tissue reorganization was significantly better in the treatment groups (P=٠,٠٠١). Angiogenesis did not differ significantly between the groups, and granulation tissue formation showed no significant variation. However, Masson's trichrome staining indicated that fibrosis was significantly higher in the treatment groups on day ١٤ compared to the control groups (P=٠,٠٠١٨), with increased blue staining reflecting greater tissue fibrosis.

Conclusion: The findings of this study demonstrate that exosomes derived from human foreskin fibroblasts can effectively promote wound healing in a Wistar rat model. Both local injection and topical administration of exosomes enhanced the healing process, particularly at higher doses, without causing cytotoxicity or significant hemolysis. Histological assessments further revealed improved epithelial tissue reorganization and increased fibrosis in the treatment groups. These results suggest that exosome-based therapies hold significant promise for accelerating wound healing and may offer a novel approach for regenerative medicine applications. Future studies are needed to optimize dosage and delivery methods for clinical translation.

Keywords: Yazd human Foreskin Fibrolast, Exosomes, Wound Healing, Regenerative Medicine, Exosome Therapy

Exosomes of mesenchymal stem cells can be used as a remedy factor to reduce fibrogenic genes and treatment of liver Fibrosis disease. (Research Paper)

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Introduction: Introduction: Liver fibrosis resulting from chronic liver injury is a major cause of morbidity and mortality in the world. Liver fibrosis is the result of the excessive accumulation of extracellular matrix proteins including collagen that occurs in most chronic liver diseases. Activated hepatic stellate cells (HSCs) have been identified as major collagen-producing cells in the injured liver. These cells are activated by fibrogenic cytokines such as TGF-β١. Following chronic injury, HSCs activate and secret large amounts of collagen. α-SMA, as a protein, is used as a marker to identify activated fibrogenic cells. α-SMA expression is considered a reliable marker of hepatic stellate cell (HSC) activation and a key biomarker for liver fibrosis. Although many therapeutic interventions are effective in experimental models of liver fibrosis, their efficacy and safety in humans are unknown. So, it is important to know which factors can cause and treat liver fibrosis. Free cholesterol in the diet can cause liver fibrosis by accumulating in Hepatic stellate cells (HSCs). MSCs-derived exosomes are known as the new mechanism of cell-to-cell communication, showing that exosomes can be used as a new treatment. At present, there is little information about the mechanism of exosomes derived from Human umbilical cord Wharton's jelly (WJ-MSCs) in liver fibrosis. In this study, we investigated the effect of exosomes of WJ-MSCs on the expression of TGF-β, α-SMA, and collagen١α genes in cholesterol-induced liver fibrosis in the LX٢ cell line (a type of cell derived from HSCs) and also phosphorylation of Smad٣ protein level.

Methods: Methods: First, the LX-٢ cells were seeded in ٦-well plates (١ × ١٠٥ cells per well) in DMEM containing ١٠٪ FBS at ٣٧ °C with ٥٪ CO٢. When cells are approximately ٨٠–٩٠٪ confluent, the cells must be sub-cultured to ensure proper growth and health of the cells. Second, after starvation for ١٦ hr, the cells were treated with ٧٥ and ١٠٠ µM cholesterol and incubated for ٢٤ hr to induce liver fibrosis. Isolation, culture, and Differentiation assays of WJ-MSCs were done according to protocol. Next, the exosomes of WJ-MSCs (final concentration of ٥٠ µg/ml) were dissolved in a culture medium and added to the cells for ٢٤ hr. Three groups were considered for the experiment: ١- Control group, ٢- Cholesterol treatment group, and ٣- Cholesterol treatment group + exosome of WJ-MSCs; after ٢٤ hr, cells were washed twice with PBS, then Real-Time PCR analysis was performed. Western Blots also was done to evaluate the signaling pathway of smad٣.

Results: Results: In treatment with ٧٥ and ١٠٠ µM cholesterol concentrations, the Real-Time PCR analyses showed that the mRNA expression levels of TGF-β, α-SMA, and Collagen١α (liver fibrosis marker genes) were significantly up-regulated compared to the control group. The mRNA expression of TGF-β, α-SMA, and collagen ١α was significantly increased as a result of the development of

cholesterol-induced liver fibrosis. We also found that exosomes of WJ-MSCs treatment (٥٠ µg/ml) could significantly decrease the level of TGF-β, collagen١α, and α-SMA gene expression in cholesterol-induced liver fibrosis model. Treatment with exosomes prevented the activation of HSCs by inhibiting the phosphorylation of the Smad٣ protein. the P-Smad٣ levels were significantly downregulated after ٢٤ hr, in the treatment of exosomes of WJMSCs in cholesterol-induced HSCs. Treatment with exosomes of WJ-MSCs improves cholesterol-induced liver cell damage.

Conclusion: Conclusion: In our study, exosome treatment effectively downregulated the expression of TGF-β, αSMA, and collagen١α and it also reduced the phosphorylation of Smad٣ levels in cholesterol-treated LX٢. Thus, suppression of TGF-β expression can improve hepatic fibrosis, and its mechanism of action is through the Smad٣ signaling pathway. This study suggests the use of exosomes of WJ-MSC for developing effective therapies for hepatic fibrosis. Cholesterol accumulation in HSCs can activate them and increase fibrosis genes expression, leading to the progression of liver fibrosis. The exosomes of WJ-MSCs can inhibit the TGFβ/Smad٣ signaling pathway, and prevent further activation of HSCs and progression of liver fibrosis. So, the exosomes of WJ-MSCs can reduce the expression of fibrosis genes. According to our data, the exosome of WJ-MSCs can be introduced as an effective remedy for liver fibrosis.

Keywords: Cholesterol, Exosomes, Liver fibrosis

Explaining the experiences of female-headed households covered by the Imam Khomeini Relief Committee: the results of a phenomenological study (Research Paper)

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Introduction: Background and Objectives: Female-headed households are one of the socially vulnerable groups, since the number of them is on the rise due to the increase in divorce rates, social crimes, or addiction rate. Considering the vulnerability of this group, the purpose of this study is to explain the experiences of female-headed households covered by the Imam Khomeini Relief Committee.

Methods: Materials and Methods: The present study is a qualitative phenomenological study that was conducted in ۲۰۱۸. To collect data, semi-structured interviews with open-ended questions about life experience as a female-headed household were used. The interviews were conducted in the Imam Khomeini Relief Committee center in Behshahr city. Sampling continued purposefully until data saturation was achieved with the participation of ۱۰ participants. The recorded interview was written down line by line and analyzed according to Collaizi's descriptive phenomenological approach. Lincoln and Guba's criteria were used for the strength of the study.

Results: From the data analysis, two main concepts including "change in normal life routine" and "problems of managing life" and four sub-concepts including "change in the role and feeling of the parent", "life progress"," loneliness" and "worried about the future of children " were extracted.

Conclusion: Considering the mentioned results and especially the basic concerns of female-headed household, it is necessary to take steps toward redusing problems of this group of society through the psychosocial empowerment programs

Keywords: Women, family, household, female-headed, qualitative research

Exploring anti-metastatic potential of Sutent on U۸۷ cells via computational and experimental analyses (Research Paper)

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Introduction: Glioblastoma multiforme (GBM) is the most aggressive and infiltrative form of brain tumor. While standard treatment typically involves surgical resection, followed by radiotherapy and chemotherapy, patient survival rates remain low. The poor prognosis associated with GBM is largely due to metastasis, as both local and distant invasions result in tumor recurrence, even after intensive treatment. The objective of current research was to determine whether Sutent has the potential to reduce the metastatic potential of GBM cells in silico and in vitro.

Methods: For computational analysis, potential molecular targets of Sutent and pathogenic targets of GBM were identified and Venn diagram was created to illustrate their overlap. Then, protein-protein interaction network was constructed, and enrichment analysis was performed. For in vitro studies, U۸۷ cells were cultured in ۲٤-well plates, and once a cell monolayer was established, a vertical scratch was introduced. Then, cells were treated with ۱۲,٥ µM Sutent, while untreated cells and those treated with DMSO solvent served as controls. Four microscopic fields were subsequently selected to observe the migration of U۸۷ cells over a ۲٤ h period.

Results: Seventy six overlapping targets were detected for Sutent and GBM, and CytoHubba plugin identified SRC, JAK۲, and EGFR as top hub genes, which are known to be involved in cell migration and invasion processes. Enrichment analysis also confirmed the involvement of hub genes in several biological processes and pathways. Results of migration assay showed that the migration of untreated cells and those treated with DMSO after ۲٤ h was ۹۸,۲٪ and ۹۸,٥٪, respectively. Notably, treatment with Sutent significantly ($p<۰,۰۰۱$) reduced cell migration to ۱۳,۷٪.

Conclusion: The study findings suggest that Sutent has significant potential to reduce the metastatic capabilities of GBM cells, supporting its further investigation as a therapeutic agent.

Keywords: Metastasis, Glioblastoma multiforme, Sutent, Migration assay.

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Exploring apoptosis-inducing effects of Sutent on human glioblastoma cells (Research Paper)

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Introduction: Sutent, a small molecule with the chemical formula C٢٢H٢٧FN٤O٢, functions as an inhibitor of multiple receptor tyrosine kinases. This drug has been approved by the FDA for the treatment of metastatic renal cell carcinoma and gastrointestinal stromal tumors. Preclinical studies have demonstrated the anticancer potential of Sutent against various solid tumors; however, no report has been published on toxic effects of this agent in glioblastoma cells. The present study aimed to investigate anticancer potential of Sutent on human glioblastoma cells for the first time.

Methods: U٨٧ cells were treated with ١٢,٥, ٢٥ and ٥٠ µM Sutent for ٢٤, ٤٨ and ٧٢ h. At the end of each time point, cell viability was determined by alamarBlue test. Subsequently, the cells were treated with ٥٠ µM Sutent, stained with propidium iodide and FITC-annexin V, and analyzed using flow cytometry to evaluate the mechanism of cell death.

Results: Findings of viability assay indicated that Sutent induced significant ($p<٠,٠٠١$) toxic effect on glioblastoma cells in a time- and dose-dependent manner. Viability of U٨٧ cells was calculated as ٥٠,٥٪, ٣٠٪ and ٢٥,٥٪ upon ٢٤, ٤٨ and ٧٢ h treatment with ٥٠ µM Sutent, respectively. Flow cytometry analysis confirmed results of alamarBlue test, as ٤٥,٣٪ of cells treated with Sutent were detected in the early and late stages of apoptosis.

Conclusion: The current study emphasizes the significant toxic effects of Sutent on U٨٧ cells, suggesting its potential as a novel therapeutic option for glioblastoma.

Keywords: Sutent, Apoptosis, Glioblastoma, Anti-cancer.

Exploring common and distinctive causes of idiopathic and familial dilated cardiomyopathies via bioinformatic analysis (Research Paper)

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Introduction: Dilated cardiomyopathy (DCM) is a cardiac disorder that leads to the enlargement of left/both ventricles and systolic dysfunction which may contribute to heart failure. The causes of DCM include metabolic, inflammation, infection, neuromuscular disease, tachyarrhythmia, toxins, pregnancy, autoimmune system dysfunction, genetics, and idiopathic. In Patients with idiopathic DCM, the precise etiology of the disease is not clarified, but its familial subtype has a genetic basis. In this study transcriptome data of idiopathic and familial DCM patients were analyzed to identify possible common and distinct genetic and molecular events in these conditions.

Methods: Left ventricular gene expression data of DCM patients and healthy donors (GSE١١٤٥) was downloaded from (GEO) database (https:// www. ncbi. nlm. nih. gov/). Differentially expressed genes (DEGs) were identified utilizing (TAC) ٤,٠ software with false discovery rate (FDR) ≤ ٠,٠٥ and log٢fold change: > ٢ or < -٢. The protein-protein interaction (PPI) network was constructed using STRING and Cytoscape, to recognize hub genes. Gephi software was utilized to create functional modules. Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway, Gene Ontology (GO), and DisGeNET enrichment analysis were conducted (P <٠,٠٥) to scrutinize the biological functions of DEGs.

Results: A total of ٢٤٣ DEGs were identified with ١٥٤ upregulated and ٨٩ downregulated genes in idiopathic DCM. In familial DCM, ٢٨٢ DEGs including, ١٩٩ upregulated and ٨٣ down-regulated genes were recognized. The PPI network analysis detected ١١٥ proteins, ١٠٦ edges for idiopathic, and ١٨٦ proteins, ٢٨٦ edges for familial DCMs. The hub genes with the highest degree in idiopathic DCM were GSPT١, SCN٢B, ANOS١, MT-ND٦, BTN٣A٢, BTN٣A٣, CCNG٤, KLHL٢٤, ENPP٢, PLA٢G٢A while, in familial were CCL٢, IGF١, LUM, DC١٦٣, ASPN, ITGA٥, OGN, JAK٢, FLNC, SOCS٣. Besides, ١٢ and ١٥ interconnected modules were recognized in DEGs for idiopathic and familial DCMs respectively. In idiopathic DCM the KEGG pathway analysis indicated, DEGs were enriched in Type I diabetes mellitus, Th١ and Th٢ cell differentiation, Hematopoietic cell lineage, dilated cardiomyopathy, etc. In familial DCM, influenza A, type I diabetes mellitus, etc. enriched. Both diseases share many pathways, such as Th١ and Th٢ cell differentiation, viral myocarditis, hematopoietic cell lineage, etc. The mainly enriched Go biological processes in idiopathic DCM encompassed: myotube Cell development, positive regulation of cell-substrate adhesion, extracellular matrix organization, and for familial DCM were: immunoglobulin mediated immune response, MHC Class II protein complex assembly, peptide antigen assembly. Nevertheless, both entities share myotube Cell development, muscle Contraction, systemic arterial blood pressure, regulation of potassium Ion export across plasma membrane, and myotube differentiation. The mainly enriched (GO) molecular functions in idiopathic DCM included ciliary neurotrophic factor receptor binding and cytokine Receptor Binding.

In familial DCM MHC Class II Protein Complex Binding and MHC Class II Receptor Activity enriched. In addition, enrichment analysis across important modules was assessed. KEGG pathways enrichment analysis of disease modules demonstrated module ٠ of idiopathic DCM was extremely similar to module ١ of familial DCM. Both are involved in amino acid and protein metabolism, however module ١ was also enriched in cancer-related pathways. Enrichment analysis of these modules in DisGeNET showed that both retrieve very similar illnesses, Marinesco-Sjogren syndrome, Oncogenic osteomalacia, Heart failure, etc. Moreover, module ٥ of idiopathic DCM was very similar to module ٣ of familial DCM which enriched the immune system, infections, etc. Nevertheless, more immune pathways were influenced by module ٣. It is also specified in dilated cardiomyopathy, p٥٣ signaling pathway, PI٣K-Akt signaling pathway. Therefore, the disease list for module ٣ of familial DCM was longer in DisGeNET. Both modules enriched in vascular diseases, myocardial infarction, coronary Arteriosclerosis. The main KEGG-enriched terms were identical in module ٩ of idiopathic and module ٨ of familial DCMs including cGMP-PKG signaling pathway and Cardiac muscle contraction. In both DCMs main enriched diseases were muscular dystrophies, Limb-Girdle, and Cardiomyopathies. Module ١٠ of familial DCM indicated unique characteristics. DisGeNET enrichment analysis showed affective Disorders Psychotic, Completed Suicide, and child abuse behavior. It is well-documented that there are strong connections between heart disease and mental illness.

Conclusion: Dilated cardiomyopathy is a genetically and clinically heterogeneous disorder. The exact etiology of idiopathic DMC has not been defined however its familial subtype has a genetic base. This bioinformatic analysis revealed that they have interweaved causes and their distinctive pathophysiology may be distinguished by meta-analysis methods.

Keywords: Idiopathic dilated cardiomyopathy, Familial, dilated cardiomyopathy, bioinformatic analysis

Exploring Diagnostic Biomarkers in Hepatocellular Carcinoma (HCC): A Study Based on The Cancer Genome Atlas and Bioinformatics Analysis. (Research Paper)

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Introduction: One of the serious cancers on a global scale is Hepatocellular Carcinoma (HCC). HCC is the most prevalent form of primary liver cancer and one of the leading causes of cancer-related death globally. Therefore, early recognition of this issue is essential. This study aimed to identify promising biomarkers for early detection and timely treatment and finding potential approaches to save more patients struggling with this morbidity.

Methods: First, the TCGA dataset named LIHC was acquired from TCGA database and expression matrix was generated using a function called assay in R programming language. Expression matrix was normalized with TMM method of edgeR and limma packages and afterwards, criteria of |log٢FC|>٢ and P.value< ٠,٠٥ were set to select target genes. Differentially Expressed Genes (DEGs) were used to perform Protein-Protein Interaction (PPI) network and its outcome was utilized to visualize and for further analysis with two plug-ins of Cytoscape software, CytoHubba and MCODE. Furthermore, Cytoscape analysis revealed the highly ranked genes which were calculated by several algorithms of CytoHubba plug-in, as our hub genes. Besides, Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis conducted using Enrichr database and finally, the value of hub genes were evaluated through the Gene Expression Profiling Interactive Analysis (GEPIA) web-based survival analysis tool.

Results: Overall, ٤٣٤ genes comprising ٦٧ up-regulated and ٣٦٧ down-regulated genes were detected. According to the results of PPI network analysis utilizing Cytoscape, the first and top-ranked cluster (٣٥,٨٣٣) was selected due to the MCODE plug-in and Top ٥ genes ranked by MCC, Degree, MNC, EcCetricity and Closeness methods of CytoHubba plug-in were distinguished. In the next step, Survival analysis ascertained that up-regulation of KIFC١, CDK١, CCNB١, KIF٢C and AURKA were strongly involved in hepatocellular carcinoma progression. Further analysis revealed an outstanding enrichment of target genes in Retinol metabolism in KEGG pathway. In addition, DEGs were significantly engaged in Arachidonic Acid Monooxygenase Activity (GO:٠٠٠٨٣٩١), Collagen-Containing Extracellular Matrix (GO:٠٠٦٢٠٢٣) and Epoxygenase P٤٥٠ Pathway (GO:٠٠١٩٣٧٣) in molecular function, cellular component and biological process, respectively.

Conclusion: In conclusion, the results of our research and survival analysis demonstrated a remarkable association between the expression of CCNB١, KIF٢C, CDK١, AURKA and KIFC١ and the mortality in hepatocellular carcinoma cases.

Keywords: Hepatocellular Cancer, Differentially Expressed Gene, Bioinformatics, Biomarker, TCGA

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Exploring Melatonin as a Targeted Inhibitor of EGFR in Colorectal Cancer: Insights from In Silico Techniques (Research Paper)

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Introduction: Colorectal cancer (CRC) is a formidable health challenge, often characterized by limited treatment success due to the development of drug resistance and high rates of cancer recurrence. Angiogenesis is a significant factor in cancer progression and metastasis that is known for its nourishment ability in pathophysiological conditions and is regulated by several proteins including vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), and endocan (ESM-1). EGF affects cell behavior through its interaction with the receptor protein called EGFR which is a transmembrane protein that plays crucial roles in regulating cell differentiation, survival, proliferation, and angiogenesis. In the context of CRC, EGFR is frequently overexpressed, contributing to the survival, proliferation, and metastasis of cancer cells. This overexpression makes EGFR an attractive target for therapeutic intervention. Melatonin, a naturally occurring molecule renowned for its anticancer properties, has shown promise in impeding the progression of CRC by exerting inhibitory effects on EGFR. This emerging evidence underscores the potential of melatonin as a valuable component in the treatment of CRC. Moreover, in silico techniques, such as bioinformatics, molecular docking, and virtual screening, offer invaluable tools for investigating molecular interactions, thereby facilitating the process of drug discovery and development. By leveraging these advanced computational methods, researchers can gain comprehensive insights into potential therapeutic compounds and their interactions with specific targets, ultimately expediting the characterization and establishment of molecules and target proteins. These techniques not only accelerate the pace of research but also provide a robust framework for designing efficient in vitro and in vivo studies, thus significantly reducing the time required for comprehensive characterization and validation.

Methods: Durggability of the EGFR was assessed through the ProteinsPlus web portal. Vandetanib was selected as an approved EGFR inhibitor molecule from the drug bank database and the 3D structure of melatonin and vandetanib was extracted from PubChem. The 3D structures of the target protein and the selected molecules were reduced using the Ligprep and the Protein preparation wizard application from Schrodinger, EGFR was docked with both molecules using the Glide application from the Schrodinger software.

Results: Docking results proved that vindetanib couples with EGFR and melatonin can interact with the same pocket showing the tyrosine kinase inhibition potential of melatonin.

Conclusion: The results of this research emphasize the potential of melatonin as a treatment that can inhibit the activity of EGFR in colorectal cancer, working alongside current treatments such as vandetanib. Through computational analysis, it was discovered that melatonin binds to the same active site on the EGFR as vandetanib, indicating its ability to potentially inhibit its tyrosine kinase

activity, which is crucial for the proliferation and survival of cancer cells. This study validates the molecular interaction between melatonin and EGFR, providing promising insights into the use of natural compounds as supplementary treatments to target EGFR in colorectal cancer. Additionally, the research showcases the effectiveness of computational methods such as bioinformatics and molecular docking in accelerating the discovery of potential therapeutic compounds, thereby reducing the necessity for extensive in vitro and in vivo experiments. Future research should concentrate on further confirming these findings through experimental studies, potentially opening the door for innovative melatonin-based therapeutic approaches in addressing drug-resistant and recurrent colorectal cancer. Future studies may consider other angiogenic proteins such as VEGFR and endocan that show important roles in cancer progression and metastasis.

Keywords: Colorectal Cancer, Melatonin, VEGF, Angiogenesis, Molecular Docking

Exploring Mycobacterium avium subsp. paratuberculosis: Antibiotic Resistance and Its Implications for Chronic Diseases (Review)

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Introduction: Mycobacterium avium subsp. paratuberculosis (MAP) is a pathogenic bacterium primarily known for causing Johne's disease in ruminants, particularly cattle. This chronic enteric disease leads to significant economic losses in the livestock industry. It raises concerns regarding its potential zoonotic implications, particularly its association with chronic inflammatory diseases in humans, such as Crohn's disease. The increasing prevalence of antibiotic resistance among MAP strains complicates treatment strategies and highlights the need for comprehensive research into its pathogenic mechanisms and public health implications.

Methods: This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A comprehensive literature search was performed using databases such as PubMed, Scopus, and Web of Science to identify relevant studies published up to October ٢٠٢٣. The search terms included "Mycobacterium avium subsp. paratuberculosis," "antibiotic resistance," "chronic disease," and "zoonosis." Inclusion criteria comprised peer-reviewed articles discussing MAP's antibiotic resistance, its role in chronic diseases, and any associated epidemiological studies. Data extraction focused on study design, sample size, findings related to antibiotic resistance patterns, and associations with chronic diseases.

Results: Antibiotic Resistance Patterns A total of ١٢٨ studies were included in this review. The findings indicated that MAP exhibits significant antibiotic resistance, particularly against commonly used antibiotics such as tetracycline and sulfonamides. Resistance mechanisms involve efflux pumps and biofilm formation, which enhance survival in hostile environments. A meta-analysis revealed that approximately ٦٠٪ of MAP isolates from cattle were resistant to at least one antibiotic, with multi-drug resistance observed in about ٣٠٪ of cases. Association with Chronic Diseases The review also highlighted a potential link between MAP infection and several chronic diseases in humans. Crohn's Disease: Epidemiological studies consistently indicate a significant association between MAP presence and Crohn's disease, with odds ratios ranging from ٤,٢٦ to ٨,٤٤. Type ١ Diabetes: A notable association was found between MAP exposure and Type ١ diabetes (odds ratio range: ٢,٩١–٩,٩٥). Multiple Sclerosis: Similar associations were observed for multiple sclerosis (odds ratio range: ٦,٥–٧,٩٩). The evidence suggests that MAP may induce autoimmune responses through mechanisms such as molecular mimicry, where the bacterium's antigens resemble host tissues, leading to immune dysregulation. Knowledge Gaps Despite these findings, substantial knowledge gaps remain regarding the precise mechanisms by which MAP contributes to chronic diseases. Variability in diagnostic methodologies (e.g., PCR primers) and study populations complicates the interpretation of results.

Conclusion: Conclusion Mycobacterium avium subsp. paratuberculosis is a significant pathogen with implications for both animal health and human chronic diseases. The documented antibiotic resistance poses challenges for effective treatment and control measures. While there is growing evidence linking MAP to conditions like Crohn's disease and other autoimmune disorders, further research is essential to clarify these associations and understand the underlying pathogenic mechanisms. Comprehensive surveillance of MAP in both livestock and human populations is crucial to mitigate its impact on public health and develop effective prevention strategies.

Keywords: Mycobacterium avium paratuberculosis (MAP), Antibiotic resistance, Chronic diseases, Zoonotic infect

Exploring the Link Between Type ٢ Diabetes and Alzheimer's Disease: The Potential of MRPL١٩ as a Biomarker (Research Paper)

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Introduction: Introduction: Alzheimer's disease (AD) and diabetes mellitus (DM), particularly type ٢ diabetes (T٢DM), are significant global health concerns with increasing prevalence. Recent research highlights a potential link between DM and an elevated risk of AD. Mitochondrial function is critical for neuronal survival, energy metabolism, and cell death, with mitochondrial dysfunction and excessive oxidative damage being early indicators of AD. As key sites for glucose and lipid metabolism, mitochondria are often implicated in the functional impairments seen in T٢DM. Damaged mitochondria release pro-inflammatory factors, triggering inflammatory pathways and oxidative stress responses. Despite these associations, the specific role of mitochondrial ribosomal proteins (MRPs) in the link between T٢DM and AD remains underexplored. MRPL١٩, a mitochondrial ribosomal protein and housekeeping gene with stable expression across various tissues, is involved in the cytosolic stress response and promotes Hsp٧٠ translation

Methods: Method: We explored the relationship between Alzheimer's disease and diabetes using the Rattus norvegicus model. We identified dataset GSE٣٤٤٥١ from the GEO database and grouped the results accordingly. Using the limma package in R, we analyzed the data to identify differentially expressed genes. The query and biobase packages facilitated data manipulation and annotation. To identify common genes between type ١ and type ٢ diabetes, we utilized the Venny Diagram website and identified ٤٥٦ common genes. We then generated a network diagram of these common genes using the String_db.org database and Cytoscape software, identifying ١٠ hub genes based on centrality and connectivity within the network. Further literature review led to the selection of MRPL١٩, a mitochondrial ribosomal gene, as a candidate biomarker. The Alliance database provided additional gene information, and we employed Prism software to assess MRPL١٩'s potential to differentiate between type ١ and type ٢ diabetes through p-value and area under the curve (AUC) analysis

Results: Result: Analysis using Prism showed that MRPL١٩ demonstrates promise as a potential biomarker for Alzheimer's disease in type ٢ diabetes but not in type ١ diabetes. The biomarker's performance was statistically significant

Conclusion: Conclusion: This study highlights the potential of MRPL١٩ as a biomarker for Alzheimer's disease in patients with type ٢ diabetes, implicating it in the mitochondrial stress response and AD pathogenesis. Future research should focus on elucidating the mechanisms by which MRPL١٩ contributes to AD development in diabetic patients and explore its potential as a therapeutic target

Keywords: Alzheimer's disease (AD),Diabetes mellitus (DM),Mitochondrial dysfunction,MRPL١٩ gene, Biomarker,

Exploring the Relationship Between Alzheimer's Disease and the Metabolome: Insights from mRNA Expression Analysis (Research Paper)

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Introduction: Alzheimer's disease (AD) is a debilitating neurodegenerative disorder characterized by progressive cognitive decline. The metabolome, comprising small molecule metabolites, plays a crucial role in the pathogenesis of AD. This study aims to investigate the association between AD and the metabolome through mRNA expression analysis, providing insights into disease mechanisms and potential therapeutic targets.

Methods: A cohort study was conducted involving ۱۵۰ participants, including ۷۵ AD patients and ۷۵ age-matched controls. Blood samples were collected from each participant, and mRNA expression levels were quantified using quantitative real-time PCR. Metabolomic profiling was performed using mass spectrometry to analyze the abundance of metabolites in plasma samples. Demographic data, including age, gender, and clinical characteristics, were collected for all participants.

Results: The demographic characteristics of AD patients and controls were comparable in terms of age and gender distribution. Analysis of mRNA expression revealed dysregulation of key genes associated with AD pathogenesis, including APP (mean mRNA copies: ۲۰۰۰ in AD patients vs. ۵۰۰ in controls; p<۰,۰۰۱) and BACE۱ (mean mRNA copies: ۱۵۰۰ in AD patients vs. ۳۰۰ in controls; p<۰,۰۰۱). Metabolomic profiling identified alterations in several metabolites associated with AD, including dysregulation of lipid metabolism pathways and changes in levels of neurotransmitter precursors.

Conclusion: This study provides evidence for the association between AD and the metabolome through mRNA expression analysis. Dysregulation of key genes involved in AD pathology and alterations in metabolite levels highlight the intricate interplay between molecular pathways underlying disease progression. These findings offer novel insights into the pathogenesis of AD and potential targets for therapeutic intervention. Further research is warranted to elucidate the causal relationships between metabolic alterations and AD pathophysiology, paving the way for personalized treatment approaches.

Keywords: Alzheimer's Disease, Neurodegenerative Disorder, Metabolomic profiling, Pathway Dysregulation

Exploring the relationship between circadian rhythm regulators and brain aging (Review)

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Introduction: Introduction: The interplay between chronobiology and neuroscience has garnered significant interest in recent years, particularly regarding the impact of molecules that regulate circadian rhythms on brain aging. The present review investigates the relationship between circadian rhythm regulators and the biological processes that contribute to age-related neurodegeneration. We examine how the disruption of circadian rhythms influences the expression and up/downregulation of specific molecules and how these variations correlate with cognitive decline, synaptic plasticity alterations, and the accumulation of neurotoxic proteins.

Methods: Methods: Through a comprehensive literature review and analysis of empirical studies in major databases using several set of keywords, we elucidated the potential relationship between circadian rhythm regulator molecules, neuroinflammatory pathways and oxidative stress responses in the aging brain.

Results: Results: Based on the observations we gathered from most recent studies, Brain and Muscle Arnt-Like 1 (BMAL1) transcription factor which plays an important role in generation of circadian rhythms, has also been associated with the process of memory formation and aging. BMAL1, and its binding-partner CLOCK, were found to correlate negatively with age. Oxidative stress and inflammation pathways appear to play mediators in this interplay.

Conclusion: Our findings suggest that maintaining circadian rhythm stability may be crucial for promoting neuronal resilience and cognitive health in aging populations. This research underscores the significance of circadian rhythm regulators as potential biomarkers and therapeutic targets for mitigating the effects of brain aging, paving the way for novel interventions that align with the body's natural rhythms.

Keywords: Circadian rhythm; Circadian rhythm regulation; brain aging

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Exploring the Synergistic Potential of Thymol/Ceftazidime against Acinetobacter baumannii: A Novel Therapeutic Approach (Research Paper)

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Introduction: This study aimed at the antimicrobial effects of thymol/ceftazidime on Acinetobacter baumannii bacteria.

Methods: Antimicrobial effects of thymol/ceftazidime were performed first individually and then combined on A. baumannii ATCC ١٩٦٠٦ by the MIC-MBC method. Therefore, the antimicrobial effects of the compounds that had a synergistic impact were performed on eighteen clinical strains using the MIC-MBC method. The identification of chemical bonds, functional groups, and molecular interactions of the mentioned compounds was investigated using an FTIR device. Checkered method, time killing curve, and biofilm inhibition on A. baumannii ATCC ١٩٦٠٦, investigation of cytotoxicity on red blood cells (RBCs) by hemolysis method and human skin fibroblast cells (Ffk) by MTT method were performed. Thymol/ceftazidime had synergistic effects.

Results: The study's findings demonstrated that when applied to A. baumannii ATCC ١٩٦٠٦, the antimicrobial activities of thymol, ceftazidime, and thymol/ceftazidime (A٤ compound) were, respectively, ٢٥٦ µg/ml, ١٢٨ µg/ml, and ١٠٢٤/٢٥٦ µg/ml (FICI: ١ µg/ml). The A٤ compound exhibited antibacterial activity of ٢٥٦-١٠٢٤/٤-١٦ µg/ml on clinical strains of A. baumannii, respectively. Compared to the individual modes, the combined mode had a longer time curve for eliminating A. baumannii. Examination with FTIR showed that these two compounds have C=C conjugated, C≡C compound. Thymol, ceftazidime, and other chemicals have biofilm inhibition rates of ١١٪, ١٨,٥١٪, and ٢٣,٤١٪, respectively against A. baumannii bacteria. The toxicity of thymol, ceftazidime, and A٤ compound against human RBCs were ٣٦,١٢, ٨,٣٣, and ٨,٣٨, and against human Ffk cells were ١٩,٦٦, ٧,٠٨, and ٩,٠٣ respectively.

Conclusion: This study proved that the thymol/ceftazidime could become one of the new drugs for treating A. baumannii infections due to its high antimicrobial effects and low toxicity.

Keywords: Acinetobacter baumannii, Thymol, ceftazidime, Antimicrobial

Exploring the Therapeutic Potential of Exosomes in the Fight Against Cancer (Review)

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Introduction: Over the last few decades, astronomical amounts of research funding and efforts have been invested in cancer research, with a primary aim of understanding and eradicating cancer. Cancer remains the second most prevalent cause of death worldwide despite the significant progress made in discovering new diagnostic, therapeutic, and preventive techniques over the past ٤٠ years. While research has demonstrated that genetic mutations are the primary cause of carcinogenesis and cancer progression, there is limited knowledge about the causes or mechanisms behind their occurrence and progress. Exosomes are a class of extracellular vesicles approximately ١٠٠ nm in diameter, secreted by most cells and contain various bioactive molecules reflecting their cellular origin and the function of intercellular communication. The development of therapeutic and diagnostic approaches using exosomes for the treatment of cancer has resulted from studies on these exosomal features in tumor pathogenesis. Exosomes have a number of advantages for the transmission of therapeutic agents such as small interfering RNAs, microRNAs, membrane associated proteins and chemotherapeutic compounds; therefore, they are considered to be a potential delivery tool for cancer therapy. The use of exosomes to activate specific immune stages of cancer has led to the creation of bioactive molecules that act as cancer immunotherapies, as they provide an optimal microenvironment for immunomodulatory factors. The benefits of exosomes for cancer treatment and the challenges that need to be overcome in developing them are discussed in this review article.

Methods: Exosomes, between macromolecules and cells, can be classified as organelles that are becoming more widely known for their diagnostic qualities and therapeutic applications. Exosomes are considered to be an appropriate tool for the treatment of a variety of diseases, including cancer, since they contain molecules with different functions but lack their complexity in cells and tissues; unlike proteins or small molecules. Furthermore, exosomes offer a number of advantages in terms of biocompatibility, immunogenicity, stability, pharmacokinetics, biodistribution and cell uptake mechanism which make them candidates for anticancer treatment. These characteristics can lead to an improvement in the therapy index for exosomes based cancer treatments, through preferential treatment of tumor cells while avoiding side effects that are unpredictable.

Results: The purpose of this review was to highlight the usefulness and potential of exosomes in cancer therapy. Until recently, cancer treatment has relied mainly on physical surgery, chemotherapy, target therapy, or radiotherapy; however, these therapeutic modalities are commonly accompanied by side effects, acquired resistance, frequent metastasis, and recurrences. Cancer immunotherapy has emerged as a promising alternative to these conventional therapies to treat a variety of malignancies and has demonstrated remarkable clinical results, gaining considerable attention as a next-generation cancer treatment. Recently, with the popularity of proteomics analyses, the secretion and function of exosomal proteins obtained from cell lines or

body fluids have been revealed, and more attention has been given to their role in predicting tumor development. Exosomal surface proteins hold clues to the mechanisms of exosome biogenesis, secretion, protein–protein interactions, and recipient cell targeting. exosomal proteins play essential roles in many aspects of cancer, including EMT, ECM remodeling, angiogenesis, tumor-related immune regulation, premetastatic behavior, and therapeutic resistance. The characteristic proteins of cancer lesions are concentrated in the exosomes from human body fluids. Exosomal surface biomarkers have been detected, indicating that the identification of exosomal surface biomarkers may provide biological information on tumours, using known cancer surface marker antibodies attached to a chip. New biomarkers will be identified for early cancer diagnosis, prognosis and treatment assessment with more sensitive methods to be developed.

Conclusion: All over the world, exosomes are being studied and developed. In addition, to develop medicinal products based on exosomes a number of studies have been carried out both in vitro and in vivo as well as at the laboratory level. Despite various studies conducted on cancer treatment, cancer remains the leading cause of death globally. Chemotherapy, targeted therapy, and ICI have not effectively controlled cancer progression. Because chemotherapy has multiple side effects, targeted therapy has a limited indication, and ICI has a low response rate, better cancer treatment strategies are needed.ICI's low response rate is often improved by ex vivo immunotherapies.By using it as a means of chemotherapy, it can decrease the side effects of conventional chemotherapy and improve its effectiveness. However, because exosomes, particularly tumor-released exosomes, have a pro-tumorigenic proclivity and show excessive immune responses, further studies on their pro-tumorigenic and anti-tumorigenic functions are required. It is essential to establish a gold standard for a large scale, scalable manufacturing process to produce and purify exosomes for clinical trials. Despite a number of challenges, exosomes have great potential for drug development and delivery in the treatment of cancer.

Keywords: Exosomes‹Therapeutic ‹cancer

Exploring TP٥٣ and HER٢ Interactions in Breast Cancer: From Genetic Mutations to Therapeutic Resistance (Review)

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Introduction: Uncontrolled mammary epithelial cell development causes breast cancer for several reasons. Several genes that cause mutations concurrently cause cellular cancer. Cancer can result from many mutations. Mutations raise cancer phenotypic complexity and treatment difficulty. These are frequent breast cancer mutations:TP٥٣-PIK٣CA_HER٢_BRCA١_BRCA٢,base on Gene expression pattern classifies breast cancer as: luminal (A and B), Basal like, Normal like, Her٢ positive. P٥٣ mutation is lowest in luminal, Mostly p٥٣ mutations. Base like In more than half of HER٢-type proliferative tumors, p٥٣ mutations are present, and HER٢ overexpression is associated with a worse prognosis. combines We examine these two's effects and therapy in recent publications. Background: A ١٩٧٩ study found p٥٣ participation in the cell cycle and cancer cell invasion and metastasis.HER٢ discovery in١٩٨٥, These studies linked p٥٣ and HER٢ to aggressive cancers, notably breast cancer. It led to making important drugs like trastuzumab , Her٢(ErbB٢)is a tyrosine kinase receptor with inactive membrane monomers that promotes cell growth and survival. HER٢-positive breast cancer accounts for ١٠-١٥٪ .٣٠ to ٤٠٪ of breast cancer patients with higher HER٢ levels also have high estrogen receptor levels, which worsens prognosis due to high and early recurrence and metastatic potential. Breast cancer cells overexpressing HER٢ proliferate aggressively and have poor prognosis. Her٢ mutation drives advanced breast cancer The tumor suppressor P٥٣ is encoded by TP٥٣. Over ٥٠٪ of neoplasm related mutations include p٥٣ mutation the important role of p٥٣ is regulating the cell cycle, proliferation, senescence, apoptosis, metabolism in response to cellular stress, this protein protects genetic integrity. particularly in breast cancer, most typically modify this suppressor's gene because it inhibits carcinogenesis. About a third of TP٥٣ point mutations change amino acids in these locations:R١٧٥_G٢٤٥_R٢٤٨_R٢٤٩_R٢٧٣_R٢٨٢_ Spots of p٥٣ DNA domain mutations. The DNA sequence is directly affected by mutations like R٢٤٨_R٢٧٣. Other types include as R١٧٥ structural mutations: P٥٣R٢٧٣C_P٥٣R٢٤٨Q Two TP٥٣ gene variations create P٥٣. Point mutations make p٥٣ bind or negatively affect dominantly- Gain of function increases carcinogenesis, independent cell proliferation, chemotherapeutic sensitivity, metastasis, invasion, spindle checkpoint disruption, topoisomerase activity, and gene replication. The E٣ ligase MDM-٢, which prevents p-٥٣ gene activation, controls p٥٣ levels and binds to it. Inactivating p٥٣ is frequent with negative regulator overexpression or mutation. The promoter's negative feedback loop lowers p٥٣. Overproducing MDM٢ accelerates p٥٣ degradation, allowing uncontrolled cell proliferation. Indeed, p٥٣ dysfunction and HER٢ overexpression can abolish p٥٣'s repression and enhance HER٢. This stimulates tumor development and survival. HER٢ signals alter p٥٣ stability and function. Due to p٥٣ mutations changing HER٢ expression, the tumor microenvironment changes p٥٣-HER٢ interactions.

According to the study, mutant p٥٣ (p٥٣R١٧٥H) stabilizes HER٢.It can transcribe EGFK and stabilize HER٢, and both mutants P٥٣R٢٤٨Q and P٥٣R٢٧٣C acetylate histones H٣ and H٤ at the promoter, becoming proximal to HER٢. These mutations increase HER٢ in cell lines.

Methods: Since this is a review article we are working on the interaction between P٥٣ and HER٢ and targeted therapy.

Results: some of Working breast cancer treatments: trastuzumab Monoclonal antibody inhibits HER٢ signaling To inhibit homodimerization and overexpression, trastuzumab binds to the HER٢e ectodomain. The medicine pertuzumab is effective too. This monoclonal antibody inhibits dimer formation with other HER٢ receptors by binding to HER٢.Recent drugs that target HER٢ and other cancer cell proteins are more effective. Research tries to destroy cancer cells with immunotherapy and Her٢-targeted treatments. The trastuzumab-chemotherapy combination T-DM١ also works for HER٢ cancer. Checkpoint inhibitors PD-١/PD-L١ Breast cancer clinical studies show significant improvements. New breast cancer treatments include TKIs, tumor vaccines, and adoptive T-cell immunotherapies. Nice breast cancer results Lapatinib TKI targets Her١ and Her٢, It substantially blocks lapatinib's ATP binding pocket. Blocking receptor phosphorylation inhibits downstream processes, Prevents MAPK/Erk١/٢/PI٣K/AKT .Here are P٥٣-based treatments: A unique small-molecule chemical inhibitor, stapled peptide, PROTAcs, and GE vectors and antibodies.

Conclusion: Recent research shows that understanding mutation connections that promote cancer cells is essential to treat it. The processes controlling these components' interactions can be studied to improve breast cancer therapies that prevent neoplastic cell invasion and metastasis. Targeting HS٩٠is one of researching studies that Supports P٥٣ folding and HER٢ stability, Targeting HS٩٠can prevent signaling path way of HER٢and gain of function of mutated P٥٣. Cancer cell treatment with targeted immunotherapy is one of the effective ways and recent research includes adoptive cell treatment, monoclonal antibodies, oncolytic viruses, immune system modulators, and P٥٣-regulates MDM٢.more Research on p٥٣ specific mutations that change HER٢ activity may prevent cancer cell growth.

Keywords: Targeted therapy-Immunotherapy-p٥٣ muta٤ons-Breast cancer-Her٢ Over expression

Expression and solubility of Teriparatide peptide in fusion of Ssp DnaB mini-intein in E. coli

(Research Paper)

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Introduction: Osteoporosis is a common disease in the world, which is prevalent especially in aging societies. Teriparatide is a synthetic peptide amino acids ١-٣٤ of the N-terminal of human parathyroid hormone (PTH) and approved by FDA in ٢٠٠٢ for treatment of osteoporosis. Ssp DnaB mini-intein with ١٥٤ amino acids is a protein which has self-splicing property. It acts as a fusion tag/fusion partner for expression of peptides and proteins in biological tools. Bioseparation technique is mediated by self-splicing inteins has become an excellent tool for affinity tag-based protein purification techniques and an alternative to conventional splicing by site-specific endoproteases. In this study the effects of Ssp DnaB mini-intein on expression and solubility of Teriparatde peptide during expression in E. coli was evaluated.

Methods: The fusion of Ssp DnaB mini-intein and Teriparatide encoding sequences was achieved through the PCR technique. The fusion gene was then cloned in pET٢٨a plasmid containing a N-terminal Histidin-tag. Subsequently the construct was introduced into E. coli BL٢١ strain through the process of transformation. The E. coli cells was then grown in Luria Broth (LB) medium supplemented with kanamycin antibiotic to produce the desired recombinant protein. Upon completing the solubilization process of the protein, the intein and peptide are separated under certain conditions (pH, temperature) and purified, resulting in the successful production of the desired peptide.

Results: The finding of this study revealed the potential of Ssp DnaB mini-intein in preparation of Teriparatide in E. coli and the expression and solubility of peptide be in acceptable level.

Conclusion: Using the inteins facilitate the purification of peptides and proteins without need to endoproteases therefore this fusion tag can be used for producing this peptide in industry scale in easier way.

Keywords: Teriparatide, Ssp DnaB mini-intein, Expression, E. coli

Fabrication and Characterization of PMMA-Based Bone Cement Enriched with Chitosan and Allograft Bone Powder (Research Paper)

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Introduction: Polymethyl methacrylate (PMMA) and its derivatives have been proficiently utilized in orthopedic surgeries aimed for filling the undesired cavities in similar forms of the surrounding tissue and eventually, stablishing a strong integration with the native tissue. However, the insufficient mechanical compatibility as well as the lack of bioactivity of PMMA bone cements has led to several investigations in case of the enhancement of their structural and biological characteristics. It has been reported in previous literature that loading chitosan in PMMA resulted in reducing the polymerization temperature and improving bone regeneration capability of the compound. Moreover, regarding the reported biocompatibility of allograft bone substitutes such as bone powders, the biological performance of the cement could be promoted via using this human-derived material and the mineral phase of bone would be mimicked optimally. Therefore, in the following project, a developed bone cement composed of PMMA, chitosan and allograft bone powder was fabricated and characterized.

Methods: Allograft bone powder was processed chemically and mechanically after donor screening and assuring of lack of any bioburden (bacteria, viruses, molds, etc.) in Iranian Tissue Product Company (ITP). A solution consists of bone powder and chitosan in acetic acid ٢٪ was produced. A homogenous powder was prepared by freeze-drying the solution and ball-milling the resulted bulks. The powder was then added to the PMMA powder (٣٠٪ w/w). The liquid phase of the cement (methyl methacrylate monomer) was poured on the final powder in a ١:٢ ratio. Benzoyl peroxide and N,N-Dimethyl-p-toluidine were also used as initiator and catalyzer of the polymerization process. The microstructure of the cement was observed by scanning electron microscopy (SEM). Furthermore, the bioactivity of the sample was evaluated through immersing in simulated body fluid (SBF) and examining the created crystals on the surface after ٢١ days. The biocompatibility was investigated by the ٣-(٤,٥-dimethylthiazol-٢-yl)-٢,٥-diphenyl-٢H-tetrazolium bromide (MTT) assay and culturing human mesenchymal stem cells (hMSCs) on bone cements after ٧٢h.

Results: According to the SEM images, a well-defined arrangement of PMMA and the chitosan-bone powder was observed as evidence of the efficient polymerization of PMMA and no unsuitable intervention of chitosan – bone powder in the process. After ٢١ days of soaking the cement in SBF solution, its surface was covered with apatite-like formations. On this basis, the bioactivity of the cement due to its mineral compound similar to the native bone tissue was approved. Also, its biocompatibility was demonstrated via a ٩٨٪ cellular viability reported by MTT assay after ٧٢h.

Conclusion: Considering the well-arranged structural characteristics, the optimum bioactivity, and the improved biocompatibility of the prepared bone cement, it could be revealed that the PMMA-Chitosan-Allograft Bone Powder bone cement is a promising candidate for successfully employing in orthopedic surgeries.

Keywords: Bone Cement, PMMA, Allograft Bone, Chitosan, Tissue Engineering.

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Fabrication and optimization of co-administrated Elaeagnus Angustifolia extract and Rosa canina isolated polysaccharide-loaded electrospun gelatin/polycaprolactone nanofibers as the burn wound dressing (Research Paper)

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Introduction: Modified wound dressings by providing a regenerative and anti-bacterial environment can accelerate the healing of wounds and prevent infection. This study aims to fabricate and evaluate the healing effect of an electrospun wound dressing containing polycaprolactone (PCL), gelatin (Gel), and extracts of Elaeagnus Angustifolia and isolated polysaccharide from Rosa canina on a burn wound model.

Methods: Characteristics analyses including scanning electron microscopy (SEM), FT-IR spectroscopy (FTIR), and X-ray diffraction (XRD) were performed to survey the physical and chemical properties of PCL/Gel/Polysaccharide and PCL/Gel/Extract mats. Water contact, mechanical properties, control release, cellular behavior, and microbial penetration were investigated to optimize dressings. The cytoprotective effect of wound dressing was evaluated on fibroblast cells. The rat burn model was used to examine the accelerative healing potentials of scaffolds.

Results: PCL/Gel mats containing Rosa canina polysaccharide or Elaeagnus Angustifolia extract as the well-known therapeutic agents showed that they can reduce pain, stimulate re-epithelialization, induce vascular propagation, and reduce infection.

Conclusion: The designed wound mat seems to be a novel mat to heal several wounds compared to others.

Keywords: Electrospining,; Gelatin; Polycaprolactone; Polysaccharide; Wound dressing

Factors associated with the quality of life of the elderly in the Middle East: a systematic review

(Review)

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Introduction: Identifying factors related to the quality of life of the elderly can be effective in finding ways to improve their quality of life. Therefore, the aim of the present study is to investigate the factors related to the quality of life of the elderly in Middle Eastern countries.

Methods: This study is a review and systematic search. In March and April ۲۰۲۰, browsing Persian and English articles in databases, (Elderly (* quality of life"), with the keywords of quality of life, Magiran, SID, Noormags, Scopus, WOS, Pubmed Irandoc, Proquest elderly, older adults, aging, aging, seniors) and each Middle Eastern country was conducted in English and Farsi, and according to the entry and exit criteria, related articles were included in this research in the period from the beginning to April ۲۰۲۰ The quality of life of the elderly in the Middle East was obtained, and after screening and evaluating the articles based on the inclusion and exclusion criteria, ۸۲ articles were finally included in the study.

Results: The results showed that most of the studies in the Middle East were conducted with a cross-sectional method and using the quality of life tool SF۳٦, and the quality of life of the elderly in the Middle East is influenced by socio-demographic, psychological, physical and spiritual factors.

Conclusion: Based on the results of the present study and several factors related to the quality of life of the elderly in the Middle East countries; It is suggested that in formulating and implementing policies and programs related to the elderly, attention should be paid to various social, psychological, physical and spiritual dimensions in order to improve their quality of life as much as possible.

Keywords: quality of life , elderly , Middle East

Factors of exacerbation and stimulation of varicella-zoster virus during the incubation period that lead to herpes zoster (Review)

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Introduction: VZV particles, classified as one of the herpes viruses, can undergo retrograde axonal transmission in the dorsal root ganglia and sensory ganglia of the cranial nerve. Following a period of inhibition caused by reactivated factors, it manifests as shingles or herpes zoster. This viral agent commences its replication within the nerve cells and is innervated by the ganglia of the same nerve, wherein it remains concealed, eventually affecting a specific area of the skin or other bodily organs. The intimate association between nerves and the circulatory system facilitates the virus's ability to extend its reach to blood vessels.

Methods: A literature search on PubMed, Google Scholar, and Web of Science databases used the terms herpes zoster and Nervous system immunity. Publications that were not available or were not in the English language were excluded, as were publications that were not related to the topic.

Results: Various studies indicate that viruses are among the most astute microorganisms and, undoubtedly, the most perilous. Consequently, in the case of the varicella-zoster virus, following an encounter with an individual's immune system and subsequent failure, these viruses remain dormant until a suitable opportunity arises. This opportunity for re-infection, which is significantly more severe and detrimental, is afforded to the virus by a multitude of factors. These factors can be delineated as follows: ١. advancing age is one of the most prevalent risk factors. In fact, statistical evidence indicates that individuals who have previously contracted this virus face a heightened susceptibility to developing shingles after reaching the age of ٥٠. Additionally, other influential factors include the presence of a tumor, as well as viral or bacterial infections. Moreover, both acute and chronic diseases, as well as autoimmune disorders necessitating corticosteroids, can contribute to the increased vulnerability. Furthermore, individuals who have undergone organ or bone marrow transplantation, which results in a reduction in white blood cell count, are also at a heightened risk. Avarand also highlighted the importance of considering asthma, chronic obstructive pulmonary disease, diabetes, depression, and chemotherapy as contributing factors. ٢. Occasionally, herpes zoster may manifest in children due to the immaturity of their immune system. To illustrate, children who contract varicella-zoster before reaching ١٢ months of age have a higher likelihood of developing herpes zoster during their childhood. An example is an ١١-year-old girl who exhibited symptoms in the genital area, prompting doctors to suspect sexual abuse. However, further testing revealed that it was indeed an infection, specifically herpes zoster. Additionally, mothers who acquire the varicella-zoster virus (VZV) during pregnancy may experience changes in maternal antibodies, resulting in the conversion of the initial varicella infection into a subclinical form.

Consequently, these individuals may initially present with clinical manifestations of herpes zoster. Furthermore, other contributing factors observed in adults, particularly in children, include traumatic injuries that provoke nerve irritation and subsequent shingles symptoms. An instance of this is a ١٥-year-old boy who experienced a fall while riding a bicycle, leading to the gradual onset of symptoms. ٣. One of the most significant precipitants of this virus during its incubation period is certain conditions within the immune system, which are influenced by various factors. For instance, the antibodies produced during the initial infection are virtually ineffective. Varicella-zoster virus (VZV), by impacting the release of active immune substances like cytokines, neurotrophic factors, and chemokines, instigates the suppression of T lymphocytes. The inhibition of JAKi inhibitors and monoclonal antibodies raises the susceptibility to contracting herpes zoster by suppressing the immune system. The existence of specific proteins or defects in the genes responsible for encoding the signal transduction factors of the IFN pathway contributes to the malfunctioning of IFN activity, ultimately yielding ISGs. Specifically, these ISGs restrict the infiltration and replication of the virus in a particular region of the central nervous system. The antiviral response of the dorsal root ganglia relies on the dual functionality of antiviral ISGs and the activation of autophagy. ٤. Hypothyroidism, smoking, mental and physical stress, and emotional failures are other factors that provoke and aggravate this virus.

Conclusion: During the research that was conducted, it has been observed that the debilitation of the immune system through various means is the paramount element in the provocation and revival of the virus. With further investigation and many examinations of these factors, it is anticipated that the primary cause will be ascertained. Subsequently, appropriate precautions were taken to avert the occurrence.

Keywords: Varicella zoster/ VZV/ immune system/ Herpes zoster/ shingles/ nerve cells

Favism disease review article (Review)

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Introduction: Favism is a condition that affects people who have a genetic deficiency of an enzyme called glucose-٦-phosphate dehydrogenase (G٦PD). This enzyme protects red blood cells from damage caused by certain substances, such as fava beans, some drugs, and some infections. People with favism can develop a type of anemia called hemolytic anemia, which occurs when red blood cells are destroyed faster than they can be replaced. Favism, a genetic disorder caused by a deficiency in the enzyme glucose-٦-phosphate dehydrogenase, is a major public health concern in many regions of the world. Understanding the underlying causes and treatment options for this disorder is essential for improving the health outcomes for those affected.

Methods: The mechanism by which G٦PD deficiency confers protection against malaria is not fully understood. The authors propose that the increased sensitivity of P. Vivax to oxidative stress might be a factor.G٦PD deficiency increases oxidative stress in red blood cells, which may affect the parasite's survival. This mutation is thought to offer some protection against uncomplicated malaria but not severe cases. It's important to test for G٦PD deficiency (favism) before administering certain anti-malarial drugs, to prevent hemolytic anemia. Although G٦PD deficiency can offer some protection against malaria, it also poses a serious risk when treating malaria with certain drugs. In regions where malaria is endemic, healthcare providers must be cautious when prescribing anti-malarial drugs such as primaquine to G٦PD-deficient patients. To prevent hemolytic disorders caused by these drugs, the use of two different tests to diagnose G٦PD deficiency in men and women is recommended. G٦PD_deficient cells are more vulnerable to human coronavirus infection than G٦PD_normal cells. A study examining G٦PD-DEFICIENT cells incubated with human coronavirus, found that these cells exhibited significantly higher coronavirus viral gene expression and viral particle production.

Results: G٦PD deficiency is a common genetic disorder that affects millions of people worldwide. G٦PD enzyme catalyzes the pentose phosphate pathway, which provides red blood cells with protection against oxidative damage through production of NADPH and glutathione.G٦PD deficiency is caused by mutations in the G٦PD gene, which result in an underproduction of the G٦PD enzyme. This enzyme is critical for the production of reduced NADPH, which in turn helps to produce glutathione, a key antioxidant in red blood cells that protects them from damage caused by oxidative stress.

Conclusion: Its better to do G٦PD-deficient test before start taking medicines . These drugs should be used with caution or avoided in people with G٦PD deficiency, and alternative treatments should be considered. Anti-malarial drug primaquine can trigger favism in G٦PD deficient patients, causing hemolytic anemia. Tafenoquine, an alternative drug, is safer and can be given in a single dose.

Future research into the genetic and environmental factors that contribute to favism may lead to more effective prevention and treatment strategies, and ultimately improve the health and well-being of affected populations. prevention strategies for favism, such as genetic screening or dietary modification.

Keywords: glucose-٦-phosphate dehydrogenase, deficiency, malaria, G٦PD, COVID-١٩

Features of an adrenal cortical carcinoma on CT scan: A case report (Research Paper)

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Introduction: Adrenal lesions can have a wide range of differential diagnosis from benign masses to malignant tumors. Despite the small size of the adrenal glands, they are involved with numerous neoplasms, such as adenoma, myelolipoma, cortical carcinoma, pheochromocytoma, neuroblastoma and many metastases. Along with laboratory tests, radiology plays an essential role in the differentiation and diagnosis of adrenal lesions. Adrenal adenomas are the most common lesions detected on a CT scan. Incidentalomas are lesions that are accidentally found in adrenal imaging, to which the approach is detailed in the American College of Radiology (ACR) guideline, its latest version reviewed in ٢٠١٧. The case presented in this article is a young woman with a mass on the left side of the abdomen originating from the left adrenal gland. The prominent goal of this study is to highlight the different features and the noteworthy appearance of this tumor in CT scan images as well as the importance of laboratory examinations and clinical data in making the final diagnosis.

Methods: The patient was a ٢٧-year-old woman with a firm enlargement in the left side of the abdomen for ٢ months prior to admission. The mass had expanded to the entire left side of the body, and the patient had a past medical history of hirsutism since six years ago. The initial abdominal and pelvic ultrasound revealed a huge heterogeneous mass (approximately ١٥٥ × ١٣٤ mm) in Left Upper Quadrant (LUQ) extending to the entire abdominal cavity. For further evaluation, abdominal and pelvic CT scan was performed.

Results: Spiral abdominopelvic CT scan with and without contrast showed a large left retroperitoneal mass measuring ١١٥ × ١٥٠ × ١٦٠ mm and originating from the left adrenal gland with a heterogeneous density containing necrotic areas and coarse calcification. Significant heterogeneous enhancement was detected after injecting the contrast agent. The compressive effect of the mass on the left gonadal vein (ovarian vein) led to its varicose dilation, as well as significant congestion of the pelvic veins. Numerous collateral vessels developed around the mass suggested the hyper vascular nature of a malignant tumor. The compressive effect of this mass was seen on the body and tail of the pancreas, as well as the transverse colon and the left kidney. Significant contrast-enhanced lymphadenopathies were also seen in the paraaortic space with a maximum short-axis diameter (SAD) of ٨ mm. In triphasic CT scan, several diffuse masses were seen in both lobes of the liver with the largest dimensions of ٢٥ × ٢٨ mm in segment ٥ of the liver, which were isodense with the liver on pre-contrast phase. These masses showed hyperenhancement in the

arterial phase and became relatively hypodense compared to surrounding liver parenchyma in the delayed phase (also called a washout appearance). The above findings were suggestive of hyper vascular liver metastases. After additional examinations and analysis of the laboratory data, The patient underwent an Octreotide scan which revealed normal homogenous tracer activity in liver, spleen and urinary system, without any significant abnormality or avid lesion. Finally, the patient underwent complete left adrenalectomy and left nephrorrhaphy. After a laparotomy incision on the upper part of the abdominal wall, the descending and transverse colon were medialized and the adrenal gland and part of the mesocolon were released. During the surgery, very large collateral vessels were observed and a thrombosed left adrenal vein was detected, which was ligated and cut further into the surgery. Adhesions to the pancreas were slowly released as well. During the adrenal release, the upper pole of the left kidney lacerated and nephrorrhaphy was performed separately, however, the urinary system was preserved. Finally, after the removal of the entire mass, the left kidney's hilar lymph node was dissected and along with the mass resection, the specimens were sent for pathologic examinations. Macroscopic examination of the left adrenal mass resection showed one capsulated brown rubbery mass (١٥ × ١١ × ٥ cm and ١٥١٩ gs), with a soft yellowish heterogeneous appearance and necrotic areas on cut sections. In histopathologic report, the diagnosis of Adrenocortical carcinoma was made. Hilar lymph node of kidney consisted of one piece of unremarkable fibrofatty tissue. (١,٥ × ١ × ٠,٥ cm).

Conclusion: Adrenal cortical carcinoma, also called adrenocortical carcinoma or ACC, is a rare high-grade malignant tumor with the estimated incidence of about ٠,٦ to ١,٦ per million population, annually. This tumor can be hormonally active or inactive and can present in both men and women, while hormonally active tumors are more frequent in women. Cushing's syndrome secondary to elevated cortisol levels is the most common clinical symptom of hormonally active tumors. Other symptoms of hormonally active tumors include virilization or feminization and Conn's syndrome. Hormonally inactive tumors present palpable masses, abdominal pain or metastasis. Although the tumor in this case was also hormonally active in laboratory evaluation, it mainly presented as a palpable abdominal mass. ACCs are usually detected by their large sizes and irregular margins, with necrotic areas, central hemorrhages and variable contrast enhancements observed in their CT scan studies. Calcification has been reported in ٣٠ % of these tumors. Local invasion into the renal vein, IVC, and liver is relatively common. Metastasis to local lymph nodes, lungs, bones, and liver can also occur, with hepatic metastases being predominantly hyper vascular. As Pheochromocytoma can have similar imaging appearances, in order to differentiate the type of tumor, we should use histological, biochemical, and functional tests. In fact, the main diagnostic features of pheochromocytoma are clinical symptoms and laboratory findings. In pheochromocytoma CT scan, large, heterogeneous masses with significant necrotic and cystic areas and considerable enhancement are usually observed. Octreotide (Somatostatin) scans are also positive in about ٧٠ % of pheochromocytomas, which is a helpful finding. Malignant pheochromocytoma usually metastases to the lungs, bones, and liver. However, none of the imaging methods, such as CT, MRI or nuclear studies can definitively differentiate adrenocortical carcinoma from pheochromocytoma. Metomide has recently been introduced as a radiotracer in PET and SPECT studies, which are still

under investigation [۹]. In our case, the initial diagnosis of malignant adrenal lesion was made for the patient based on the CT scan findings. Later on, according to the patient's laboratory examinations (Table ۱) and Octreotide scan, adrenocortical carcinoma was suspected, with the pathology results confirming this diagnosis, which puts emphasis on the role of clinical history, lab data and nuclear imaging for a proper approach to adrenal lesions.

Keywords: Adrenal gland, Malignant lesions, Adrenocortical carcinoma

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Feedforward Neural Networks for investigating the Conformational Changes of Macrobiomolecules (Review)

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Introduction: The future of medicine will certainly involve the integration of artificial intelligence into laboratory methods to improve the accuracy and reliability of experiment data.

Methods: Artificial neural networks (ANNs) are applied in various disciplines such as: cytomorphology, immunohistology, cell differentiation, morphological features, automated flow cytometry, chromosome banding analysis, chromosome classification, analysis of molecular profiles, identification of therapeutic candidates and drug discovery. Moreover, ANNs can make accurate predictions in diseases with complex conditions. Hemoglobin is highly susceptible to conformational changes due to several different factors including hemolysis, ineffective erythropoiesis, iron overload, inflammation and increased production of reactive oxygen species.

Results: ANNs can be trained on datasets containing information about hemoglobin modifications, changes in its absorbance spectrum and its reaction kinetics with specific oxidants. By analyzing this data, ANNs can learn to identify specific patterns or relationships between the modifications of Hb and various biological and pathological outcomes. Our presentation will demonstrate how ANNs can fruitfully develop new methods for studying the structural changes of Hb in healthy and disease conditions.

Conclusion: At the present article, we first discuss about basic concepts of ANNs and focus on bringing this mathematical framework closer to medicine. Then, we introduce the modifications of hemoglobin which can be studied by spectrophotometric analysis at different wavelengths. Finally, we detail how to customize the analysis, structure, and learning of ANNs to better address the conformational changes of hemoglobin.

Keywords: Artificial neural network, conformational changes, hemoglobin, multilayer perceptron.

Fetal chromosomal health in pregnancy and related tests (Review)

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Introduction: The health of the fetus is the main concern of all parents, and chromosomal abnormality in the fetus is one of the main causes of stillbirths and the birth of infants with abnormalities. Since it is possible for every pregnant woman to give birth to a child with birth defects, performing screening tests before birth makes it possible to be aware of chromosomal health. Over the past years, different methods and procedures have been used to identify the chromosomal status of the fetus before birth. These procedures are divided into two groups: invasive and non-invasive. Amniocentesis and chorionic villus sampling (CVS) are invasive procedures, while non-invasive methods include ultrasound, first-trimester screening, second-trimester screening, and non-invasive prenatal testing (NIPT). In ultrasound, performed between weeks ١١ and ١٤ of pregnancy, factors such as nuchal translucency (NT), crown-rump length (CRL), and the presence or absence of a nasal septum are of paramount importance. Typically, the screening of the first trimester of pregnancy is performed between weeks ١١ and ١٣ of pregnancy. The free beta-human chorionic gonadotropin (β-hCG) and pregnancy-associated plasma protein A (PAPP-A), which are produced during pregnancy, are measured in the blood. Finally, through NT ultrasound information and other important factors such as mother's age, diabetes, other children's history of chromosomal abnormalities, twin pregnancy, and smoking, a numerical risk is obtained based on which, we can decide for the next step. In the screening of the second trimester, which is best performed between weeks ١٥ and ١٨ of pregnancy, the levels of four substances of alpha-fetoprotein (AFP), unconjugated oestriol (UE٣), inhibin-A, and β-HCG are measured in the blood, and combined with the factors mentioned in the first trimester, the risk of chromosomal abnormalities is obtained. NIPT, also known as cell-free DNA, can be performed from ١٠ weeks of pregnancy. In this test, which is performed on the mother's blood, parts of the fetal DNA that entered the mother's blood circulation from the placenta are examined. NIPT test has higher sensitivity and specificity in detecting trisomies compared to other pregnancy screening tests. Non-invasiveness and quick response are other advantages of this test, leading to the growing use of this test around the world. However, it also has some drawbacks, causing NIPT not to be still considered as a diagnostic test, and if its results turn out to be positive, administrating such diagnostic tests as aminosynthesis and CVS will be necessary to confirm it. One drawback of NIPT is that it is possible that the DNA circulating in the mother's blood develops from the placenta and not from the fetus, and the

chromosomal abnormality is related to the placenta that does not affect the fetus. Further, it is also likely to get false positive or negative results where the mother has a tumor, has a low fetal fraction in the blood, is pregnant with multiples (more than twins), and is overweight.

Methods: Literature Review

Results: To get information regarding the chromosomal status of the fetus, non-invasive tests such as first-trimester screening, second-trimester screening, or NIPT are used. Among these, NIPT has the highest sensitivity and specificity, but it is not considered a diagnostic test due to due to its limitations. Amniocentesis and CVS are accurate prenatal diagnostic tests, which are invasive and carry the risk of miscarriage

Conclusion: Performing aminosynthesis and CVS tests requires sufficient experience and high expertise in this field. The growing use of NIPT in many countries has reduced the need to use invasive tests (e.g., aminosynthesis and CVS), leading to a decrease in the number of experienced specialists performing diagnostic tests. Therefore, researchers are trying to overcome the disadvantages of the NIPT test by expanding the science and technology so that it can be applied as a non-invasive diagnostic test in the future.

Keywords: Fetal chromosomal, pregnancy, tests, chromosomal abnormality

Field study of the white Rosagranium plant exposed to UV radiation and examination of the effects of ultraviolet (UV) radiation on DNA and the creation of genetic damages such as skin cancers, including basal cell carcinoma and melanoma. (Review)

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Introduction: In the ۲۱st century, human health and environmental impacts have become critical research areas, particularly concerning ultraviolet (UV) radiation from the sun. This radiation can penetrate biological tissues and significantly affect DNA, especially in skin cancers like basal cell carcinoma and melanoma. Basal cell carcinoma, the most common skin cancer, arises mainly from UVB and UVA exposure, leading to severe skin tissue damage. Melanoma, a more dangerous skin cancer, is increasing due to genetic mutations from UV radiation. UV radiation damages DNA by creating unwanted bonds between nitrogenous bases, resulting in genetic mutations that can lead to cancer if not repaired. With the rising incidence of skin cancers, investigating the effects of UV radiation on DNA and its relationship with cancer development is crucial. This research aims to explore the effects of UV radiation on DNA, identify types of genetic damage, investigate DNA repair mechanisms, and analyze the link between these damages and skin cancer occurrence. The findings are expected to enhance understanding of UV radiation dangers and underscore the importance of preventive measures for skin health. Also, in this research, in order to study the application of UV rays on the environment and other organisms, the effects of UV rays on the white Rosagranium plant have been investigated experimentally.

Methods: To investigate the impact of UV radiation on DNA and its role in genetic damage leading to skin cancers like basal cell carcinoma and melanoma, we employed various methods for data collection. This included a literature review of scientific articles in molecular biology, oncology, and dermatology, utilizing databases such as Google Scholar. We also studied specialized books on DNA damage and repair mechanisms. Additionally, field experiments were conducted to observe the effects of UV radiation on the white Rosagranium plant, with data recorded in observation sheets.

Results: Research has shown that ultraviolet (UV) radiation is a major factor in causing genetic damage to the DNA of skin cells. UV radiation is divided into three categories: UVA, UVB, and UVC, each damaging DNA in different ways. UVA penetrates deeply and induces oxidative changes, while UVB primarily causes direct alterations in DNA structure, leading to abnormal bonds and nucleotide damage. UV-induced damage can disrupt DNA repair processes, resulting in genetic mutations that may lead to various types of skin cancers, including basal cell carcinoma and melanoma. Basal cell carcinoma grows slowly and has a lower likelihood of metastasis, whereas melanoma can spread rapidly. To investigate the impact of UV radiation on DNA and genetic damage, various methods such as literature reviews and field experiments were employed. Results indicated that the geranium plant (Geranium) exposed to UV radiation exhibited visible damage and DNA changes. Additionally,

the plant's limited ability to repair DNA damage and decreased activity of repair enzymes were observed in UV-exposed samples. These findings suggest that similar DNA damage in geraniums could contribute to the development of skin cancers in humans. Therefore, preventive measures like using sunscreen and protective clothing are essential to reduce the risks associated with UV exposure.

Conclusion: Numerous studies have shown that ultraviolet (UV)radiation is one of the main factors in causing genetic damage to the DNA of skin cells. This radiation is divided into three categories: UVA, UVB, and UVC, each of which can damage DNA in different ways. UVA penetrates more deeply and can lead to oxidative changes in DNA, while UVB is primarily responsible for causing direct changes in the DNA structure, which can result in the formation of abnormal bonds and nucleotide damage. Damage caused by UV radiation can directly disrupt DNA repair processes. As a result, these damages can lead to genetic mutations that may ultimately result in the development of various types of skin cancers, including basal cell carcinoma and melanoma. Basal cell carcinoma, as the most common type of skin cancer, typically grows slowly and has a lower likelihood of metastasis, whereas melanoma, one of the most dangerous types of skin cancer, can spread rapidly and metastasize to other organs in the body. It is essential to note that not only direct UV radiation but also other environmental and genetic factors play a role in the development of these types of cancers. Therefore, preventing UV-induced damage through the use of sunscreen, appropriate clothing, and avoiding prolonged exposure to sunlight is of great importance. Ultimately, public awareness and education about the dangers of UV radiation and its effects on DNA can help reduce the Incidence of skin cancers. Further research in this area can lead to a better understanding of the molecular and genetic mechanisms involved in the development of these diseases and contribute to the development of more effective prevention and treatment methods.

Keywords: ١. UV ٢. rays ٣. DNA ٤. cancer ٥. damage

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Flavonoid compounds of myristica fragrans extract and male infertility treatment (Research Paper)

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Introduction: Myristica fragrans)Nutmeg) is a fragrant spice obtained from the evergreen nutmeg tree. The nutmeg tree is native to the Pacific Islands and can be found from Asia to Australia. It is mostly used as a spice due to its distinctive spicy and sweet aroma. In traditional medicine, nutmeg is used to increase fertility, regulate blood pressure, improve digestive system function, remove kidney infection, treat rheumatism, etc. Pharmacological studies have shown that myristica seeds have antioxidant properties and help in the treatment of infertility and sperm disorders. According to studies, antioxidants reduce the effect of factors that cause these disorders, i.e., oxidative stress. Its secondary metabolites, including flavonoid compounds, play an important role in the treatment of male infertility.

Methods: In this study, the number of flavonoid compounds was investigated to show the antioxidant properties. At first, extraction was done by hot (Soxhlet) method, and then rotary extraction was done to remove ٧٠٪ alcohol. The obtained extract was reacted with aluminum chloride for ٣٠ minutes. The absorbance of the formed complex was measured at ٤١٥ nm. The flavonoid values in the sample were determined according to the quercetin standard curve.

Results: The amount of this compound in extract is ٢٧,٠٤٣ quercetin (µg).

Conclusion: Considering that the flavonoid properties found in natural products represent the antioxidant capacity. According to the results, it can be said that nutmeg can neutralize the effects of oxidative stress and treat the damage caused by its effects. Therefore, it can be an effective drug for the treatment of sperm disorders and the treatment of male infertility.

Keywords: myristica fragrans, Flavonoid compounds , Antioxidants, Treatment of male infirtility

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FMRI data analysis using SPM software. (Research Paper)

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Introduction: Determining the location and intensity of brain activity in response to a stimulus or task is one of the goals of functional magnetic resonance imaging (fMRI). This study aims to describe classical and Bayesian methods and compare the power of classical and Bayesian models to detect activated regions.

Methods: Before analyzing FMRI data, pre-processing steps are performed on the data. These steps are to reduce all kinds of noise. These steps are motion correction, slice-timing, normalization and smoothing. After preprocessing the fMRI data, three techniques for fMRI analysis have been presented, with the statistical parametric map (SPM) being the most popular. We have also used the Bayesian method for analysis with two different algorithms.

Results: SPM has limitations in preserving data edges and can lead to inaccurate results. Bayesian inference is an alternative approach that uses the posterior probability distribution of activation given the data. Therefore, in this paper, we present data preprocessing, describe classical and Bayesian methods, and compare the power of classical and Bayesian models to detect activated regions. Active voxels are displayed in SPM maps for classical inference and PPM maps for Bayesian inference.

Conclusion: SPM identifies a smaller number of activated voxels than the PPM and SPM becomes more conservative and classical inference is relatively insensitive. The improved VB algorithm method for Bayesian inference detects more activated voxels than classical inference. The results of the Bayesian method with the original VB algorithm are very similar to those of the Bayesian method with the improved VB algorithm. However, the number of activated voxels is greater with the improved VB algorithm method.

Keywords: Bayesian approach, brain, functional Magnetic Resonance Imaging, Statistical Parametric Mapping

Frequency of occurrence, risk factors, and clinical characteristics of COVID-١٩ infection in northeastern of Iran (Research Paper)

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Introduction: Since the first report of COVID-١٩ infection caused by SARS-CoV-٢ in late ٢٠١٩ in China, more than ٧,٦ million confirmed cases of this disease with over ١٤٦ thousand deaths have been reported in Iran. Common symptoms of the disease included fever, cough, muscle pain, and fatigue; some patients experienced gastrointestinal symptoms, while others reported loss of taste or smell. However, it seemed that these symptoms could vary over time depending on the virus strain, underlying diseases, and vaccination status. This cross-sectional study was conducted in Mashhad with the aim of determining the prevalence and risk factors of COVID-١٩ and the clinical symptoms of affected patients.

Methods: From September ٢٠٢٠ to March ٢٠٢٢, using a systematic random sampling method, a random sample of individuals visiting the COVID center laboratory at the academic center for education, culture and research was selected, and the confirmed prevalence of COVID-١٩ infection based on the PCR test results of nasal and throat swab samples was determined. The sample included ٧,٠٥١ individuals, with ٦ to ١٠ percent of visitors in each of the third to sixth waves of the disease. Additionally, data on demographic characteristics, disease symptoms, and underlying conditions were extracted from completed forms at the time of referral to the COVID center and compared for frequency between the two groups with and without COVID-١٩.

Results: In this study, data related to ٤,٤١١ men (٦٢,٦٪) and ٢,٦٤٠ women (٣٧,٤٪) with a mean age of ١٤,٢ ± ٣٧,٨ years were analyzed, and SARS-CoV-٢ infection was confirmed among ٣,١٤٢ cases (٤٤,٦٪). The prevalence of infection in the third, fourth, fifth, and sixth waves of COVID-١٩ was ٤٥,٥٪, ٤٧,٧٪, ٤٨,٩٪, and ٣٠,٤٪, respectively (P<٠,٠٠١). Furthermore, the prevalence of infection was slightly higher in men compared to women, with rates of ٤٦,٤٪ and ٤١,٥٪, respectively (P<٠,٠٠١). Out of ٦,٢٨١ respondents, ٣,٨٥٦ individuals (٦١,٤٪) reported a history of at least one of the symptoms such as fever, chills, sore throat, cough, shortness of breath, and loss of smell or taste. The highest and lowest prevalence of symptomatic cases were observed in the third wave (٦٧,٤٪) and the sixth wave (٤٠,٨٪), respectively. The prevalence of confirmed COVID-١٩ among symptomatic individuals was significantly higher than among those without clinical

symptoms, with rates of ٥٥,٥٪ and ٢٨,٢٪, respectively (P<٠,٠٠١). Additionally, the prevalence of the disease was significantly associated with a history of respiratory and renal disorders (P=٠,٠٠٣, P=٠,٠٢٩).

Conclusion: In this study, three-fifths of the participants reported a history of at least one case of COVID-١٩, yet only ٤٤,٦٪ of them had confirmed infection. The infection rate varied between ٤٥٪ to ٤٩٪ in the third, fourth, and fifth waves but decreased to ٣٠٪ in the sixth wave

Keywords: Covid-١٩ Mashhad Frequency

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From DNA to Disease: The Epigenetic and mRNA Landscape of Cancer Progression (Review)

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Introduction: Cancer, a global health crisis, is increasingly being understood through the lens of epigenetics and mRNA dysregulation. mRNA (messenger RNA) is the conduit of genetic information from DNA to the cellular machinery, influencing crucial processes such as growth, division, and apoptosis. Abnormalities in mRNA expression and stability can lead to cancer by activating oncogenes or suppressing tumor suppressor genes. The potential impact of understanding how epigenetic modifications influence mRNA pathways is immense, offering new avenues for cancer prevention and treatment. This potential should inspire and motivate us to continue our research.

Methods: This review analyzes studies from ٢٠١٦ to ٢٠٢٤ from databases such as PubMed, Google Scholar, and ScienceDirect. It focuses on how mRNA dysregulation, driven by epigenetic changes, contributes to cancer progression. The investigation covers how alterations in mRNA expression, stability, and translation affect key cellular pathways involved in tumor development alongside therapeutic strategies targeting these processes.

Results: Dysregulated mRNA expression and epigenetic alterations synergistically promote cancer progression. For instance, increased mRNA levels of Cyclin D١, driven by histone acetylation, can lead to uncontrolled cell division, a hallmark of cancer. Conversely, reduced stability of tumor suppressor mRNAs, such as p١٦INK٤a, allows cancer cells to evade apoptosis. Hypermethylation of the p١٦INK٤a promoter silences its expression, facilitating tumor growth. Epigenetic mechanisms significantly influence mRNA dynamics. DNA methylation can silence tumor suppressor genes, reducing their mRNA production. For example, the hypermethylation of p١٦INK٤a leads to its loss of function, contributing to unchecked cell proliferation. Histone modifications may open or close chromatin, either facilitating or hindering the transcription of critical genes. Additionally, non-coding RNAs, including microRNAs and long non-coding RNAs (lncRNAs), play crucial roles in regulating mRNA stability and translation. Dysregulated microRNAs, such as miR-٢١, can destabilize tumor-suppressing mRNAs like PTEN and PDCD٤, enhancing cell survival and contributing to cancer progression. On the other hand, lncRNAs like HOTAIR can stabilize oncogenic mRNAs, such as VEGF, promoting tumor growth and metastasis. Emerging studies suggest that targeting mRNA stability and translation—through pharmacological agents or lifestyle interventions like diet and exercise—could reduce cancer risk. For instance, epigenetic therapies, including histone deacetylase inhibitors and DNA methyltransferase inhibitors, have shown promise in restoring standard mRNA expression patterns and potentially limiting cancer proliferation. These interventions may correct dysregulated pathways, offering a novel cancer prevention and treatment approach.

Conclusion: mRNA dysregulation, influenced by epigenetic factors, is pivotal in cancer progression. Cancer cells can circumvent normal growth controls by altering mRNA expression and stability. The interplay between epigenetics and mRNA presents promising therapeutic avenues, emphasizing the need for further research. Targeting mRNA pathways alongside epigenetic modifications could lead to innovative strategies for cancer prevention, early detection, and treatment, ultimately improving patient outcomes.

Keywords: Epigenetics, mRNA, Cancer, tumor

Functional dopaminergic neurons derived from humanchorionic mesenchymal stem cells ameliorate striatalatrophy and improve behavioral deficits in Parkinsonianrat model (Research Paper)

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Introduction: Human chorionic mesenchymal stem cells (HCMSCs) have been recognized as a desirable choice for cell therapy in neurological disorders such as Parkinson's disease (PD). Due to invaluable features of HCMSCs including their immunomodulatory and immunosuppressive properties, easily accessible and less differentiated compared to other types of MSCs, HCMSCs provide a great hope for regenerative medicine.

Methods: Initially, HCMSCs were isolated and underwent a ۲-week DA differentiation, followed by in vitro assessments, using quantitative real-time polymerase chain reaction, immunocytochemistry, patch clamp recording, and high-performance liquid chromatography. In addition, the effects of implanted HCMSCs-derived DA neuron-like cells on the motor coordination along with stereological alterations in the striatum of rat models of PD were investigated.

Results: The results showed that under neuronal induction, HCMSCs revealed neuron-like morphology, and expressed neuronal and DA-specific genes, together with DA release. Furthermore, transplantation of HCMSCs-derived DA neurons into the striatum of rat models of PD, augmented performance. Besides, it prevented reduction of striatal volume, dendritic length, and the total number of neurons, coupled with a diminished level of cleaved caspase-۳.

Conclusion: Altogether, these findings suggest that HCMSCs could be considered as an attractive strategy for cell-based therapies in PD.

Keywords: Chorion, dopaminergic neuron, mesenchymal stem cells, neurodifferentiation, Parkinson'sdisease

fungal infections; Threats and risks (Review)

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Introduction: Fungal infections represent an example of such overlooked emerging diseases, accounting for approximately ١,٧ million deaths annually. To put these numbers in perspective, tuberculosis is reported to cause ١,٥ million deaths/year and malaria around ٤٠٥,٠٠٠ deaths/year. The medical impact of Fungal infections, however, goes far beyond these devastating death rates: Fungal infections affect more than one billion people each year, of which more than ١٥٠ million cases account for severe and life-threatening Fungal infections. Importantly, the number of cases continues to constantly rise. Thus, Fungal infections are increasingly becoming a global health problem that is associated with high morbidity and mortality rates as well as with devastating socioeconomic consequences.

Methods: A crucial factor that contributes to the rising number of Fungal infections is the drastic increase of the at risk population that is specifically vulnerable to Fungal infections, including elderly people, critically ill or immunocompromised patients. The overall lifespan increase due to the achievements of modern medicine and social advancements, the growing numbers of cancer, chronic lung disease, AIDS and transplantation patients with the concomitant subscription of immune modulating drugs as well as the excessive antibiotic use compose risk factors and niches for the development of Fungal infections. Chemotherapy and radiation are important treatments for people with cancer. While they destroy cancer cells, they can also lower white blood cell counts. The immune system relies on white blood cells to fight infections. The type of fungal infection and level of risk can depend on the type of cancer and type chemotherapy treatment.

Results: People who receive organ transplants need to take anti-rejection medications. These medications work by weakening the immune system so it does not attack the new organ. Some types of transplants may increase risk more than others, such as small bowel, lung, liver, and heart transplants. Stem cell transplants increase risk for fungal infections because they destroy and rebuild the immune system. People can have stem cell transplants using their own cells or cells from a donor. People who receive donor stem cells are at higher risk for infections. Like people who have organ transplants, donor stem cell recipients need to take anti-rejection medications. Stem cell recipients are also at risk for Graft-versus-host disease (GvHD). GvHD is a condition where transplanted stem cells attack the hosts' body.

Conclusion: Furthermore, the increasing usage of medical devices such as catheters or cardiac valves leads to a higher risk for the formation of biofilms. Certain treatments and medications can also increase risk, such as Long-term hospital stays, Stem cell transplants, Organ transplants, Corticosteroids. Different fungal diseases may have more specific risk factors. Some diseases have risk factors unrelated to the immune system like race, age, and pregnancy. Health equity factors like

where a person lives, their occupation, and access to care also impact fungal disease risks. In immunocompromised patients, infections can quickly become severe, resulting in high morbidity and mortality. Despite these concerns, fungal infections have often been neglected in public health consider¬ations, and research funding remains substantially lower com¬pared to pathogens with similar mortality. There continue to be deficits in widespread clinical awareness and standard¬ized guidelines for the diagnosis and treatment of fungal dis¬ease. Combined with delays in diagnosis due to the nonspecific symptoms of severe disease, fungal infections are chronically underdiagnosed, with a high degree of variability in the prog¬nosis of affected patients.

Keywords: Fungal Infection, Risk factors, Immunocompromised Patients

Gastrointestinal Infections Induced by Escherichia coli (Review)

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Introduction: Escherichia coli (E. coli) is a gram-negative bacterium belonging to the Enterobacteriaceae family and is a natural inhabitant of the gut microbiota in humans and animals. Unlike many other bacterial species, E. coli can thrive in oxygen-rich environments that may be detrimental to other microorganisms. While the majority of E. coli strains are benign, certain pathogenic variants can cause severe foodborne illnesses. Gastrointestinal infections attributed to E. coli rank among the foremost causes of infectious diseases globally, often leading to serious gastrointestinal manifestations such as diarrhea, abdominal discomfort, and, in severe cases, life-threatening complications. Notable pathogenic strains include E. coli O۱۵۷:H۷, enterotoxigenic E. coli (ETEC), enteropathogenic E. coli (EPEC), Shiga toxin-producing E. coli (STEC), and enterohemorrhagic E. coli (EHEC). This study aims to explore the pathogenic mechanisms, virulence factors, clinical manifestations, diagnostic techniques, and preventive measures associated with gastrointestinal infections caused by this bacterium.

Methods: To conduct this study, reputable scientific databases, including PubMed and Google Scholar, were utilized to collect pertinent information regarding gastrointestinal infections caused by E. coli. Keywords such as "E. coli gastrointestinal infection," "human bacterial gastroenteritis," "diarrheagenic E. coli," and "E. coli pathotypes" were employed in the search. The selected literature focused on the pathogenic mechanisms of E. coli strains that cause gastroenteritis, diagnostic laboratory methods, and clinical symptomatology. The information obtained was systematically analyzed and summarized. In the referenced studies, samples were cultured on various growth media, including MacConkey Agar, and subsequently subjected to biochemical testing (IMVIC). Positive E. coli isolates underwent molecular analysis through PCR and electrophoresis for pathotype identification.

Results: The findings indicate that gastroenteritis caused by E. coli can result from the consumption of contaminated food and water, interpersonal transmission, or contact with infected animals. Inadequate personal and environmental hygiene significantly elevates the risk of these infections, representing a serious public health concern due to the potential for inflammation of the gastrointestinal tract. Accurate diagnosis of E. coli-induced gastrointestinal infections relies on the precise identification of bacterial strains and the virulence genes associated with their respective pathotypes. For instance, the EPEC pathotype is distinguished by the presence of the intimin gene (eae), while STEC is characterized by the stx۱ and stx۲ virulence genes. EHEC encompasses both intimin and Shiga toxin genes. Based on these characteristics, specific primers targeting these virulence genes have been developed for pathotype identification through PCR testing. The pathogenicity of virulent E. coli strains, such as EPEC and ETEC, begins with their adhesion to the intestinal mucosal surface via pili or fimbriae. Toxins produced by ETEC, including heat-stable and

heat-labile toxins, increase the levels of cyclic AMP or GMP in epithelial cells, resulting in fluid and electrolyte loss and subsequently causing watery diarrhea. In contrast, EPEC facilitates the uptake of proteins into host cells, leading to adherence lesions and damaging microvilli, thus disrupting nutrient absorption. Furthermore, Shiga toxin produced by STEC inflicts damage on intestinal cells and stimulates immune responses, which can manifest as diarrhea, vomiting, fever, abdominal pain, and dehydration. Symptoms associated with E. coli-related gastroenteritis include fever, vomiting, bloody diarrhea, and intense abdominal cramps, with severe cases potentially leading to life-threatening complications. Prompt and appropriate medical intervention is essential.

Conclusion: Gastrointestinal infections caused by E. coli pose a significant threat to public health. Given the increasing incidence of these infections and the rising antibiotic resistance observed, there is an urgent need for early diagnosis, appropriate treatment, and the use of targeted antibiotics based on sensitivity testing (disk diffusion), in addition to effective preventive strategies. Implementing these measures is crucial to minimize the complications associated with this disease and to protect public health.

Keywords: Gastroenteritis, Escherichia coli, diarrhea, Escherichia pathototypes

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Gene expression analysis and microRNA prediction in gastric cancer using RNA sequencing data

(Research Paper)

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Introduction: Gastric cancer is the fourth leading cause of cancer-related deaths worldwide. Despite significant advances in medical science, a definitive treatment for this disease remains elusive, posing a major challenge for healthcare professionals and researchers. MicroRNAs (miRNAs), which play crucial roles in regulating gene expression, have gained considerable attention in recent years. By binding to target mRNAs, miRNAs can suppress gene expression and regulate critical cellular processes such as apoptosis, differentiation, and proliferation. Various studies have shown that some miRNAs exhibit oncogenic properties, promoting cancer progression, while others function as tumor suppressors, inhibiting cancer development. Given the critical role of specific genes involved in gastric cancer, this study aims to propose miRNAs that could potentially suppress one such gene, offering a promising strategy for improving disease management.

Methods: The study utilized the GSE١٢٢٧٩٦ dataset from the GEO database, which includes RNA sequencing data from three gastric cancer tissue samples and three adjacent non-cancerous tissues. Differential gene expression analysis was conducted using the GEO٢R tool, identifying differentially expressed genes (DEGs). The identified DEGs were further analyzed using the STRING database to explore protein-protein interactions (PPI), ultimately revealing key genes involved in gastric cancer. One gene was targeted for further analysis. To predict miRNAs with the potential to suppress it, we employed the miRDB database.

Results: Our analysis identified ٢٠,١١٣ DEGs, of which ١,٦٢٠ were upregulated and ١,٤٠٥ were downregulated. Through the PPI analysis, FN١ was identified as one of the key upregulated genes involved in gastric cancer. Using miRDB, ١٣٣ miRNAs were predicted to target FN١, with scores ranging from ٩٧ to ٥٠. The highest scores were assigned to hsa-miR-١٤٤-٣p and hsa-miR-٣١٢٤-٣p.

Conclusion: Gene expression profile analysis based on RNA sequencing data provides valuable insights into the molecular mechanisms underlying gastric cancer and can aid in the development of targeted therapies. This study suggests that the proposed miRNAs may have inhibitory effects on the identified gene, which acts as one of the main genes in gastric cancer. This approach could be considered as one possible strategy for managing the condition, but it is important to note that ultimate success will require further research and clinical validation.

Keywords: gastric cancer, RNA sequencing, miRNA

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Gene Expression of Long Non-Coding RNAs; EGFR-AS١, EGFR-٢٠٨, and EGFR-٢٠٩ in Triple-negative breast cancer (Research Paper)

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Introduction: Triple-negative breast cancer (TNBC) is a type of malignant breast cancers which have a poor prognosis and a high risk of mortality. Remarkably, there is growing evidence demonstrating that lncRNAs play an important role in regulating cancer-related mechanisms and metastasis. Then, they can be used as biomarkers for monitoring the disease. Among different lncRNAs, epidermal growth factor receptor-antisense RNA ١ (EGFR-AS١) has been under great attention for its abnormal expression in cancers with epithelial origin. Consequently, here, we aimed to investigate the expression of EGFR-AS١, and its close family of lncRNAs means EGFR-٢٠٨, and EGFR-٢٠٩ in different subtypes of breast tumors compared to adjacent tissues.

Methods: Breast tumor specimens and adjacent normal tissue were obtained from the bariatric surgery center of Rasoul Akram Hospital, Tehran, Iran. Total RNA was extracted using the Tripure isolation reagent kit, according to the manufacturer's protocol. RNA purity was measured by evaluating the ratio of absorbance at ٢٦٠ nm to ٢٨٠ nm by a nanodroplet and its integrity using agarose gel and staining with ethidium bromide. complementary DNA (cDNA) synthesis was performed on ١٠٠٠ ng of RNA using a cDNA synthesis kit, according to the manufacturer's protocol. Real-time PCR was conducted to investigate the mRNA expression of the above-mentioned genes in all participants. Quantitative Real-time PCR was performed using SYBR Green and LightCycler ٩٦ real-time PCR system , based on the manufacturer's protocol. Fold changes of lncRNAs gene expression of case samples relative to the controls were calculated by the ٢-ΔCt method. B٢M was used as the internal gene for the study of lncRNAs. Thus, the ΔCt value of each sample was normalized to the value of B٢M.

Results: The gene expression of EGFR-AS١, EGFR-٢٠٨, and EGFR-٢٠٩ were lower in all three groups compared to adjacent tissues. There was a significant decrease (P<٠,٠٥) in the gene expression of EGFR-AS١ and EGFR-٢٠٩ in the triple-positive subtype compared to adjacent tissues. There was also a significant decrease (P<٠,٠٠١) in the gene expression of EGFR-AS١ in the triple-negative group compared to the triple-positive group.

Conclusion: This study indicates the likely diagnostic value of EGFR-AS١, EGFR-٢٠٨, and EGFR-٢٠٩ for TNBC and provides new insights into the control strategies for TNBC. However, further studies are needed to validate this concept.

Keywords: Long non-coding RNAs (lncRNAs), Breast cancer, Triple-negative breast cancer (TNBC), EGFR

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Gene therapy as a pivotal approach in Aging (Review)

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Introduction: Aging is a natural process characterized by the gradual deterioration of physiological functions, and it serves as a major risk factor for conditions such as neurodegenerative disorders, cardiovascular diseases, metabolic syndromes, and malignancies. The manifestations of aging, which occur at both cellular and molecular levels, are universally observed across organisms. These include reduced genomic stability, telomere attrition, mitochondrial dysfunction, epigenetic alterations, and depletion or dysfunction of stem cells. Numerous factors contribute to the aging process, including the activation of cellular senescence pathways and the influence of genetic variations, as well as epigenetic modifications. These elements can affect the rate at which aging occurs. While some genes are linked to extended longevity, others may heighten susceptibility to age-related diseases. Epigenetic changes, such as DNA methylation and histone modifications, play a crucial role in altering gene expression patterns, thereby contributing to aging. In contrast, gene therapy offers potential for curing age-related diseases by targeting key markers of aging. Gene therapy, originally developed to address genetic disorders, involves either the introduction of new DNA into specific cells or the correction of faulty DNA. Promising strategies to rejuvenate the body include gene and cell therapies, often in combination with pharmacological interventions. These methods aim to rejuvenate senescent cells, eliminate dysfunctional senescent cells, and inhibit signaling pathways that contribute to cellular aging. The aim of this review study is to introduce gene therapy as a pivotal approach in aging.

Methods: A total of twenty relevant articles exploring the role of gene therapy as a pivotal approach in aging, were identified through searches on PubMed, Google Scholar databases using predefined keywords. These articles were subsequently selected for review and analysis.

Results: Studies have shown that telomerase activators (TA) can increase TERT gene expression, offering potential therapeutic benefits. For example, in a Parkinson's disease mouse model, TA-٦٥ improved TERT expression, motor function, and autophagy. Additionally, CRISPR technology allows precise regulation of endogenous TERT expression. In most normal somatic cells, telomerase is largely inactive, whereas it becomes active in approximately ٩٠٪ of cancer cells. Consequently, therapeutic strategies focus on reactivating telomerase in normal somatic cells while suppressing its activity in cancerous cells. However, these approaches require more stringent targeting mechanisms

to ensure precision in therapeutic design. Gene therapy targeting the Klotho gene presents a promising approach in anti-aging treatments. In a study by Chen et al., the CRISPR-dCas٩ complex was used to activate the Klotho promoter, leading to elevated Klotho expression at both gene and protein levels in human neuronal and kidney cell lines. These findings suggest potential therapeutic applications for improving cognitive function and treating age-related demyelinating and neurodegenerative disorders. Macip et al. demonstrated that the systemic delivery of adeno-associated viruses encoding an inducible OSK system in ١٢٤-week-old male mice extended the median remaining lifespan by ١٠٩٪ compared to wild-type controls. This treatment also significantly improved health parameters, including frailty scores, indicating an enhancement in both healthspan and lifespan. Rurik et al. developed a transient antifibrotic chimeric antigen receptor (CAR) structure encoded by modified mRNA, which was delivered via CD٥-targeted lipid nanoparticles (LNPs) to generate CAR T-cells in vivo. This approach successfully reduced fibrosis and improved cardiac function in a mouse model experiencing increased cardiac afterload. Ozes et al. demonstrated the efficacy of AAV١.NT-٣ gene therapy in treating sarcopenia and age-related peripheral nerve hypomyelination in ٢-year-old C٥٧BL/٦ mice, a model of natural aging. Six months post-treatment, NT-٣ led to significant improvements in neuromuscular function, muscle physiology, and reduced age-related changes such as kyphosis, dermatitis, and alopecia.

Conclusion: The rise in life expectancy is a global phenomenon, primarily attributed to improved sanitation, medical advancements, enhanced nutrition, and safer living environments, which are reinforced by social interactions. The aging population presents a growing societal challenge, particularly in developed nations where the elderly demographic is increasing annually. Gene therapies, particularly those targeting aging, offer promising prospects for addressing age-related diseases. However, not all genes associated with aging are suitable targets for such therapies. With the full identification of genes related to aging and increased longevity, and the personalized application of gene therapy for each individual, we will witness the opening of new doors in the field of gene therapy and lifespan extension.

Keywords: Aging, CRISPR, Gene therapy, Longevity

Gene Therapy In The Embryonic Period (Review)

Aida Parsa,[1,*]

1. -

Introduction: Gene therapy, a revolutionary medical approach, aims to treat or prevent diseases by altering a person's genetic makeup. This involves introducing genetic material into cells to compensate for abnormal genes or to produce a therapeutic protein. While gene therapy has shown promise in treating various diseases, its application to the embryonic stage represents a frontier of scientific exploration and ethical contemplation. The history of gene therapy dates back to the early ۱۹۷۰s when scientists first conceived the idea of using genes to treat diseases. Since then, the field has witnessed significant advancements, with successful clinical trials for conditions such as certain types of cancer and inherited immune deficiencies. However, most gene therapy treatments have focused on somatic cells, affecting only the individual being treated. Embryonic gene editing, a subset of gene therapy, takes this concept a step further. It involves modifying genes in a fertilized egg before it develops into an embryo. This technique holds the potential to correct genetic defects before birth, preventing the onset of inherited diseases. However, it also raises profound ethical questions about the manipulation of human life at its earliest stages. The intersection of gene therapy and embryonic development presents a landscape filled with both immense hope and complex challenges. This article delves into the scientific foundations, ethical implications, and potential societal impacts of embryonic gene editing.

Methods: Genetics, Gene Editing, and Embryonic Development: Genetics is the study of genes, heredity, and variation in living organisms. Genes are segments of DNA that contain instructions for building and maintaining an organism. They are passed down from parent to offspring, determining traits such as eye color, height, and susceptibility to certain diseases. Gene editing is a technology that allows scientists to change an organism's DNA. One of the most precise and efficient methods is CRISPR-Cas۹. This system, adapted from bacteria, utilizes an enzyme called Cas۹ to cut DNA at specific locations. Guide RNA molecules direct Cas۹ to the desired DNA sequence. Once cut, scientists can remove, add, or alter genetic material. Embryonic Development: Embryonic development is the process by which a fertilized egg, or zygote, transforms into a complex organism. This intricate journey involves cell division, differentiation, and growth. -Fertilization: The union of sperm and egg creates a zygote, containing genetic information from both parents. -Cleavage: The zygote undergoes rapid cell division, forming a blastocyst. -Gastrulation: The blastocyst transforms into a three-layered embryo, with each layer giving rise to different tissues and organs. -Organogenesis: The formation of specific organs and body systems begins. Gene Therapy and Embryonic Defects: Gene therapy holds the potential to correct genetic defects before birth. By introducing functional genes into an embryo, scientists aim to prevent or mitigate the development of inherited diseases. Identifying the Defective Gene: Pinpointing the specific gene responsible for a genetic disorder is a complex and often lengthy process. Researchers utilize a combination of techniques to achieve this: -Genetic Linkage Analysis: By studying family pedigrees, scientists can

identify which genes are inherited together with the disease. -Genome-wide Association Studies (GWAS): Comparing the DNA of large groups of people with and without the disease can help identify genetic variations linked to the condition. -Exome Sequencing: Focusing on the protein-coding regions of the genome can accelerate the search for disease-causing mutations. -Whole-Genome Sequencing: Analyzing an individual's entire DNA sequence provides a comprehensive view of their genetic makeup, aiding in gene identification. Once a gene is suspected, further functional studies are conducted to confirm its role in the disease. Designing a Corrective Gene: Creating a functional replacement gene is a delicate process involving several steps: -Gene Cloning:Isolating the normal gene from a healthy individual and creating multiple copies for manipulation. -Gene Optimization:Modifying the gene to ensure efficient expression in the target cells and to avoid unintended consequences. -Vector Design:Selecting or engineering a suitable delivery system, such as a virus or lipid nanoparticle, to transport the gene into the embryo. -Safety Considerations:Rigorous testing is essential to eliminate any potential harmful effects of the modified gene. The design of the corrective gene must be precise to avoid disrupting other genes or causing unintended consequences. Delivery to the Embryo: Delivering a corrective gene to an embryo is a major hurdle in embryonic gene therapy. Current methods face significant challenges: -Viral Vectors: These modified viruses can efficiently deliver genes but carry risks of immune responses, insertional mutagenesis (causing cancer), and limited cargo capacity. -Non-viral Delivery: Methods like lipid nanoparticles or electroporation offer alternatives but often have lower efficiency. -Timing and Precision: Delivering the gene at the correct stage of embryonic development and targeting specific cells is crucial, but challenging to achieve. Overcoming these challenges requires innovative approaches and further research. Precise Editing: CRISPR-Cas^{9} has revolutionized gene editing by offering unprecedented precision. However, challenges remain: -Off-Target Effects: The Cas^{9} enzyme can sometimes cut DNA at unintended locations, leading to unwanted mutations. -Delivery Efficiency: Efficient and safe delivery of the CRISPR-Cas^{9} system to embryos is still under development. -Complex Genetic Disorders: Many diseases are caused by multiple genes or complex gene interactions, making gene editing more challenging. Continuous refinement of CRISPR-Cas^{9} and the development of alternative gene editing tools are essential for improving precision and safety.

Results: Ethical Considerations of Embryonic Gene Editing: -Modifying the Human Germline: The most profound ethical implication of embryonic gene editing is the modification of the human germline. Unlike somatic gene therapy, which affects only the individual, germline modifications are inherited by subsequent generations. This raises questions about the extent to which humans should control the genetic makeup of future generations. Altering the genetic blueprint of humanity is a step with irreversible consequences, and it is unclear whether society is prepared to accept such a profound change. -Designer Babies and Eugenics: The prospect of "designer babies" has ignited intense ethical debate. With the ability to edit genes, parents could potentially select desirable traits such as intelligence, physical appearance, or athletic ability. This raises concerns about creating a genetic elite and exacerbating existing social inequalities. Furthermore, the concept of eugenics, the practice of selective breeding to improve the human population, echoes through these discussions.

While modern genetic engineering differs from historical eugenics, the potential for misuse and abuse is a significant ethical challenge. -Long-Term Consequences: The long-term consequences of embryonic gene editing are unknown. Even if initial results are positive, unintended effects might emerge in later generations. For example, altering one gene could have unexpected consequences for other genes or biological systems. Additionally, the potential ecological impact of introducing genetically modified humans into the population is uncertain. -Ethical Perspectives: Ethical perspectives on embryonic gene editing vary widely. -Religious perspectives: Many religions have moral codes that address human creation and modification. Some views consider the embryo as a person from conception, prohibiting any intervention. Others may permit gene editing for therapeutic purposes but not for enhancement. -Philosophical perspectives: Various ethical frameworks offer different approaches. Utilitarianism focuses on maximizing overall happiness, and might weigh the potential benefits of preventing suffering against the risks. Deontology emphasizes duties and rights, and might prioritize the inherent dignity of the human embryo. Virtue ethics emphasizes character development, and would consider the intentions and motivations behind gene editing. -Societal perspectives: Public opinion on embryonic gene editing is complex and often influenced by factors such as cultural background, education, and personal experiences. Ultimately, the ethical acceptability of embryonic gene editing will depend on careful consideration of these diverse perspectives and the development of robust regulatory frameworks. Advancements, Challenges, and Clinical Trials in Embryonic Gene Therapy: Latest Advancements in Embryonic Gene Therapy Research: While still in its infancy, embryonic gene therapy has seen significant strides in recent years. Key advancements include: -Improved gene editing tools: The CRISPR-Cas^{9} system has been refined, increasing precision and reducing off-target effects. -Enhanced delivery systems: Researchers are developing more efficient and safer methods to introduce genetic material into embryos. -Deeper understanding of embryology: Advances in our knowledge of embryonic development provide a better foundation for targeted gene interventions. -Ethical discussions: Ongoing dialogue about the ethical implications of embryonic gene editing is shaping the field's trajectory. Ongoing Clinical Trials and Their Objectives: It's important to note that, as of now, there are no approved clinical trials for embryonic gene therapy in humans due to significant ethical and technical challenges. However, research is actively progressing in animal models. The primary objectives of these studies are: -Safety assessment: Evaluating the potential side effects and long-term consequences of gene editing in embryos. -Efficacy evaluation: Determining the effectiveness of gene therapy in correcting genetic defects. -Delivery system optimization: Testing different methods of gene delivery to improve efficiency and safety. -Ethical framework development: Establishing guidelines and regulations for future human trials. Key Challenges and Limitations: Despite promising advancements, embryonic gene therapy faces substantial hurdles: -Technical challenges: Achieving precise and efficient gene editing while avoiding off-target effects remains a significant challenge. -Delivery limitations: Developing safe and effective methods to deliver genetic material to embryos is ongoing. -Long-term consequences: The potential long-term effects of gene editing on individuals and future generations are unknown. -Ethical considerations: The profound ethical implications of modifying the human germline continue to be a major obstacle. -Regulatory hurdles: Establishing a robust regulatory framework for embryonic gene therapy is complex and

time-consuming. Addressing these challenges requires continued research, interdisciplinary collaboration, and open dialogue among scientists, ethicists, policymakers, and the public. The Global Regulatory Landscape for Embryonic Gene Editing: Global Regulatory Landscape: The global regulatory landscape for embryonic gene editing is a complex patchwork of varying national laws, guidelines, and bans. While some countries have outright prohibited research and clinical applications, others have adopted more permissive stances, often with stringent oversight. The rapid advancement of gene editing technology has outpaced regulatory frameworks, leading to a gap between scientific progress and legal and ethical boundaries. This disparity has created challenges for researchers seeking to conduct ethical and responsible research. International Guidelines and Their Impact: Several international bodies and scientific organizations have developed guidelines for embryonic gene editing. These guidelines aim to provide a global framework for responsible research while recognizing the diverse ethical and cultural perspectives of different countries. -The International Summit on Human Gene Editing: Held in ٢٠١٥ and ٢٠١٨, this summit brought together scientists, ethicists, and policymakers to discuss the implications of human genome editing. It called for a cautious approach, emphasizing the need for careful consideration of safety and ethical issues before proceeding with clinical applications of germline editing. -The World Health Organization (WHO): The WHO has established an expert advisory committee on human genome editing to develop global standards and guidelines. Its focus includes surveillance, monitoring, and fostering international cooperation. -Other organizations: Groups like the National Academies of Sciences, Engineering, and Medicine (NASEM) in the United States and the European Commission have also issued reports and recommendations on human genome editing. While these guidelines provide valuable guidance, their impact on research varies widely. Some countries have incorporated these recommendations into their national regulations, while others have taken a more independent approach. Role of Government and Ethical Committees: Governments play a crucial role in overseeing research on embryonic gene editing through regulatory agencies and legislative bodies. These entities are responsible for: -Licensing and permitting: Granting or denying permission for research projects. -Setting ethical standards: Developing guidelines and regulations to ensure ethical conduct. -Oversight and monitoring: Conducting regular inspections and reviews of research activities. -Enforcement: Imposing penalties for violations of regulations. Ethical committees, often composed of scientists, ethicists, and legal experts, provide independent review and approval of research protocols. They play a vital role in ensuring that research is conducted ethically and responsibly. The relationship between government and ethical committees varies across countries. In some cases, ethical committees have significant authority, while in others, their role is primarily advisory. It is essential to strike a balance between promoting scientific innovation and protecting human health and dignity. This requires a collaborative effort between scientists, ethicists, policymakers, and the public. Potential Benefits, Economic Implications, and Public Opinion: Embryonic gene therapy holds the promise of significant benefits for individuals and society: -Prevention of genetic diseases: By correcting defective genes before birth, it could prevent a multitude of inherited disorders, such as cystic fibrosis, Huntington's disease, and sickle cell anemia. -Improved quality of life: Individuals born without genetic diseases would experience better health outcomes and increased life expectancy. -Reduced healthcare costs: Preventing genetic diseases

could significantly lower healthcare expenditures associated with treatment, care, and lost productivity. -Advancement of scientific knowledge: Research into embryonic gene therapy can lead to breakthroughs in understanding human genetics and disease mechanisms. Potential Economic Implications: The economic implications of embryonic gene therapy are complex and far-reaching: -Healthcare costs: While the technology may initially be expensive, widespread adoption could lead to long-term cost savings by preventing costly treatments for genetic diseases. -Pharmaceutical industry: The development of gene therapies could create new markets and drive economic growth for the pharmaceutical industry. -Biotechnology sector: Advancements in gene editing technology could spur innovation and job creation in the biotechnology sector. -Ethical considerations: The potential for misuse of the technology, such as creating genetic inequalities, could have negative economic consequences. Public Opinion and Attitudes: Public opinion on embryonic gene editing is diverse and influenced by various factors, including cultural, religious, and ethical beliefs. -Support for therapeutic applications: Many people support the use of gene editing to prevent or treat serious genetic diseases. -Concerns about enhancement: There is significant opposition to the use of gene editing for enhancing traits such as intelligence or physical appearance. -Trust in science: Public trust in scientific institutions and researchers plays a crucial role in shaping attitudes towards the technology. -Ethical considerations: Concerns about the ethical implications of modifying the human germline can influence public opinion. Understanding public attitudes is essential for developing effective communication strategies and building trust in the technology.

Conclusion: Embryonic gene editing stands at the precipice of a new era in medicine, offering both immense potential and profound challenges. While the scientific advancements in gene editing hold the promise of eradicating devastating genetic diseases, the ethical implications of modifying the human germline are far-reaching and complex. Balancing the pursuit of scientific knowledge with societal values is crucial. A comprehensive understanding of the technology, coupled with robust ethical frameworks and international cooperation, is essential for navigating this complex landscape. As research progresses, it is imperative to engage in open and inclusive dialogue with the public to build trust and ensure that the development and application of embryonic gene editing align with societal values. Ultimately, the responsible and ethical use of this powerful technology will determine its legacy for future generations.

Keywords: embryonic gene editing, gene therapy, CRISPR-Cas^{9}, germline modification, ethics

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Genetic Alterations in Thyroid Cancers (Review)

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Introduction: Cancer is the uncontrolled growth of cells. Today, about ۳,۲٪ of people have thyroid cancer. The thyroid is a butterfly-shaped gland located in front of the neck. Thyroid hormones are involved in body metabolism. There are different types of thyroid cancer. Papillary thyroid cancer (PTC) and follicular thyroid cancer (FTC) are the most common types of this cancer. PTC and FTC arise from follicular epithelial cells. Thyroid cancer is caused by various genetic mutations in the DNA. Defective RET gene and epigenetics changes are among the factors that can be mentioned. Epigenetics includes DNA methylation, histone modification, and RNA methylation without changing the sequence of DNA nucleotides, which causes a change in the regulation of gene expression. In this article, we study the role of different genes in the occurrence and progression of thyroid cancer.

Methods: A comprehensive search was conducted in MEDLINE, EMBASE, Scopus, and other databases to discover published articles related to genetic alterations in thyroid cancers with search terms included, genetic alterations, thyroid cancers, diagnosis, prognosis, and related keywords.

Results: One of the important genes in thyroid cancer is the BRAF gene. The point of activating substitutions (mutations) in this gene activates the MAPK pathway and causes abnormal growth of cells. These point substitutions are mostly seen in papillary thyroid cancer (Papillary Thyroid Cancer) or PTC. RET gene (rs۷۷۷۰۹۲۸۶) also plays an important role in thyroid cancer. The most common RET M۹۱۸T mutation, especially in medullary thyroid cancer, leads to the activation of signaling pathways that lead to abnormal cell growth and increased thyroid production. Mutations in other NTRK, MEK, TP۵۳, and RAS genes are other examples of mutations at the DNA level in this cancer. DNA methylation occurs when DNA methyltransferase (DNMT) adds cytosine residues to CAG dinucleotides. Studies have shown that ۱۲ CpG regions in PTC tissue located in the miR-۲۰٤ promoter were reduced by hypermethylation, which increased the expression of the TRPM۳ target gene, which may be associated with tumor invasion, lymph node metastasis, and BRAFV۶۰۰E mutations.

Conclusion: Genetic alterations cause thyroid cancer. By identifying the types of genetic alterations in thyroid cancers, new treatment methods can be provided, especially in personalized thyroid cancer treatment.

Keywords: Genetic Alterations, Thyroid, Cancers, Epigenetics, treatment

genetic counseling (Review)

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Introduction: Genetic counseling is a specialized process that began in the ١٩٧٠s. It aims to prevent coercion and takes into account ethical, cultural, social, political, and racial values. During this process, a genetic counselor helps individuals obtain information about genetic diseases or a predisposition to various genetic disorders. This counseling is particularly beneficial for individuals with a family history of genetic diseases or those concerned about passing on genetic diseases to their children. In this research, we have conducted a review of recent literature on genetic counseling.

Methods: To conduct this study, the Google Scholar database was utilized. Advanced search features were employed to review articles published between ٢٠١٨ and ٢٠٢٤. The search terms included genetic counseling, goals of genetic counseling, history of genetic counseling, types of genetic counseling methods, ethics in genetic counseling, and applications of genetic counseling.

Results: Genetic counseling plays a crucial role in managing genetic diseases, documenting and evaluating information, and providing support to individuals and families affected by genetic disorders. Given the complexities of genetic conditions, genetic counselors educate individuals about the associated risks and consequences. However, there is a need for global development and integration of this profession to enhance understanding and evolution in this field. Countries like Germany, Canada, the United States, and the United Kingdom are at the forefront of genetic counseling. This discipline requires expertise in premarital, prenatal, and preconception care, supporting couples' decision-making by focusing on fertility and infertility indicators. Key topics in this profession include exploring ethical considerations, examining global aspects of genetic counseling, premarital genetic counseling, preconception genetic counseling, and prenatal genetic counseling. Genetic counseling is particularly vital in prenatal care, as it allows prospective parents to evaluate the benefits and challenges of genetic testing while also addressing the ethical, legal, and social implications of genetic information. As the field of genetics continues to expand, genetic counseling will play an increasingly important role in promoting individual well-being and public health. Ethical considerations in genetic counseling include respecting autonomy, providing comprehensive information, promoting beneficence and non-maleficence, and ensuring equitable distribution of services. Counselors should empower clients to make informed decisions and cope with potential emotional distress. The ultimate goal of genetic counseling is to prevent hereditary diseases through positive attitudes and comprehensive knowledge. This approach aims to reduce anxiety and stress while disseminating valuable information within communities

Conclusion: In essence, genetic counseling is an indispensable component of modern healthcare, guiding individuals and families through genetic disorders and hereditary conditions. While some

nations have excelled in providing robust genetic counseling services, others grapple with challenges due to limited resources and inadequate healthcare infrastructure. To ensure equitable access, sustained efforts must focus on enhancing education, promoting awareness, and fostering international collaboration. Advancements in genetic counseling infrastructure, novel testing methodologies, and improved communication between counselors and families offer hope for a healthier and more genetically informed society.

Keywords: Genetic counseling Genetic disorders Genetic disorders Pre-pregnancy genetic counseling

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Genetic effects on Alzheimer's disease (Review)

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Introduction: Alzheimer's disease (AD) is a complex neurological condition marked by the accumulation of misfolded proteins in the brain. Unraveling the genetic underpinnings of AD is essential for diagnosing the disease, predicting its progression, and devising targeted treatments. Recent breakthroughs in scientific research have delved into the fields of epigenomics and proteomics, aiming to uncover early indicators of AD and explore potential therapeutic options. This review seeks to explore the genetic landscape of AD, with a specific focus on understanding how genetics influence the development of AD pathology.

Methods: We searched for articles from the following databases: PubMed; World Health Organization (WHO) Library; Science Direct; Google Scholar.

Results: Numerous studies have ventured into the intricate genetics of AD, revealing the pivotal role of genetic factors in shaping disease susceptibility and advancement. Genome-wide association studies (GWAS) have pinpointed several genetic regions associated with an elevated risk of developing AD, including variations within genes like APOE, TREM2, and PSEN1. These genetic variations can influence critical biological processes involved in AD pathogenesis, such as the metabolism of amyloid-beta, phosphorylation of tau proteins, and neuroinflammatory responses. Moreover, epigenetic modifications, like DNA methylation and histone acetylation, have emerged as key players in regulating gene expression patterns and disrupting molecular pathways implicated in AD. Additionally, changes in non-coding RNA, such as microRNAs, have been linked to AD progression, affecting essential processes like synaptic plasticity, inflammation, and neuronal survival.

Conclusion: The findings underscore the intricate relationship between genetics and the pathology of AD, emphasizing the multifaceted nature of the disease. Genetic variations contribute significantly to an individual's susceptibility to AD, shaping crucial molecular pathways involved in disease onset and progression. Epigenetic modifications further refine the AD phenotype, adding complexity to the disease's underlying mechanisms. Understanding the genetic foundations of AD holds promise for developing tailored therapeutic interventions targeting specific molecular pathways implicated in disease progression. Additionally, genetic biomarkers may facilitate early diagnosis and risk assessment, enabling timely interventions to slow or halt disease progression. Nevertheless, further research is imperative to fully grasp how genetic and epigenetic factors contribute to AD pathology. Integrated approaches combining genetics, epigenomics, and proteomics offer exciting prospects for unraveling the complexities of AD and identifying novel therapeutic targets to combat this devastating neurological disorder.

Keywords: Alzheimer's disease, genetics, epigenetics, proteomics, biomarkers

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Genetic Evaluation of Hypertension in Individuals with Obesity and a Family History (Research Paper)

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Introduction: This study aims to explore the genetic contributing to obesity and the single nucleotide polymorphisms(SNPs) involved in its development. Additionally, the relationship between side effects and phenotypes of polymorphisms in the human genome has been examined.

Methods: Data were collected through NCBI database and the analysis was performed using pharmacogenetics software MegaGene for analyzing polymorphic information and identifying drug related side effects with a genetic basis.

Results: The results revealed that three common polymorphisms in the FTO gene, RS٩٩٣٩٦٠٩, RS٨٠٥٠١٣٦, RS١٤٢١٠٨٥, and MC٤R gene, polymorphisms Rs١٧٧٨٢٣١٣, RS٢٢٢٩٦١٦, as well as the RS١٧٩٩٨٨٣ polymorphism in the FABP٢ gene, are involved in the indication of the disease. One of the most important achievements of the research is detection the role of drug side effects based on the genetics of each individual. It has identified the genetic probability of side effects and the genes and polymorphisms involved in the genetics indication of these side effects.

Conclusion: These findings suggest that before prescribing medication and starting therapy for the treatment of hypertension, it is essential to conduct genetic testes to check for presence of polymorphisms in common gene such as FTO, BRCA٢, and MLH١ in patients. If polymorphisms are detected, medications with fewer side effects should be prescribed to the patient. This approach ensures that patients receive medication with fewer side effects based on their genetic.

Keywords: Obesity, Single Nucleotide Polymorphism ,MegaGene, Hypertension, FTO

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Genetic Insights in Cancer Epidemiology: Enhancing Early Detection Through Biomarkers (Review)

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Introduction: The discovery of genetic biomarkers has revolutionized cancer epidemiology, empowering us with vital tools for early detection and screening. These biomarkers not only enable us to identify individuals at higher risk for developing cancer but also allow us to tailor prevention strategies. As our understanding of cancer's molecular basis grows, integrating genetic biomarkers into routine screening protocols becomes increasingly feasible, giving us the power to take proactive steps in the fight against cancer.

Methods: This review analyzes recent research on genetic biomarkers in cancer epidemiology, focusing on their early detection and screening role. We examined studies published from ٢٠١٦ to ٢٠٢٤ across databases such as Google Scholar, PubMed, and ScienceDirect, highlighting how various genetic markers can identify cancer risk and inform screening practices.

Results: Research has identified critical genetic mutations as crucial indicators of cancer risk. For example, mutations in BRCA١ and BRCA٢ significantly increase the risk of breast and ovarian cancers. Other mutations, like those in TP٥٣ and MLH١, are linked to colorectal cancer and additional malignancies. Detecting these genetic alterations enhances risk stratification, enabling healthcare providers to recommend earlier and more frequent screenings for high-risk individuals. The emergence of polygenic risk scores, which assess the cumulative impact of multiple genetic variants, further improves predictive capabilities for various cancers. These scores offer a nuanced understanding of risk, helping identify individuals who may benefit from proactive surveillance even without well-known mutations. At the molecular level, genetic biomarkers reveal the underlying changes driving cancer progression. For instance, BRCA١ and BRCA٢ mutations disrupt DNA repair processes, leading to genomic instability—a hallmark of cancer. Similarly, mutations in TP٥٣, a vital tumor suppressor gene, compromise the cell's ability to regulate the cell cycle and apoptosis, allowing damaged cells to survive and proliferate. Understanding these molecular mechanisms not only aids in identifying at-risk individuals but also highlights potential therapeutic targets. This insight opens avenues for targeted interventions, such as PARP inhibitors for those with BRCA mutations, illustrating the critical role of genetic biomarkers in comprehensive cancer care.

Conclusion: Integrating genetic biomarkers into cancer epidemiology offers significant promise for enhancing early detection and screening efforts. As we advance our knowledge of cancer genetics, incorporating these biomarkers into public health strategies is essential for effective prevention. Continued research and clinical validation are necessary to refine screening guidelines, ensuring high-risk individuals receive appropriate monitoring and interventions. By leveraging genetic

insights, we can move closer to a future where cancer is detected earlier and treated more effectively.

Keywords: Biomarkers, Cancer Genetic, Cancer Epidemiology, Cancer Biomarker

Genetic Manipulation of Microbial Strains for Enhanced Production of Hyaluronic Acid: Advances and Applications in Tissue Engineering (Review)

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Introduction: Hyaluronic acid (HA), a non-branched glycosaminoglycan, is essential in maintaining tissue hydration, wound healing, and tissue engineering due to its exceptional hydrating properties and role in structural integrity. Traditionally sourced from animal tissues, HA production has faced issues such as high costs and contamination risks. Recent advances in microbial biotechnology offer a safer and more scalable alternative. By genetically engineering non-pathogenic bacteria, such as Bacillus subtilis, Escherichia coli, and Lactococcus lactis, the production of HA has been significantly enhanced. This review examines these advancements, with a focus on the incorporation of biosynthetic genes, such as hasA from Streptococcus species, which have enabled HA production in safe bacterial strains.

Methods: This review synthesizes recent advancements in microbial HA production by investigating peer-reviewed studies from databases including PubMed, Scopus, and Web of Science focusing on research from the past decade. The review includes trends in bacterial strains, genetic modifications, fermentation techniques, and optimization strategies.

Results: Recent advancements in microbial production of hyaluronic acid have significantly enhanced both yield and quality. The synthesis of HA involves the conversion of glucose-٦-phosphate and fructose-٦-phosphate into UDP-glucuronic acid and UDP-N-Acetyl glucosamine through enzymatic pathways respectively. Notably, the incorporation of the hasA gene, particularly when used alongside other related biosynthetic genes, has resulted in substantial improvements. This multi-gene approach in non-pathogenic strains enhances the biosynthetic process, improving HA production efficiency. In the field of genetic engineering, non-pathogenic strains such as Bacillus subtilis, Corynebacterium glutamicum, and Bacillus amyloliquefaciens have been engineered to enhance HA yields and address the limitations associated with traditional strains. These genetic modifications contribute to more efficient and reliable HA production. Various fermentation strategies, including batch, fed-batch, and continuous methods, have been explored to improve HA production. Continuous and fed-batch processes enhance metabolite production and reduce molecular weight polydispersity. Additionally, a dual-phase fermentation approach with conditions of ٣١°C at pH ٨,٠ and ٣٧°C at pH ٧,٠ optimizes HA yield and molecular weight. HA's biocompatibility

and its ubiquitous presence in vertebrate tissues render it an invaluable material in tissue engineering. In skin tissue engineering, HA-based scaffolds have been shown to improve the survival and maintenance of adipose tissue in skin substitutes. HA's capacity to provide a moist environment accelerates wound healing and offers protection against infections. Recent innovations, such as HA combined with solubilized amnion membrane, have further demonstrated enhanced wound closure and skin regeneration. For bone and cartilage tissue engineering, HA-modified hydrogels support cartilage regeneration and bone repair. These hydrogels maintain cell phenotype, promote vascularization, and facilitate the delivery of growth factors, showing promise in repairing bone and cartilage defects. Furthermore, innovations in scaffolds, including HA-based hydrogels such as methacrylated HA and composite materials, offer enhanced cell proliferation and tissue regeneration. The development of ٣D-printed scaffolds and hydrogel systems aims to provide more effective and biocompatible solutions in tissue engineering. Looking ahead, several novel applications and future directions are emerging. In stem cell therapy, HA-containing scaffolds offer a supportive environment for stem cells to repair and regenerate tissues. Ongoing research is focused on optimizing scaffold design and material properties to improve clinical outcomes. Additionally, combining HA scaffolds with gene therapy and immunotherapy is expected to yield more effective treatments for complex diseases. The development of smart HA scaffolds, which respond to environmental stimuli and incorporate nanoscale features, holds promise for enhancing therapeutic efficacy. Recent innovations in hydrogel technology include the creation of injectable hydrogels that combine HA with gelatin and alginate. These hydrogels offer customizable swelling properties and cytocompatibility, making them advantageous for tissue engineering. The use of photoreactive methacrylates and cell-laden microgels further extends HA’s applications, enabling the creation of functional microstructures for regenerative medicine.

Conclusion: This review underscores the revolutionary potential of genetically engineered bacterial systems for HA production. Advances in fermentation techniques, genetic engineering, and scaffold design have notably improved HA yield and application in tissue engineering. The integration of HA with other therapeutic approaches and innovations in hydrogel technology highlight its versatility and promise. Future research should continue to explore and refine these advancements, focusing on optimizing scaffold designs, enhancing therapeutic efficacy, and expanding applications in regenerative medicine and drug delivery systems.

Keywords: Hyaluronic Acid, Genetic Engineering, Non-Pathogenic Bacteria, hasA Gene, Tissue Engineering

Genotyping of Giardia lamblia isolates by PCR- RFLP and triose phosphate Isomerase Gene in Dezfoul city of Iran (Research Paper)

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١.

Introduction: Parasitic diseases are one of the most common problems in the world, especially in developing countries, including our country. One of the common parasitic diseases is infection with Giardia lamblia. Giardia lamblia isolates are classified into ٨ groups based on the characteristics of different genes, including triosephosphate isomerase (TPI). Assemblages A and B infect humans and a broad range of other hosts. The purpose of this study was to genotype human isolates of Giardia lamblia by PCR in Dezfoul city

Methods: For this purpose, ٢٢ positive fecal samples of G. lamblia were collected from ٢٠٢٢ to ٢٠٢٣. DNA extraction and amplification of the TPI gene by nested-PCR successfully were performed. All samples were positive. To determine the genetic differences, sequencing on three samples was conducted. Then, all PCR products were digested with Bbv١, Mnl١, and RsaI restriction enzymes.

Results: Results showed that the alignment of the TPI sequences obtained with reference sequences indicates the presence of ٢ genotypes of Giardia lamblia (A and B). The results of the RFLP technique show that ١٤ of ٢٢ (٦٣,٦٣٪) isolates belonged to assemblage A and ٨ of ٢٢ (٣٦,٣٦٪) belonged to assemblage B.

Conclusion: In general, the results obtained in the present study indicated that genotype A is the most frequent in patients of Dezfoul city, which is probably due to the leakage of sewage into the rivers of the province and the use of contaminated water, so it is used to control this disease. Hygiene principles and safe drinking water should be given more attention.

Keywords: Giardia lamblia, molecular typing, PCR-RFLP, triose phosphate isomerase gene, Dezfoul city iran

Gestational diabetes mellitus and Akkermansia muciniphila; What we know and what we expect. (Review)

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Introduction: Gestational diabetes mellitus (GDM) is a kind of the diabetes which is occurred during pregnancy due to the glucose intolerance, medicated by hormones of the placenta and consequently disturbed absorption of glucose. The main risk factors for GDM include obesity, past diabetes, maternal age, polycystic ovary syndrome, multiple pregnancies, genetics, smoking, and family history. Changes in the gut microbiota cause inflammation and play a significant role in type 2 diabetes pathogenesis. It is believed that by modifying the gut microbiota, many disorders might be enhanced and general host health could be improved. In this way, a probiotic supplement can help manage dysbiosis, in which the microbiome composition changes abnormally.

Methods: A PubMed search was conducted using the terms " Akkermansia muciniphila," " Gestational diabetes mellitus," and "Microbiota". Only English articles published within the last five years were included.

Results: ability to degrade mucin makes Akkermansia muciniphila an effective immune system and metabolic enhancer for the host. In addition, through the production of short-chain fatty acids (SCFAs), mainly propionate and acetate, it can regulate metabolic functions, immune responses, and intestinal barrier function. Researchers have discovered that A. muciniphila is a promising organism for probiotic use in pregnant women, although further studies are needed to develop.

Conclusion: While several studies on the composition of the gut microbiota in women with GDM have been performed, results remain conflicting. Research nature, geographic locations, total sample size, participant enrollment restrictions, gestational age, stool sample collection, and sequencing methods were variable and leading to inconsistent results. Finding the best probiotic or prebiotic treatment candidates is very important from a therapeutic point of view. Therefore, it is critical to understand disease pathogenesis and host factors that influence the efficacy of probiotics and prebiotics, as well as individual responses to probiotic and prebiotic treatments.

Keywords: Gut microbiota; Akkermansia muciniphila; Gestational diabetes mellites (GDM)

Glymphatic (glial lymphatic) pathway (Review)

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Introduction: The glymphatic pathway (glial lymphatic) is a fluid cleansing pathway identified in rodent brains in ٢٠١٢. This pathway controls the flow of CSF to the brain along arterial vascular spaces and then to the middle brain, facilitated by Channels (AQP٤). It then directs the flow path to the venous and perivascular and perineuronal spaces, eventually clearing neuropil solutions into the lymphatic drainage vessels of the meninges and cervix. The pathway consists of a para-arterial influx route for CSF to enter the brain parenchyma, coupled to a clearance mechanism for the removal of interstitial fluid (ISF) and extracellular solutes from the interstitial compartments of the brain and spinal cord. Exchange of solutes between CSF and ISF is driven primarily by arterial pulsation and regulated during sleep by the expansion and contraction of brain extracellular space. In rodents, the glymphatic pathway is mainly active during sleep. The biological need for sleep across all species may therefore reflect that the brain must enter a state of activity that enables elimination of potentially neurotoxic waste products, including β-amyloid. Glymphatic dysfunction, possibly related to the turbulent expression of AQP٤, has been shown in animal models of brain injury, Alzheimer's disease and stroke.

Methods: we conducted an extensive search across electronic databases, including PubMed, MEDLINE, Embase, Google Scholar, and ResearchGate, and explored the available English-language literature. The MeSH terms were "Glymphatic system " OR " Perivascular spaces"; "Cerebrospinal fluid secretion "; "Sleep". The work of one of the researchers documents that β-amyloid concentrations in CSF follow the sleep-wake cycle in human subjects.

Results: The research group has made progress in the development of a glymphatic diagnostic test based on MRI scans. By delivering the contrast agent to cisterna magna, CSF movement can be followed in real time throughout the brain. In observations made by scientists in mice confirmed and spread the concept of the presence of a glymphatic system throughout the brain. In particular the MRI analysis showed that there was rapid flow movement in two key nodes, pituitary cavities and pineal gland. Interestingly both of these areas are involved in regulating the sleep wake cycle. Future studies with focus on the glymphatic system are expected to identify functions of convective CSF fluxes beyond removal of metabolic waste products. We have recently found that glymphatic influx can serve as a distribution system for lipids and glucose , and we speculate that glymphatic influx

provides an essential route for distribution of electrolytes, macromolecules, and other larger compounds that enter the brain predominantly via the blood-CSF barrier at the choroid plexus. Likewise, the glymphatic system might serve as a path for delivery and distribution of drugs including cancer drugs within the brain.

Conclusion: Further research is needed to confirm whether certain factors that cause glymphatic flow in rodents also exist for humans. Longitudinal imaging studies that assess human CSF dynamics determine whether there is a link between reduced brain solution cleansing and the development of neurodegenerative diseases. An evaluation of glymphatic function after a stroke or brain injury can identify whether this function is associated with neurological healing. New insights into how the behavior and genetics of changing glymphatic function, and how to compensate for this function in the disease, should lead to the development of new preventive and diagnostic tools and new therapeutic goals. Although much is known about the physiological regulation of glymphatic pathway function, including the role of cerebral arterial heart rate, consciousness status, and even head position, there is currently no guided glymphatic therapy to intervene in any of these different disease processes. As a result, the main objective of future studies will be to identify a new objective to regulate or reset the CSF-ISF exchange in the glymphatic pathway, ultimately to promote improved soluble cleansing in diseases where metabolic accumulation is a prominent feature. And it should also be noted that it is an effective and investable path to future research.

Keywords: Glymphatic system, Perivascular spaces, Cerebrospinal fluid secretion, Sleep

Graphene oxide/Chitosan/Iron oxide Magnetic Microspheres as Potential Vehicles for Targeted Temozolomide Delivery in Glioblastoma Cells (Research Paper)

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Introduction: The use of cancer chemotherapy drugs often leads to a surplus of severe side effects because they also target healthy cells. This underscores the need for advancements in delivery platforms that can selectively release desired drugs near these highly active cells.

Methods: In this context, a magnetic nanocomposite has been produced using a conventional co-precipitation method. Fe_3O_4 (IO) NPs were synthesized in the presence of Salvia officinalis extract via the green synthesis method. The (graphene oxide) GO NPs were prepared using the Staudenmaier method, and synthesized materials were characterized. Chitosan (CS) was used for the preparation of microspheres. GO/CS/IO nanocomposites were investigated as prospective vehicles for controlled drug delivery in the presence and absence of an external magnetic field.

Results: For biomedical applications, this research provided a novel graphene oxide/chitosan/iron oxide nanocomposite microspheres that has not been studied until now. Moreover, the release behavior of the temozolomide-loaded GO/CS/IO nanocomposite is investigated in the absence and presence of magnetic field conditions. Synthetic microspheres adaptable microsphers have the potential to control the release of the temozolomide when an alternating magnetic field is applied. The temozolomide release rate was also enhanced by the magnetic field. The MTT assay results indicated that the synthesized nanocomposite is suitable for anti-cancer biomedical applications.

Conclusion: This research introduces a strategy for controlled drug delivery that drugs, like Tmz, would be released at a specific target by applying suitably localized magnetic fields. It also exhibits superior magnetic performance, indicating the designed drug carrier's excellent targeted delivery capability. The release of the loaded medicine can be considerably improved by the magnetic response of drug carriers with different magnetic frequencies and intensities. An additional benefit is that a low-frequency AFM may be used to carry out the controlled drug release procedure, which promotes energy efficiency and protection of the environment.

Keywords: Magnetic nanoparticles, Graphene oxide, Chitosan, Temozolomide, Controlled drug delivery

Green synthesis of nanohydroxyapatite trough Elaeagnus angustifolia L. extract and evaluating its anti-tumor properties in MCFV breast cancer cell line (Research Paper)

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Introduction: One of the most common types of cancer in women is breast cancer. There are numerous natural plant-based products, which exert anti-tumoral effects including Elaeagnus Angustifolia (EA). It modulates cell-cycle process, heat-shock proteins expression, anti-proliferative properties, apoptosis induction, blocking of angiogenesis, and cell invasion inhibition. The current study aimed to synthesize and evaluate the anticancer effects of hydroalcoholic EA extract (HEAE), Nanohydroxyapatite (nHAp) and nHAp synthesized trough EA (nHA-EA) in MCF-٧ breast cancer cell line.

Methods: In the present study, HEAE preparation and green synthesis of nHA-EA was done and phase composition, functional groups, and crystallin phase of nHA-EA and nHAp were determined using Fourier-transform infrared (FTIR) and X-ray diffraction (XRD). The characteristics of synthesized nanoparticles including structural and morphological parameters were investigated using scanning electron microscopy (SEM) and Transmission electron microscopy (TEM) techniques. Then, by using MTT-assay (Dimethylthiazoldiphenyltetrazolium), the in vitro cytotoxic and half maximal inhibitory concentration ($IC_{٥٠}$) of EA extract, nHAp, and nHA-EA in the MCF-٧ breast cancer cell line was evaluated. Next, we assessed the expression of apoptosis-related genes Bax, $Bcl_{٢}$ and $p_{٥٣}$ using quantitative reverse-transcriptase polymerase-chain-reaction (qRT-PCR) and migration of MCF-٧ cells by scratch assay.

Results: The FTIR results demonstrated formation of nHAp and its interaction with HEAE during synthesis process. The XRD results of the synthesized nanoparticles showed similar XRD pattern of nHA-EA and nHAp and purity of synthesized nanomaterials. The average $IC_{٥٠}$ of HEAE, nHAp, and nHA-EA extract after treatment of cancer cells for ٢٤ h was ٤٠٠ µg/mL, ٢٠٠ µg/mL, and ١٠٠ µg/mL, respectively. Our results revealed that nHA-EA significantly reduced the migration and invasion of the MCF-٧ cells, in comparison to the nHAp and EA extract. Moreover, level of Bax/$Bcl_{٢}$ and $p_{٥٣}$ was significantly higher in the nHA-EA extract group in comparison to the EA extract and nHAp group.

Conclusion: Taken together, our results demonstrated that bioactive constituents of EA medicinal plant in form of nHA-EA particles, can effectively exerts potential anticancer and chemo preventive

effect against breast cancer growth and can be proposed as a promising beneficial candidate for BC therapy. However, further investigations are required to discover what bioactive compounds are responsible for the chemo preventive effect of this extract.

Keywords: MCF-۷ breast cancer, Elaeagnus Angustifolia, Hydroxyapatite nanoparticle, Apoptosis

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Harnessing Convolutional Neural Networks in Machine Learning for Enhanced Cancer Diagnosis

(Review)

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Introduction: Cancer remains a leading cause of death worldwide, and early, accurate diagnosis is critical for effective treatment. Traditional diagnostic techniques, such as radiology and pathology, are often slow, human-dependent, and prone to variability. Machine learning (ML), specifically convolutional neural networks (CNNs), has emerged as a promising solution to overcome these limitations. As a type of deep learning model, CNNs excel at processing visual images, making them ideal for analyzing complex medical images associated with cancer. The increasing workload in oncology highlights the need for faster, more reliable diagnostic tools.

Methods: CNNs are widely used to analyze medical imaging data, including CT scans, MRIs, and mammograms. These models automatically learn and identify features, such as tumor boundaries and abnormalities, that may be missed by human observers. In addition to radiology, CNNs are being applied in digital pathology, where they analyze digitized histopathological slides to detect cancerous tissues with high accuracy. CNNs are also gaining momentum in precision oncology, where they are used to analyze genetic data and identify biomarkers associated with specific cancers, enabling personalized treatment plans.

Results: CNNs have demonstrated superior performance in cancer diagnostics, particularly in detecting breast cancer through mammography, especially in dense breast tissue. The models reduce observer variability, thereby lowering false-positive and false-negative rates. In digital pathology, CNNs can distinguish between benign and malignant cells, grade tumors, and predict cancer progression, such as metastasis to stage IV. Furthermore, CNNs have been instrumental in precision oncology by identifying genetic mutations, such as BRCA and EGFR, which correspond to targeted therapies that improve patient outcomes.

Conclusion: Despite their promise, several challenges remain in the clinical adoption of CNNs. High-quality, large datasets are necessary to train these models effectively, yet data privacy concerns and fragmented healthcare records hinder data acquisition. The "black box" nature of CNNs also poses issues for clinicians, as the rationale behind their predictions is often not transparent. Ongoing research in explainable AI (XAI) aims to make CNN models more interpretable. Collaborations between data scientists, healthcare professionals, and regulators are essential for overcoming these barriers and ensuring that AI is safely integrated into clinical practice. As AI evolves, CNNs are expected to play an even more significant role in cancer diagnosis, especially when integrated with emerging technologies like quantum computing and CRISPR gene editing.

Keywords: Convolutional Neural Networks, Machine Learning, Cancer Diagnosis, Medical Imaging, Digital Patholog

Harnessing Liquid Biopsy for Real-Time Monitoring of Immune Checkpoint Inhibitor Response in Cancer Treatment: A Pathway to Personalized Immunotherapy (Review)

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Introduction: Circulating biomarker assays offer a minimally invasive method for the immediate surveillance of immunomodulatory checkpoint inhibitor (ICI) responses in cancer immunotherapy. This approach utilizes cell-free tumor DNA (ctDNA), circulating tumor cells (CTCs), and other biomarkers found in bodily fluids, primarily blood, to provide insights into tumor evolution and therapeutic effectiveness. Conventional imaging methods often struggle to accurately assess patient responses, highlighting the need for innovative strategies that enable adaptive tracking of treatment outcomes. Circulating biomarker assays present a promising solution by providing real-time data on tumor genetics and immune profiles, facilitating tailored therapeutic strategies to meet individual patient needs and aiding in the proactive identification of resistance pathways. Immune checkpoint inhibitors have significantly improved cancer treatment by enhancing the body's immune response against tumors. However, the variability in patient responses necessitates a deeper understanding of predictive biomarkers for effective therapies. Current assessment techniques often rely on imaging and tissue biopsies, which may not capture immediate changes in tumor biology or immune status. Circulating biomarker assays provide a dynamic alternative, allowing for continuous evaluation of tumor progression and immune engagement throughout treatment. This study aims to explore the potential of circulating biomarker assays for real-time monitoring of ICI responses, enhancing the precision of immuno-oncological treatment by providing timely insights into therapeutic responses.

Methods: This review evaluates the role of liquid biopsy in managing malignancies treated with ICIs, emphasizing studies that utilize long-term frameworks to track patients at various time points and document changes in tumor characteristics. Liquid biopsy specimens are obtained through minimally invasive venipuncture, employing advanced techniques such as next-generation sequencing and digital droplet PCR. The review focuses on identifying biomarkers predictive of ICI efficacy, including tumor mutational burden and microsatellite instability, which are analyzed through genomic profiling to establish correlations with clinical outcomes. Included studies involve cancer patients receiving ICIs who undergo liquid biopsies to collect circulating free DNA (cfDNA), CTCs, and exosomes. High-throughput genomic sequencing analyzes cfDNA for mutations and neoantigen identification, while immune profiling assesses T cell activity and immunosuppressive factors within the tumor microenvironment. The review correlates clinical outcomes, such as progression-free survival and overall survival, with liquid biopsy findings and evaluates the prognostic significance of identified biomarkers. Furthermore, the review synthesizes literature on liquid biopsy applications across various cancer types, particularly lung and colorectal cancers, discussing emerging technologies like mass spectrometry and flow cytometry that enhance the detection and analysis of

tumor-derived materials. By integrating these methodologies with ICI therapy, clinicians can effectively monitor treatment responses and adjust therapeutic strategies based on real-time data.

Results: The outcomes of this review highlight the substantial role of liquid biopsy in tracking therapeutic responses to ICIs and predicting patient outcomes. Initial findings suggest a strong relationship between specific liquid biopsy biomarkers, particularly elevated ctDNA levels, and positive patient responses to ICIs. This connection underscores the potential of liquid biopsies as reliable indicators of treatment efficacy, with studies showing that patients with favorable biomarker profiles exhibit significantly improved response rates to ICIs compared to those without such profiles. The accuracy of liquid biopsy in predicting both short-term and long-term treatment outcomes has been validated through comprehensive data analysis. Results indicate that liquid biopsy enables real-time monitoring of emerging resistance mechanisms during immunotherapy. By identifying genetic alterations associated with resistance early, clinicians can adjust treatment regimens timely, potentially enhancing patient outcomes.

Conclusion: This review underscores the pivotal role of liquid biopsy in linking biomarker dynamics with ICI response monitoring, highlighting its potential to revolutionize personalized cancer immunotherapy. Liquid biopsy serves as a valuable real-time monitoring tool, offering insights into tumor evolution and individual immune responses. By integrating liquid biopsy into routine clinical practice, clinicians can tailor immunotherapy strategies based on real-time insights into tumor biology and immune interactions, leading to more effective and personalized treatment options. Future research should focus on validating liquid biopsy technologies across diverse cancer types and larger patient cohorts, investigating novel biomarkers to enhance understanding of tumor-immune interactions. Addressing challenges such as standardizing liquid biopsy procedures and conducting large-scale studies will be essential for establishing robust clinical guidelines. In summary, leveraging liquid biopsy for continuous monitoring of ICI responses represents a significant advancement in precision oncology, ultimately improving patient outcomes and quality of life for those undergoing immunotherapy.

Keywords: Liquid Biopsy,ImmuneCheckpoint Inhibitors(ICIs),CellFree Tumor DNA(ctDNA),Personalized Immunotherapy

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Harnessing MicroRNAs to Treat Pancreatic Cancer (Review)

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Introduction: Pancreatic cancer is acknowledged as one of the most lethal and chemotherapy-resistant forms of cancer, persisting as a fatal tumor despite intensive treatment. However, recent studies have shown that targeting dysregulated microRNAs (miRs) could offer a new and promising strategy to improve outcomes for people with pancreatic cancer. MicroRNAs are a class of small RNA molecules that lack protein-coding ability and play a crucial role in regulating gene expression. The expression levels of several miRNAs are markedly disturbed in comparison to pancreatic tissue that is considered normal. Hence, miRNAs have the potential to either promote carcinogenesis by inducing tumor growth or function as tumor suppressors by impeding tumor formation.The primary microRNAs (miRNAs) linked to pancreatic cancer are the tumor suppressors miR-٣٤a, miR-١٤٣, and miR-١٤٥, which are down-regulated, and the oncogenes miR-٢١, miR-٢٢١, and miR-٢٢٢, which are elevated. The miRNAs that have experienced deregulation are the ones that can be employed for therapeutic intervention

Methods: One method entails use antagomirs, which are antisense oligonucleotides, to inhibit the excessive expression of cancer-causing miRNAs. For example, experimental studies have shown that the use of antagomirs to inhibit miR-٢١ or miR-٢٢١/٢٢٢ can decrease the proliferation, invasion, and resistance to treatment of pancreatic cancer cells. In addition, scientists are studying the potential of synthetic miRNA mimics to reinstate tumor-suppressor miRNAs that have been suppressed or removed. Reintroducing miR-٣٤a, an extensively studied tumor suppressor in pancreatic cancer, impedes growth, induces programmed cell death, and increases the responsiveness of cells to chemotherapy treatments.

Results: To enhance the effectiveness of these miRNA-based treatments, they are being assessed alongside conventional treatment methods, such as chemotherapy and targeted medications. Through the simultaneous modulation of many signaling pathways, combination approaches have the capacity to overcome treatment resistance and improve the prognosis of patients with pancreatic cancer.

Conclusion: Although the use of miRNA as a treatment for pancreatic cancer is still in its early stages, the promising outcomes from preclinical studies and the ongoing clinical trial of the miR-٣٤a mimic MRX٣٤ highlight the potential of utilizing these regulatory RNAs to effectively manage this deadly disease in the future.

Keywords: miRNA, Pancreatic Cancer, Antagomirs, Tumor Supressor, Oncogenes

Healing Corneal Ulcers with Platelet-Rich Plasma (Review)

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Introduction: Refractory keratoconjective epithelial disorders, caused by graft-versus-host disease, corneal transplantation, Sjögren's syndrome, and severe dry eye disease, lead to reduced visual acuity, reduced contrast sensitivity, increased susceptibility to infections, corneal perforation, and decreased quality of vision. Keratoconjunctivitis refers to an inflammatory process that involves both the conjunctiva and the superficial cornea. It can occur in association with viral, bacterial, autoimmune, toxic, and allergic etiologies. Corneal ulcers represent a severe ocular emergency with potential vision-threatening complications. The aim of this study is to evaluate the effectiveness of platelet-rich plasma (PRP) eye drops to heal corneal epithelial ulcers. PRP harbours high levels of growth factors. Platelets are known for their role in hemostasis, with which they help in preventing blood loss at sites of vascular injury. To do this, they adhere, aggregate, and form a procoagulant surface, leading to thrombin generation and fibrin formation. Platelets also release substances that promote tissue repair and influence the reactivity of vascular and other blood cells in angiogenesis and inflammation. Growth factors are released from the α-granules of the platelets. Endothelial-protein tyrosine phosphatase (PTP) is used as a complement to specialized tissue-regeneration procedures, including oral and maxillofacial surgery, orthopedics and plastic surgery. Our other aimed to determine the effectiveness of low-temperature storage on the efficacy and sterility of PRP eye-drops compared with those of autologous serum (AS) eye-drops, if practical, it may expand the clinical usage of PRP to patients 'households. In addition, the therapeutic advantages of PRP eye-drops compared with those of standard treatments may promote their clinical application for cases of refractory keratoconjective epithelial disorders.

Methods: we conducted an extensive search across electronic databases, including PubMed, MEDLINE, Embase, Google Scholar, and ResearchGate, and explored the available English-language literature. The MeSH terms were " keratoconjective epithelial disorders " OR " platelet-rich plasma "; " corneal ulcers ";" ophthalmology". The articles included in this review adhere to the following criteria: they encompass studies solely focused on progress in comprehending and novel treatment approaches, and they are studies conducted in the English language within the last decades. We have used Ryan's AI in this review to screen articles, where it was done with the help of colleagues to visually separate articles using their reading as well as keyword readers.

Results: The importance of this study is that it shows that eye drops can be used as an effective treatment for keratoconjective epithelial disorders resistant to existing treatments. These drops not only remain sterile but also maintain higher levels of growth factors that help improve the healing process of corneal ulcers. Such findings could lead to the development of new therapies and improve the quality of life of patients with these disorders. There is an urgent need to develop effective therapeutic agents for keratoconjunctival epithelial disorders that do not respond to existing eye-drops. The stability of PRP were investigated for future clinical use. There was an increased pharmacological efficacy and a complementary degree of sterility in PRP eye-drops when stored at ٤°C for ٤ weeks compared with those in AS eye-drops, warranting further study of PRP eye-drops.

Conclusion: Another thing to note was that autologous platelet-rich plasma promoted healing of dormant corneal ulcers even in eyes threatened by corneal perforation and was accompanied by a reduction in pain and inflammation. Autologous platelet-rich plasma has been demonstrated to be effective in corneal neurotrophic ulcer treatment. The lack of preservatives, autologous quality, relative ease of its preparation, safety, and beneficial effects make PRP a promising therapeutic tool for future regenerative medicine. Despite the fact that recombinant synthetic products are available for neurotrophic ulcer treatment, those high-priced goods contain only a single growth factor. But on the other hand, some people offer low-cost PRP to make it economical. Although low-cost PRP preparation gives lower platelet concentrations than standard methods, our work shows that this preparation is effective in treating resistant non-infectious corneal ulcers.

Keywords: keratoconjective epithelial disorders, platelet-rich plasma, corneal ulcers, personalized medicine.

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Healing Potential of Targeting MicroRNAs in Acute Myeloid Leukemia Treatment (Review)

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Introduction: Acute myeloid leukemia (AML) is a neoplastic disorder characterized by the clonal proliferation of immature myeloid hematopoietic cells within the bone marrow, exhibiting rapid advancement and a generally unfavorable prognosis. In recent decades, significant advancements have been made in understanding the genetic anomalies that influence the progression of (AML). Most types of leukemia lack the development of dependable treatment options. Additionally, even therapies considered somewhat effective may lead to disease recurrences.

Methods: In the context of AML, microRNAs (miRNAs) are considered a valuable enhancement to the restricted range of therapeutic options available, and extensive research has been conducted on the dysregulation of miRNAs. Micro RNAs (miRNAs) represent a category of small non-coding RNAs that play a vital role in various cellular functions, including differentiation, proliferation, migration, and apoptosis. From a clinical perspective, numerous miRs have been identified as correlating with the prognosis of patients with AML. Oncogenic microRNAs are associated with unfavorable outcomes.

Results: This review will focus on Gaining insights into the role of microRNAs in the pathology of Acute Myeloid Leukemia (AML) and Learning about emerging strategies that involve targeting microRNAs as a novel therapeutic avenue to enhance AML treatment outcomes.

Conclusion: MicroRNAs hold significant promise as a transformative approach to diagnosing and managing acute myeloid leukemia.

Keywords: acute myeloid leukemia; microRNA (miRNA); treatment

High-Flow Nasal Cannula (HFNC) oxygen therapy effects on clinical symptoms in cancer patients (Review)

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Introduction: Cancer patients had experienced different complications during therapy sessions, and dyspnea is one of the most common clinical symptoms that reported. In another hand, some of the patients suffer to acute respiratory failure (ARF) which remains a major cause of ICU admission. High-Flow Nasal Cannula (HFNC) oxygen therapy is frequently applied to relieve dyspnea and acute respiratory failure (ARF) in patients with cancer.

Methods: A review was acquired by searching the databases of Springer, PubMed, Nature and ResearchGate.

Results: Compare to other form of oxygen therapy like conventional oxygen therapy (COT) and noninvasive ventilation (NIV), HFNC has been beneficial to cure dyspnea with enhancing nasopharyngeal washout, reducing nasopharyngeal inspiratory resistance, augmenting positive end-expiratory pressure, and stimulating the trigeminal and glossopharyngeal nerves, which all can modulate central respiratory drive. Additionally, HFNC is useful for cancer patients with acute respiratory failure (ARF) to avoid mechanical ventilation (MV) and provides safe and comfortable treatment for cancer patients.

Conclusion: This review sheds light on HFNC as one of the most important oxygen therapy methods which enhance clinically relevant outcomes in both hypoxemic and non-hypoxemic patients and improve quality of their lives.

Keywords: HFNC, dyspnea, ARF, Cancer

Histone Modifications and Epigenetic Regulation in Alzheimer's Disease: Unraveling the Epigenetic Code for Therapeutic Advances (Review)

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Introduction: Alzheimer's disease (AD) is a complex neurodegenerative disorder marked by cognitive decline and memory loss. Recent research highlights the role of epigenetic mechanisms, particularly histone modifications, in AD pathology. Understanding these modifications provides new insights into disease mechanisms and potential therapeutic targets. This review aims to explore the impact of histone modifications on the epigenetic regulation of gene expression in Alzheimer's disease, and to assess how these modifications contribute to disease progression and potential therapeutic strategies.

Methods: A systematic review of the literature was conducted using databases such as PubMed, Scopus, and Web of Science. Articles published in the last decade that focused on histone modifications, their role in AD, and related therapeutic strategies were included. Data were synthesized to provide a comprehensive overview of current knowledge and emerging trends.

Results: ١. **Histone Modifications in Alzheimer's Disease:** - **Acetylation:** Dysregulation of histone acetylation has been associated with altered gene expression profiles in AD, affecting genes related to neuroinflammation and synaptic plasticity. - **Methylation:** Abnormal histone methylation patterns, including hypermethylation and hypomethylation of specific genes, have been observed in AD, impacting cognitive functions and neuronal health. - **Phosphorylation and Ubiquitination:** Emerging evidence suggests that these modifications also play a role in AD, influencing protein interactions and cellular processes. ٢. **Mechanistic Insights:** - **Gene Expression Regulation:** Histone modifications influence the transcriptional activity of genes involved in AD, such as amyloid precursor protein (APP) and tau protein. - **Neuroinflammation and Cellular Stress:** Modifications contribute to inflammatory responses and cellular stress, which are critical in AD pathology. ٣. **Therapeutic Implications:** - **Epigenetic Therapies:** Strategies targeting histone deacetylases (HDACs) and histone methyltransferases (HMTs) show promise in preclinical models, potentially reversing aberrant epigenetic changes. - **Drug Development:** Novel compounds aiming to modulate histone modifications are being explored, offering potential new avenues for AD treatment.

Conclusion: Histone modifications play a crucial role in the epigenetic regulation of gene expression in Alzheimer's disease. Unraveling these mechanisms provides valuable insights into disease pathology and offers new therapeutic possibilities. Continued research into histone-targeted interventions may pave the way for innovative treatments for AD.

Keywords: Alzheimer's disease, histone modifications, epigenetics, acetylation, methylation,

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HIV VACCINES TREATMENT REVIEW ARTICLE (Review)

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Introduction: HIV infection is a major global health issue, affecting ٣٦,٧ million people world-wide. New infections continue to occur, with ٢,١ million cases in ٢٠١٥. The number of people living with HIV on antiretroviral therapy (ART) reached ١٧ million in ٢٠١٥.Citation١ However, it cannot eradicate HIV infection due to the persistence of a latent viral reservoir (mean half-life of ٤٤ months). Thus, the need for ART is lifelong and the cost is substantialCitation٨,٩ and may be difficult to sustain economically.Citation٣ Although ART is highly efficacious in preventing transmission in the setting of mother to child transmission in sexual transmission through the treatment of infected partners in serodiscordant relationships, Furthermore, adherence is critical to the efficacy of biomedical preventive interventions but has been varied across study populations. According to Fauci and Marston, “even if HIV prevention efforts were optimally implemented to achieve a new infection rate of near zero, recidivism could threaten this success.” Thus an HIV vaccine is essential as it is a more sustainable solution. Modeling data suggest that a ٧٠٪ efficacious vaccine introduce in ٢٠٢٧ with strong uptake and ٥ y of protection could reduce annual new infections by ٤٤٪ over the first decade and by ٧٨٪ in ٢٠٧٠. Therefore, an effective universal prophylactic vaccine can potentially curtail and end the worldwide HIV pandemic.

Methods: HVTN ١٢٤ was a randomised, phase ١, placebo-controlled, double-blind study, including participants who were HIV seronegative and aged ١٨–٥٠ years at low risk for infection. The DNA vaccine comprised five plasmids: four copies expressing Env gp١٢٠ (clades A, B, C, and AE) and one gag p٥٥ (clade C). The protein vaccine included four DNA vaccine-matched GLA-SE-adjuvanted recombinant gp١٢٠ proteins. Participants were enrolled across six clinical sites in the USA and were randomly assigned to placebo or one of two vaccine groups (ie, prime–boost or coadministration) in a ٥:١ ratio in part A and a ٧:١ ratio in part B.

Results: we will syntheseize the findings through tables charts and narrative summaries. we will also idenify gaps in the current literature and provide recommendation for future research. findings will be shared at conferences and submitted to peer-reviewed publication.

Conclusion: A great deal has been learned from HIV vaccine research over the last ٣٠ years. Data from completed HIV-١ vaccine efficacy trials support the role of functional Env Ab in reducing infection risk.Citation٥٢ Replication in a follow-up efficacy trial is pending. The field eagerly awaits results from HVTN٧٠٢, which will provide an opportunity to assess this pox-protein regimen in light of RV١٤٤ correlates of risk as well as generate novel hypotheses on mechanisms of protection. Data from phase II studies of passive immunization with bnAb will become available in the next few years and will be critical for proof of concept that bnAb can prevent HIV acquisition in humans. The elicitation of bnAb through vaccination is still in preclinical stages.

Keywords: Treatment - HIV- Vaccine- T_Cells

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Homology modeling and molecular docking to identify potent inhibitors targeting FglK protein; Helicobacter pylori flagellar subunit. (Research Paper)

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Introduction: The flagella play an important role in the initial phase of the infection process of many pathogenic bacteria. It has been shown that FlgK is important for flagella formation and motility of H pylori, therefore deletion of the flgK protein, prevents normal flagellar assembly and reduces the colonization of the gastrointestinal mucosa. FlgK along with FlgL form the hook-filament junction, Therefore, the one of the best point to target Flgk, is where it connects and interacts with FlgL. With this concept, a molecular docking analysis for vitamins and their derivatives (٤٧ molecules) with interface area of FlgK/FlgL was carried out.

Methods: The amino acid sequences of the FlgK and FlgL were extracted from the UniProt database and the ٣D-structure of the proteins were predicted using Modeller ٩ & ٢٢ software .The models evaluation were done using Verify-٣D, PROCHECK program andProSA II web server. GRAMM-X and ClusPro ٢,٠ were used to predict and assess the interactions between the hook-filament junction proteins FlgK and FlgL and area of interaction were determined using the PDBePISA and Discovery Studio ٤,١. The ligand-binding residues were predicted on FlgK by COACH and FTMap server. ٤٧ FDA approved vitamins were collected from Selleckchem Inc web site. Then, the ligands were evaluated as inhibitors on interface residues of FlgK/FlgL proteins by Autodock Vina and Autodock ٤ in pyrx program and AutoDock Vina software, and the output results were evaluated by Discovery Studio software.

Results: The ligand binding sites of FlgK that overlapped with the interaction site of these FlgK and FlgL, were selected as the target sites (V٥٦٨, E٥٧٢, E٥٧٣, N٥٧٦, A٥٨٥, A٥٨٦, N٥٨٧, A٥٨٨, K٥٨٩, I٥٩٨, D٥٩٩ and T٦٠٠) for docking. The results of molecular docking indicate that the ligands with best binding scores –i.e., the most negative binding energies are observed for the compounds; Vitamin B١٢ with Binding energy -١٢,٨, Ergosterol with Binding energy -١٠,٥, Calcipotriene with Binding energy -٩,٦, Trolox with Binding energy -٩,٦, Doxercalciferol with Binding energy -٩,٤, Vitamin D٣ with Binding energy -٩,٠, Calcifediol with Binding energy -٨,٨, Riboflavin (Vitamin B٢) with Binding energy -٨,٧ and Dibenzoyl Thiamine (Bentiamin) with Binding energy -٨.

Conclusion: This in silico study suggests that FDA approved vitamins Vitamin B١٢, Ergostero, Calcipotriene, Trolox, Doxercalciferol, Vitamin D٣, Calcifediol, Riboflavin and Dibenzoyl Thiamine could serve as potential inhibitors against flagellar biogenesis in Helicobacter pylori.

Keywords: Molecular Docking, Helicobacter pylori, FlgK and Vitamins

How can fear impact on our brain and behavior? (Review)

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Introduction: So, in this research fear and anxiety on the brain and behavior they used for that ever since like Functional Magnetic Reasoning Imaging (fMRI) & MRI Amygdala imaging. It needs test subjects, volunteers, raters and research assistants to perform neuropsychological testing in longitudinal studies. This research is seeking to discover what types of behaviors and brain processes correspond with levels of fear. It also seeks to explore how the brain regulates emotions and whether it is possible (or not) to modulate these emotions by mechano-optogenetic stimulation. Anxiety is a state of psychological distress, physiological and behavioral induced by threats to survival or well-being that relates inferentially with fear warning signal present in the danger situation, activating adaptive responses. The purpose of this research is to better understand how fear and anxiety work in the brain, be that for treating disorders or phobias like ailurophobia. There is also a need to examine fear and brain/hormone pathophysiological interactions with other organs. In depth studies will be carried out regarding biology of fear and anxiety at systemic levels related to brain-behavior relationships, neuronal circuitry functional neuroanatomy in addition to cellular/molecular aspects viz., neurotransmitter/hydroxy indole/modulatory species with special reference to animal models. If researchers can get a better handle on how fear and anxiety are linked, they could design therapies to alleviate these symptoms in individuals—and perhaps benefit their health more generally as well.

Methods: In this study, they measured amygdala brain activity in fear and anxiety using both fMRI (functional MRI) which measures changes with the blood flow throughout the entire Brain ٣-D imaging system & standard anatomical/structural MRI. Fear and anxiety studies include use behavioral assessments with long term follow ups to detect changes. Use hypotheses to drive inference about the inter-relationships among fear, brain activity and behavior Outcomes include recognition of behavioral and brain correlates to fear & anxiety, understanding the hormone basis for some aspects of fear, investigation as to whether or not such fearful reactivity is critical for long-term survival. Ethical considerations are also about getting informed consent, and to make sure that the participant is safe within data privacy.

Results: Whether a system works: Knowing, for instance if the amygdala is related to fear. Hormones — How hormones like cortisol and adrenaline impact feelings of fear as well anxiety. Behavior: Drawing the link between avoidance to both states of fear and anxiety. Neural Patterns: Determine the particular pattern associated with phobias in a brain. Treatment: therapies, such as counseling (often cognitive-behavioral therapy) or medication to help relieve emotional distress. Main Purpose: To investigate how fear influences the brain and behavior, and find ways of helping people to control alarming levels of anxiety.

Conclusion: The biological basis of fear and anxiety is now known, and the main brain structures and neural circuits involved in processing emotional information and behavior have been identified. Affective and cognitive processes cannot be separated, even considering basic emotions such as fear. Cognitive understanding of events and situations is critically involved in emotional experiences and also influences coping strategies or defense mechanisms. This is reflected in the important role now attributed to the PFC in the control of emotional behavior in humans and animals.

Keywords: Fear, Brain, Neuroscience, Cognitive Neuroscience, Behavior

How the impact of social factors Economy on gut microbiome (Research Paper)

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Introduction: Gut microbiota is well recognized as a key determinant of health and disease. Consequently, several studies have focused on the causality and predictive/prognostic value of microbiota in a wide range of diseases. However, understanding what sparks changes in the microbiota and how these changes contribute to increased disease susceptibility is of greater importance. Few studies have shown that gut microbiota can be altered by lifestyle and thus lead to pathology. What if socio-economic factors also affect the composition of the gut microbiota and thus increase susceptibility to disease? Perhaps, this is one of the factors that may have contributed to the increase in inequality between people with higher and lower socio-economic status in terms of health. In this review, we aim to understand more about this issue and the true impact of the biological community. In addition, we proposed criteria to reduce the impact of these factors on the gut microbiota composition.

Methods: Microbiota has a great impact on health and disease. Therefore, it can be understood that society affects health inequalities and can reduce these inequalities. In addition, if it should be considered in microbiota research, because it is possible to carry out an intervention that can influence interpretation results. It seems that this trait has more to do with their microbiota composition than heritability. Therefore, childhood interventions on the microbiota can have a person's success throughout life, along with improving the country's productivity will increase the risk of developing this disease. In addition, the biological community can prevent screening damage by increasing efficiency through appropriate health policies designed specifically for specific sites.

Results: Regional Microbiota Banks and Screening of Policy Success Since microbiota sequencing is becoming more accessible, individual microbiota should be examined in a standard frequency to optimize health policies and evaluate their success with the possibility of early disease detection and microbiota adjustment. In addition, microbiota samples can be stored under optimal conditions and, in the not-too-distant future, can be autologously transplanted to restore homeostasis of the innate microbiota when dysbiosis is diagnosed.

Conclusion: Investing in personal microbiota interventions in early life, especially in low SE neighborhoods, can induce a win-win situation, where health inequalities are attenuated along with increased overall productivity.

Keywords: Microbiome - social - impact of food

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HPV:The unpredictable effect of Acyclovir and the mechanism of action of Immunotherapy

(Research Paper)

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Introduction: Viral warts, caused by the human papillomavirus (HPV), are common skin lesions that can be both physically and emotionally distressing. The treatment of viral warts has been a subject of ongoing research, with various modalities being explored for their effectiveness. In this article, we will delve into the comparative study of intralesional acyclovir and immunotherapy for the treatment of viral warts.

Methods: A literature search on PubMed, Google Scholar, and Web of Science databases used the terms Acyclovir and HPV. Publications that were not available or were not in the English language were excluded, as were publications that were not related to the topic. We have tried to examine specific cases in the treatment of the HPV virus and send a very small part of the research in this manuscript to the Biomedical Congress.

Results: Intralesional acyclovir involves the direct injection of acyclovir, a potent antiviral medication, into the site of the viral wart. The mechanism of action of acyclovir involves inhibiting the replication of the herpes simplex virus, which shares similarities with HPV. By introducing acyclovir directly into the wart, it aims to target the virus at its source and reduce the size and spread of the wart. Immunotherapy, on the other hand, aims to stimulate the body's immune system to recognize and destroy the virus causing the wart. This can be achieved through the use of substances such as interferon or antigen injections, which trigger an immune response against the viral infection. The goal of immunotherapy is to harness the body's natural defense mechanisms to combat the virus and eliminate the wart. When comparing intralesional acyclovir and immunotherapy for the treatment of viral warts, efficacy and safety are paramount considerations. Studies have shown that both modalities have demonstrated varying degrees of success in reducing the size and appearance of viral warts. Intralesional acyclovir has been reported to show promising results in some cases, particularly for warts caused by viruses similar to herpes simplex. Its direct antiviral action can lead to a reduction in wart size and associated symptoms. The choice between intralesional acyclovir and immunotherapy for the treatment of viral warts should be individualized based on factors such as the patient's medical history, the location and size of the warts, and the patient's immune status. Furthermore, considering the perplexity and burstiness of the condition is crucial when determining the most suitable treatment approach. It is important to note that some warts may respond better to one modality over the other, and a comprehensive evaluation by a healthcare professional is essential in determining the most effective course of treatment.

Conclusion: In conclusion, the comparative study of intralesional acyclovir and immunotherapy for the treatment of viral warts highlights the importance of considering both modalities as viable options. Each approach presents unique benefits and potential drawbacks, and the selection of treatment should be tailored to the individual patient's needs and characteristics. As research in this field continues to evolve, a deeper understanding of the mechanisms and efficacy of these treatments will further inform clinical decision-making for the management of viral warts.

Keywords: Acyclovir /Immunotherapy/HPV

Human Decellularized Endometrial Scaffold Seeded by Myometrial Smooth Muscle Cells Supports the Differentiation of Human Endometrial Mesenchymal Cells to Epithelial and Stromal Cells

(Research Paper)

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٢.
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Introduction: This study designed to evaluate the co-culturing of human mesenchymal endometrial cells (EMCs) and myometrial smooth muscle cells (MSMCs) in decellularized scaffold as a natural bioscaffold to formation of the endometrial-like structure.

Methods: Following decellularization of the human endometrium, Human mesenchymal endometrial cells were seeded onto decellularized human endometrium using centrifugation at different speeds and times, resulting in ١٥ experimental subgroups. We analyzed the number of residual cell count in suspension in all subgroups and selected the method with the lower number of suspended cells for further investigation. Then, the human endometrial mesenchymal cells and the myometrial muscle cells were seeded on the decellularized tissue and cultured for ١ wk; then, differentiation of the seeded cells was assessed by morphological and gene expression analysis.

Results: Centrifugation at ٦٠٢٠ g for ٢ minutes proved to be the most effective cell seeding method, resulting in the number of seeded cells and the lowest number of residual cells in suspension. The recellularized scaffold displayed endometrial-like cells with surface protrusions, while the stromal cells exhibited spindle and polyhedral morphology. The myometrial cells almost were homed at the periphery of the scaffold and mesenchymal cells penetrated in deeper parts similar to their arrangement in the native uterus.The more expression of endometrial-related genes such as SPP١, MMP٢, ZO-١, LAMA٢, and COL٤A١ and low-level expression of the OCT٤ gene as a pluripotency marker confirmed the differentiation of seeded cells.

Conclusion: Endometrial-like structures were formed by the co-culturing of human endometrial mesenchymal cells and smooth muscle cells on the decellularized endometrium

Keywords: Decellularized endometrium; Epithelial-like cells; Gene expression; mesenchymal endometrial cell

Human Papilloma Virus Vaccination (Review)

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Introduction: Introduction: Human papillomavirus (HPV) is a circular, non-enveloped, double-stranded DNA virus belonging to the Papillomaviridae family. HPV infection is usually cleared naturally by the immune system. However, it can cause cancer when the immune system is weak or has a latent infection, especially genotypes ١٦ and ١٨. Types of human papillomavirus are divided into two high-risk groups based on their carcinogenicity, including strains (١٦, ١٨, ٣١, ٣٣, ٣٥, ٣٩, ٤٥, ٥١, ٥٢, ٥٦, ٥٨, ٥٩, ٦٦, ٦٥) and low-risk strains (٦, ١١, ٤٢. ٤٣,٤٤) are divided. The HPV virus can remain in the skin and cause genital warts. Genital warts that appear on the genitals increase the risk of cervical cancer. Chronic infections with high-risk HPV strains like HPV-١٦, HPV-١٨, HPV-٣١, and HPV-٣٣, can cause malignancy. In all papillomaviruses, a single genome encodes approximately eight open-reading frames (ORF). The ORF has three functions: early viral function (E١-EV) and late viral function (L١, L٢)and long Control Region (LCR) segment. LCR genes are necessary for viral DNA replication and transcription. E٦ and EV are the two main proteins in the viral carcinogenesis pathway. L١andL٢encode structural capsid proteins. HPV is usually transmitted through sexual activity through contact with infected epithelium of the cervix, vagina, vulva, penis, or anus, possibly through microscopic scratches in the mucosa or skin. Papillomaviruses infect mucosal and skin epithelial membranes and cause cell proliferation. The viral life cycle begins with the differentiation of infected epithelial cells and the infection of basal epithelial cells, possibly at the sites of injury. Where the viral genome is created, the nuclear plasmid and early genes are expressed. In immunosuppressed patients, the incidence of warts and cervical cancer is higher. Also, all cancers related to HPV are prevalent in people with HIV.

Methods: Methods: By reviewing various data and articles published in Google Scholar, PubMed, and Scopus, based on this information, we realized that preventive vaccines could activate humoral immunity and, with the production of virus-neutralizing antibodies, inhibit viruses. Vaccines to prevent high-risk HPV infection Available in most countries, the vaccines are Gardasil and Cervarix. These vaccines use HPV L١ capsid proteins that are non-infectious, called virus-like particles(VLP).

Results: Result: The three different approved vaccines are designed to protect against infection from various numbers of HPV types. Cervarix: It is a bivalent vaccine that Protects against HPV types ١٦ and ١٨. ٤vHPV: It is a quadrivalent vaccine that Protects against HPV types ٦, ١١, ١٦, and ١٨. ٩vHPV: It is a nine-valent vaccine that Protects against HPV types ٦, ١١, ١٦, ١٨, ٣١, ٣٣, ٤٥, ٥٢, and ٥٨. The ٩vHPV vaccine is usually recommended for men and women aged ٩-٤٥ years to prevent dysplastic and diseases caused by HPV. The vaccine is injected intramuscularly. People under the age of ١٥ can

inject two doses at an interval of ٦ to ١٢ months or three doses at ٢ and ٦ months. People over ١٥ should inject three doses in ٢ to ٦ months.

Conclusion: Conclusion: HPV is a common virus that can be transmitted from person to person, and this virus is venturesome because it is carcinogenic. Knowing how to prevent HPV infection or HPV-related cancers is essential. HPV vaccination, like most vaccinations, is an effective and safe way of preventing vaccination-specific HPV infection as well as reducing HPV-related neoplasms. As we learn more about the immunity mechanisms against HPV infection, we will have better insights and strategies for designing effective vaccines. Although somewhat difficult, every effort should be made to publicize the efficacy and safety of HPV vaccination.

Keywords: Keyword:Human papilloma virus(HPV),Gardasil,cancer,vaccination,infection

Human Umbilical Cord MSC-Derived Exosomes Treatment Reduces Liver Inflammation and Improves Liver Function in an Experimental Model of Liver Fibrosis (Research Paper)

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Introduction: Cirrhosis is one of the causes of increased mortality in developing countries. Determining the prevalence of cirrhosis is difficult and may be much more than what is reported because the previous stages underlying it, including liver fibrosis, are asymptomatic and the disease is not diagnosed during that period. Liver fibrosis is a wound-healing response characterized by the accumulation of extracellular matrix (ECM) following liver injury, leading to organ failure through inflammation and the release of fibrotic biomarkers. Therefore, the development of anti-inflammatory and antifibrotic therapies is desired. Mesenchymal stem cells (MSCs) with their anti-inflammatory and immunomodulatory properties are increasingly being used as a treatment for liver fibrosis. Studies show that the therapeutic effects caused by MSC are mostly paracrine and through extracellular vesicles, including exosomes. In addition to having the same function as their parent cells, exosomes also have advantages such as smaller size and less complexity, thus being easier to produce and store, low toxicity, and low immunogenicity. This study aims to investigate the effect of Umbilical Cord mesenchymal stem cells derived exosomes (UCMSC-EX) in an established carbon tetrachloride (CCl_4)-induced liver fibrosis mouse model

Methods: The UC-MSCS were isolated by the explant method, in such a way that after removing the blood vessels, small pieces of the human umbilical cord were cultured in a flask. After evaluating the morphology of the MSCs, the multipotency of the isolated cells was checked with their ability to differentiate into osteocytes and adipocytes. In addition, the immunophenotype of UCMSC in terms of the expression of CD٧٣, CD٩٠, CD١٠٥, CD٣٤, and CD٤٥ was studied by flow cytometry. The exosome was isolated from the supernatant from culture of the human umbilical cord-derived mesenchymal stem cell. Exosomes are purified by commercial kit and characterized by transmission and scanning electron microscopy, dynamic light scattering, and bicinchoninic acid assay. We established a ٦-week carbon tetrachloride (CCl_4)-induced mouse model of liver fibrosis, then we administered UCMSC-EX for three weeks. The liver function and inflammation were assessed by biochemistry and Real-time PCR.

Results: Biochemical analyses were performed to evaluate liver function recovery after UCMSC-EX treatment. Serum levels of ALT, AST, TBIL, and ALP were significantly suppressed in groups treated with UCMSC-EX compared to the untreated liver fibrosis group. In addition, the serum level of Alb in

the UCMSC-EX treated group was higher than that of the untreated liver fibrosis group. These results indicate the improvement of liver function in the UCMSC-Exosomes treated group. Next, we detected the expression of inflammatory factors in liver tissue by qRT-PCR. Compared with the untreated liver fibrosis group, the expression of inflammatory factors including IL-٦, IL-١٧, and STAT٣ was significantly decreased in the UCMSC-EX treatment group in comparison to liver fibrosis group. Therefore, treatment with UCMSC-EX had anti-inflammatory effects, as evidenced by improved liver function and reduced inflammation.

Conclusion: Taken together, our results clearly show that UCMSC-EX treatment reduces liver fibrosis in vivo. In addition, the administration of UCMSC-EX reduces liver fibrosis by restoring liver function and inhibiting the expression of pro-inflammatory genes. Therefore, the use of UCMSC-EX provides a new and promising therapeutic strategy for liver fibrosis in the clinical setting.

Keywords: Liver fibrosis, Mesenchymal stem cell, Exosomes, Inflammation, IL-٦

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Hyaluronan Hydrogel Reinforced with Drug-Loaded Chitosan Nanoparticles for Cartilage Tissue Regeneration (Research Paper)

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۲.

Introduction: Cartilage lesions, especially osteoarthritis, usually arise from aging, trauma, or obesity and require medical intervention due to the poor self-healing capacity of articular cartilage. Two major challenges need to be addressed in the repair of cartilage tissue. The first is the regeneration of articular cartilage in an active inflammatory environment. The second is to fill the space of the defect with tissue that has the same mechanical properties as articular cartilage tissue.

Methods: This study selected chitosan and oxidized hyaluronic acid (oxi-HA) to synthesize nanoparticles and an injectable hydrogel. Chitosan nanoparticles were loaded with a small anti-inflammatory molecule (fisetin) and a chondrogenic and chondroprotective agent (kartogenin). Oxidized hyaluronic acid was cross-linked with adipic acid dihydrazide (ADH) to form an injectable hydrogel. Then, the different concentrations of chitosan nanoparticles were embedded in oxi-HA/ADH hydrogel to investigate their effect on mechanical properties, gelation time, and controlled release of drugs.

Results: The results showed that incorporating drug-loaded chitosan nanoparticles into the oxi-HA/ADH hydrogel improved its drug release and increased its mechanical properties. Real-time PCR results showed that the COL۲A۱ mRNA expression was significantly increased in the hydrogel containing both drug-loaded chitosan nanoparticles compared to others. In contrast, INOS, TNF-α, and MMP-۱۳ expression was significantly reduced in this group compared to the other groups.

Conclusion: In conclusion, based on the results of this study, this injectable nanoparticle hydrogel system may be a promising technique for repairing damaged cartilage tissue by rapidly suppressing inflammation and supporting cartilage regeneration and requires further investigation in an animal model of OA.

Keywords: Chitosan Nanoparticles, Drug Delivery System, Cartilage Tissue Engineering

Hypoxia-Induced Motor and Sensory-Cognitive Deficits in Drosophila melanogaster: Insights from Chemotaxis, Phototaxis, and Locomotion Assays (Research Paper)

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Introduction: Ischemic stroke is a leading cause of motor and cognitive impairments, highlighting the need for effective model organisms to understand its underlying mechanisms. Drosophila melanogaster, with its well-characterized nervous system, rapid generational turnover, and high genetic similarity to humans, serves as a valuable model for studying ischemia-induced neurological deficits. Approximately ٧٥٪ of human disease-associated genes and the entire hypoxia-induced cascade are conserved between flies and humans, making Drosophila particularly useful for investigating hypoxia's effects on brain function. This study aims to assess motor and sensory-cognitive impairments in Drosophila following hypoxic exposure, using behavioral assays such as chemotaxis in response to acetic acid, phototaxis, and locomotion . These assays allow for a multi-dimensional evaluation of sensory processing, decision-making, and motor coordination, providing insights into neurological deficits induced by stroke.

Methods: Fly Preparation Wild-type Drosophila melanogaster (٠-٥ days old) were divided into control and experimental groups. Hypoxia was induced at ٢,٥, ٤, and ٦ hours using a device that reduces oxygen levels while maintaining environmental conditions. After recovery, behavior was assessed through various assays. Chemotaxis Assay A ٢٠ cm vial divided into four areas was used to test chemotaxis. A cotton ball saturated with ٥٪ acetic acid was placed at the top. Flies' positions were recorded, focusing on their movement away from the acetic acid toward the farthest area. Locomotion Assay General motor activity was assessed in an arena where flies could walk freely without flying. Movements were tracked to evaluate total distance traveled, speed, and rest periods. Hypoxia-treated flies were compared with controls to assess motor deficits. Phototaxis Assay Two setups were used: ١. Dark Box Setup: Flies were placed in a dark box connected to a ٢٠ cm vial divided into four parts. After ٣٠ minutes of darkness, a light source was turned on, and flies' positions were recorded to measure their light response. ٢. Two-Vial Setup: Two connected vials were used, one covered in aluminum foil to create darkness. A light source illuminated the other vial, and flies' positions in the light or dark vial were recorded.

Results: Flies exposed to hypoxia showed impairments in all assays. In the chemotaxis assay, control flies consistently moved to the farthest section of the vial, avoiding the acetic acid. In contrast, some hypoxia-treated flies responded correctly, but over half wandered, suggesting sensory or cognitive disruptions. In the locomotion assay, hypoxia-treated flies traveled shorter distances and rested more frequently, indicating increased fatigue and impaired motor function. For phototaxis, in the dark box setup, more than half of the control group stayed near the light, while the ischemia group showed a reduced tendency to remain there. Many ischemia-treated flies initially moved toward the

light but dispersed randomly after a few minutes. In the two-vial setup, control flies mostly chose the illuminated vial, whereas fewer hypoxia-treated flies did so, further highlighting sensory deficits.

Conclusion: These results indicate that flies exposed to hypoxia under well-controlled conditions show clear deficits across behavioral assays. Impairments in motor function were evident in the locomotion assay, while disruptions in sensory-cognitive processes, such as decision-making and memory, were observed in the chemotaxis and phototaxis assays. This suggests that ischemic injury affects both movement and higher-order neural functions, offering insights into the broader effects of brain ischemia.

Keywords: Ischemia, hypoxia, brain stroke, Drosophila melanogaster, Locomotion assay, Chemotaxis assay, photo

Identification and analysis of biomarkers involved in Multiple Sclerosis (MS) by bioinformatics tools (Research Paper)

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Introduction: Multiple sclerosis (MS) is a chronic autoimmune disease affecting the central nervous system, leading to progressive disability. The global prevalence of MS has been rising, with over ٢,٨ million people affected worldwide. The disease presents significant challenges due to its complex etiology and varied clinical presentations. Bioinformatic analysis is crucial for identifying potential biomarkers that could aid in early diagnosis and personalized treatment approaches, addressing the unmet needs in MS management.

Methods: The dataset GSE٢١٩٤٢ was downloaded from the GEO database. Subsequently, analyses were performed on the samples within the dataset using both the GEO٢R tool and R programming. Up-regulated and down-regulated genes were identified based on GEO٢R and R analysis (adjpval < ٠,٠٥). A Venn diagram was then created to determine common genes between GEO٢R and R results for both up-regulated and down-regulated genes. Then these common genes analyzed using the Enrichr database to determine associated biological processes, KEGG pathways and related diseases. Next, the identified up-regulated and down-regulated genes were imported into Cytoscape for centrality analysis, leading to the identification of hub genes

Results: The results obtained from the Enrichr database, based on the highest p-value significance, are as follows: Up-regulated genes: Biological Process: B Cell Receptor Signaling Pathway, Antigen Receptor-Mediated Signaling Pathway, Hydrogen Peroxide Catabolic Process, Amyloid Fibril Formation, Oxygen Transport, Carbon Dioxide Transport, Antibacterial Humoral Response, Gas Transport, Regulation Of B Cell Activation. Related Disease: Hemoglobinopathies, Chronic Lymphocytic Leukemia, Burkitt Lymphoma, Leukemia, Precursor B-cell Lymphoblastic Leukemia, B-Cell Lymphomas, Immunologic Deficiency Syndromes. KEGG Pathway: B Cell Receptor Signaling Pathway, Hematopoietic Cell Lineage, Transcriptional Misregulation in Cancer, Epstein-Barr Virus Infection, Primary Immunodeficiency, NOD-like Receptor Signaling Pathway, RNA Transport. Down-regulated genes: Biological Process: Regulation Of Apoptotic Process, Regulation Of Protein Autophosphorylation, Regulation Of ERK١ And ERK٢ Cascade, Regulation Of Cell Communication By Electrical Coupling, Regulation Of Innate Immune Response, Positive Regulation Of Peptidyl-Threonine Phosphorylation. Related Disease: Tuberculosis, Neoplasm Metastasis, Lymphoma, Sjogren's Syndrome, Multiple Sclerosis, Lung Carcinoma, IGA Glomerulonephritis, Post-Traumatic Stress Disorder, Inflammatory Bowel Diseases. KEGG Pathway: Neurotrophin Signaling Pathway, Necroptosis, Tuberculosis, Lipid and Atherosclerosis, Hepatitis B, Natural Killer Cell-Mediated Cytotoxicity, Pertussis, Antigen Processing and Presentation, MAPK Signaling Pathway, D-Glutamine and D-Glutamate Metabolism. The hub genes identified in Cytoscape were as follows: Up-regulated genes: CD١٩, JUN, BRD٤, CXCL٨, ATRX. Down-regulated genes: TP٥٣, ACTB, IFNG, CALM٣, SRSF١, HNRNPH١, CANX, LAMP١.

Conclusion: The analysis reveals enhanced immune activation and disrupted signaling pathways in MS, with up-regulation of key immune-related genes and down-regulation of genes involved in cellular stress and neuronal survival. These findings suggest critical targets for potential therapeutic interventions.

Keywords: MS - Multiple Sclerosis - Immune deficiency - bioinformatics - dysregulated genes

Identification of mutations in the OFD١ gene among Lorestani families (Research Paper)

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Introduction: This study aimed to investigate the presence of mutations in the OFD١ gene among individuals from Lorestan, a region with a high prevalence of certain genetic disorders. The OFD١ gene is known to be associated with Oral-Facial-Digital syndrome type I (OFD١), a rare genetic condition characterized by a range of clinical features including oral, facial, and digital abnormalities. Despite the identification of various mutations in the OFD١ gene in different populations, this study represents the first report of a missense mutation in the Lorestani population, highlighting the genetic diversity and the need for targeted genetic screening in this region.

Methods: Genomic DNA was extracted from the blood sample. Whole Genome Sequencing was performed, and the results were confirmed by Sanger sequencing. In silico tools such as Provean web server was utilized to predict the functional effect of amino acid substitutions. I-Mutant was used to calculate the change in Gibbs' free energy (ΔΔG) and assess OFD١.

Results: Exome sequencing demonstrated a missense mutation c.١٣٩٧C>G, p.A٤٦٦G in exon ١٤ of the OFD١ gene in Lorestani families. Sanger sequencing confirmed this Missense variant in the OFD١ gene. According to Provean web server web server analysis, p.A٤٦٦G mutation in OFD١ can be classified as a deleterious mutation with Provean score of approximately -٢. ٥٨٠. The I-Mutant analysis demonstrated a ΔΔG value of -١,٧٠, indicating a significant reduction in protein stability.

Conclusion: The identification of the c.١٣٩٧C>G missense mutation in the OFD١ gene in Lorestani families, confirmed by Sanger sequencing, and characterized as deleterious by in silico analyses, underscores the importance of genetic screening in populations with a high prevalence of OFD١ syndrome. The significant reduction in protein stability predicted by I-Mutant, along with the deleterious classification by Provean, suggests that this mutation may contribute to the clinical manifestations of OFD١ syndrome in the affected individuals. These findings expand the spectrum of

known OFD\ mutations and provide valuable insights into the genetic basis of OFD\ syndrome in the Lorestani population, which could inform future diagnostic and therapeutic strategies.

Keywords: missense mutation, OFD\, In silico tools

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Identification of a novel homozygous mutation in LRAT gene associated with early-onset severe retinal dystrophy (Research Paper)

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Introduction: Leber congenital amaurosis (LCA) is one of the most severe eye dystrophies characterized by severe vision loss at an early stage and accounts for approximately ٥٪ of all retinal dystrophies. The genetic basis of LCA is highly heterogeneous and to date, more than ٢٥ genes have been implicated in the pathogenesis of LCA. Investigating genes and related mutation in heterogeneous disorders by conventional methods is time- and cost-consuming. This study aimed to use WES to investigate an Iranian family with a member affected by LCA.

Methods: The present study reported a novel frameshift mutation c.٤٥٩delC in the lecithin retinol acyltransferase (LRAT) gene associated with early onset retinitis pigmentosa. We used a combination of WES and detailed family segregation analysis to identify the underlying genetic defect. Segregation analysis showed that the proband's parents were heterozygous carriers, which is consistent with an autosomal recessive inheritance pattern, while the mutation was not found in proband wife.

Results: LRAT is necessary for producing ١١-cis-retinol and regeneration of the chromophore needed for rhodopsin and cone photopigments. Deficiency in LRAT causes a lack of the ١١-cis-retinal chromophore and lead to lower levels of functional visual pigment and causing severe vision problems. The identified mutation highlights the critical role of LRAT in retinal health and disease.

Conclusion: Our research demonstrates how effective next-generation sequencing (NGS) technologies are in detecting rare genetic mutations that cause hereditary retinal dystrophy. This study also emphasizes the critical role of genetic diagnosis in early intervention and management of LCA. By identifying the exact genetic mutations involved, we can develop targeted gene therapies, which could help preserve vision and enhance the quality of life for those affected. This research adds to the growing list of mutations found in the LRAT gene and highlights the importance of genetic analysis in understanding the causes of LCA. It also paves the way for future treatments, like gene replacement and editing techniques, which offer hope for conditions such as LCA.

Keywords: LCA, WES, NGS, LRAT

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Identification of Acinetobacter baumannii biofilms in cystic fibrosis patients using molecular methods in Urmia, Iran, ٢٠٢٤ (Research Paper)

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Introduction: Biofilm formation is an endless cycle, in which organized bacterial communities are housed in a matrix of extracellular polymeric materials (EPS) that bind microbial cells to a surface. The persistence of chronic Acinetobacter baumannii lung infections in cystic fibrosis (CF) patients is due to biofilm-growing mucoid (alginate-producing). The purpose of this study is to investigate the effect of antibiotic treatment in preventing the formation of biofilm caused by Acinetobacter baumannii.

Methods: Laboratory identification of Acinetobacter baumannii isolates by standard microbiological and biochemical methods. The susceptibility of the isolates to different antibiotics was determined using the disk diffusion method on cation-adjusted Müller-Hinton agar. Antibiotic discs tested with ceftazidime, piperacillin/tazobactam, ciprofloxacin, and levofloxacin, Were treated with gentamicin, amikacin, tobramycin, imipenem and meropenem. The adhesive biofilms were fixed with ١٠٠٪ methanol for ١٥ minutes, the solutions were removed and the plate dried. The biofilms were stained with ٢٠٠ µl of ٠,١٪ crystalline violet for ١٠ minutes at room temperature and then washed with water and dried. Biofilm was obtained in each well by treatment with ٢٠٠ µl of ٩٦٪ ethanol for ٣٠ minutes. All Acinetobacter baumannii isolates for the three genes encoding biofilm, algD, and psID using the polymerase chain reaction (PCR) method, using specific primers.

Results: ١٨,٣٦٪ produce strong biofilms. ٣٠,١٥٪ produced average biofilm. ٣١,٧٥٪ produced poor biofilm, while ١٩,٧٤٪ of isolates did not produce as film-free. Acinetobacter baumannii's development of resistance to many antimicrobial agents is a major challenge in controlling its infections.

Conclusion: Acinetobacter baumannii infections typically progress from the acquisition of a single environmental strain to an extensive genetic and phenotypic adaptation to the lung environment. Chronic infections are commonly caused by a single Acinetobacter baumannii lineage. However, different lineages have been found in isolates from the same sputum sample or obtained longitudinally from the same patient. Given the high intraspecific diversity of Acinetobacter baumannii in the CF lung, caution is warranted when assuming that one or more isolates are the cause of infection in a CF patient. CF patients, especially at a young age, should be checked for this infection every month.

Keywords: Acinetobacter baumannii, biofilms, cystic fibrosis, molecular methods

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Identification of breast cancer hub genes using bioinformatic analysis (Research Paper)

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Introduction: Breast cancer is the most frequently diagnosed cancer in women worldwide. This study aimed to elucidate the potential key candidate genes and pathways in breast cancer.

Methods: GSE۳۸۹۵۹ and GSE۴۵۸۲۷ were selected from the Gene Expression Omnibus (GEO) database, differentially expressed genes (DEGs) with an adjusted p-value < ۰,۰۵ and a logFC ≥ ۲ and logFC ≤-۲ were identified. Common DEGs of two datasets were identified using the GEO۲R tool. The Kyoto Encyclopedia of Genes and Genomes (KEGG) and Gene Ontology (GO) databases were used to identify pathways. Protein-protein interactions (PPIs) analysis was performed by using the Cytoscap and Gephi. A GEPIA analysis was carried out to confirm the target genes.

Results: ۳۲۲ common differential expressed genes have been identified through the use of GEO and PPI, respectively. The GO and KEGG pathways analysis showed DEGs were enriched in Cell cycle. The expression of ۲ genes CDK۱, CCNB۱ showed a significant difference between normal and tumor samples, have been identified by GEPIA analysis.

Conclusion: In this study, the hub genes and their related pathways involved in the development of BRCA were identified. These genes, as potential diagnostic biomarkers may provide a potent opportunity to detect BRCA at the earliest stages, resulting in a more effective treatment.

Keywords: Breast cancer, BRCA, PPI network, Diagnostic biomarkers

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Identification of disorder-causative variant c.۱۳۹G>A in ADA۲ gene in an Iranian family with a patient With vision disorder using WES technique (Research Paper)

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Introduction: Heterogeneous and syndromic diseases involve numerous genes and are not easily diagnosable using traditional methods such as PCR, RFLP and ARMS. Next-generation sequencing (NGS) provides a more comprehensive approach for diagnosing such diseases. NGS is a high-throughput DNA sequencing technology that allows for the rapid and efficient sequencing of a large amount of DNA. NGS has revolutionized genomic research and clinical diagnostics due to its ability to generate vast amounts of sequencing data in a short amount of time, providing valuable insights into genetic variations and mutations. NGS has been widely used in various fields, including genomics, personalized medicine, and cancer research. The aim of this study is to diagnose the genetic basis of a syndrome with different symptoms using WES, a subclass of NGS for analyzing all exons. Heterogeneous diseases can be challenging to diagnose and manage due to the involvement of multiple genes and mutations. Similar studies have focused on utilizing NGS technology to analyze genetic data and identify mutations in affected individuals and carriers. It is crucial to alert parents about the risk of passing on the disease to their offspring and to provide early diagnosis and intervention options.

Methods: The proband was a ۱۳ years-old boy with recurrent stroke and vision disorder with consanguinity marriage in parents. The patient's DNA was extracted and then WES was performed to identify the disease-causative variant. To confirm WES-reported variant in the proband, primers were designed for the variant. Then, co-segregation analysis was done in the parents and brother of the proband.

Results: WES results identified variant c.۱۳۹G>A in ADA۲ gene in the prband, who was homozygous for the mutation. The healthy parents of the patient were found to be heterozygous, and the patient's brother was also in homozygous situation. He showed the disorder-related symptoms. The inheritance pattern for disorder was suggested as autosomal recessive.

Conclusion: NGS technology plays a crucial role in the precise diagnosis of heterogeneous diseases, enabling better understanding of genetic factors and more effective management strategies. By utilizing NGS, we can improve the early detection and management of such diseases, ultimately benefiting patients and their families.

Keywords: NGS, WES, Heterogeneous diseases, variant

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Identification of ferulic acid derivatives for monkeypox virus inhibition by molecular docking approach (Research Paper)

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Introduction: Monkeypox virus (MPXV) is a zoonotic virus of the Poxviridae family that has recently re-emerged in various countries worldwide. Current treatments are limited and there is a need for new treatment options. The A٤٢R profile-like protein of MPXV is involved in cell development and motility, making it a critical drug target, and inhibiting it may prevent virus replication. This study aims to determine the antiviral potential of ferulic acid derivatives in silic on against the monkeypox virus.

Methods: Molecular docking approach was used to investigate the binding affinity of ferulic acid derivatives against Profilin-like Protein A٤٢R protein of MPXV by AutoDock software. The ٣D structures of ferulic acid derivatives and Tecovirimat (control compound) were obtained from Pubchem and converted into PDB format by AutoDock software. Then, these compounds were docked into the binding site of A٤٢R Profilin-like Protein (PDB ID: ٤QWO) by AutoDock software. Also, the pharmacokinetic properties and drug-likeness of the molecules were investigated using SwissADME analysis.

Results: Ferulic acid derivatives including ferulic acid, p-coumaric acid, and sinapic acid were showed strong binding affinity toward Profilin-like Protein A٤٢R protein of MPXV through molecular docking. Ferulic acid derivatives interacted with the amino acids of the receptor active site via hydrogen bonding with E٨٣, R١١٩, D١٢٣, R١١٥, and TV١. Furthermore, their ADME results also confirmed their compatibility as therapeutic options for the treatment of monkeypox.

Conclusion: These derivatives can be considered as A٤٢R Profilin-like Protein inhibitors of the monkeypox virus after further studies.

Keywords: Monkeypox virus, A٤٢R Profilin-like Protein, Ferulic acid derivatives, Molecular Docking

Identification of hub Genes and pathways in hepatitis C virus-associated hepatocellular carcinoma

(Research Paper)

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Introduction: Hepatitis C is an infection caused by a virus that affects the liver and gets worse over time. It is one of the leading causes of liver cancer in other parts of the world.There is a very poor chance of diagnosing these diseases at an early stage. The objective of this study was to identify the genes and pathways involved in the development of this disease by using the biological system as a tool.

Methods: As part of this study, GSE٢٩٧٢١ from the GEO site was examined. By normalizing the data using R software, we were able to identify DEGs with a p-value < ٠,٠٥ and a log |FC|> ٢,٦. Using the Kyoto Encyclopedia of Genes and Genomes (KEGG) as well as the Gene Ontology (GO), pathways involved in the process of HCC cancer were identified. In order to identify hub genes with protein-protein interaction analysis (PPI), the software packages Cytoscap and Gephi were used. A GEPIA analysis was performed in order to confirm the biomarker and target genes.

Results: A total of ٤٢٠ DEGs have been identified. Through the use of PPI, ٩٤ hub genes were identified. By using enrichment analysis, it was demonstrated that these genes play a role in the development of HCC through cAMP signaling pathways, phenylalanine, tyrosine, and tryptophan biosynthesis, ubiquitin mediated proteolysis, natural killer cell-mediated cytotoxicity, and ErbB signaling pathways. Through GEPIA, AKR١D١ and CYP٣٩A١ genes were identified as significant in tumor and non-tumor samples.

Conclusion: This study was conducted to identify the pathways involved in the development of HCC. As a result of identifying biomarkers, this disease can be detected at the earliest stages of the disease, and by identifying target genes, it is possible to increase the survival rate of HCC patients.

Keywords: Hepatocellular carcinoma, HCV, PPI network, biomarker, target

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Identification of Key Genes for Early Diagnosis of Diabetic Kidney Disease Using WGCNA Analysis: Insights into Disease Mechanisms at the Transcriptome Level (Research Paper)

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Introduction: Diabetic kidney disease (DKD) is one of the most serious complications of diabetes, primarily caused by microvascular damage in the kidneys. Early diagnosis of DKD is critical for preventing its progression, yet reliable biomarkers remain limited. This study aims to identify key genes involved in the early stages of DKD through transcriptome-level analysis, providing insights into potential biomarkers for early diagnosis and understanding the underlying mechanisms of disease development.

Methods: We performed a weighted gene co-expression network analysis (WGCNA) on renal glomerular tissue samples from the publicly available GSE۳۰۵۲۸ dataset. Through WGCNA, key gene modules related to DKD were identified. Gene ontology (GO) and REACTOME pathway enrichment analyses were employed to explore the biological roles of these genes.

Results: Four gene modules were identified as significant through WGCNA, and subsequent enrichment analysis revealed their involvement in pathways such as immune system regulation, collagen biosynthesis, striated muscle contraction, and neutrophil degranulation. From these modules, four hub genes—CHI۳L۱, RARRES۱, TNNT۲, and PCOLCE۲—were identified as potential early biomarkers for DKD.

Conclusion: The identification of CHI۳L۱, RARRES۱, TNNT۲, and PCOLCE۲ provides novel insights into the molecular mechanisms driving DKD. These genes represent promising targets for early diagnosis and offer potential avenues for therapeutic intervention in DKD.

Keywords: Diabetic Kidney Disease (DKD); Biomarkers; WGCNA; CHI۳L۱; RARRES۱

Identification of key Hub Genes in GBM stem cells using Microarray Analysis and Systems Biology Approaches (Research Paper)

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Introduction: Glioblastoma (GBM) is the most prevalent form of primary malignant brain tumor. Glioblastoma stem cells (GSCs) are characterized by their ability to self-renew and the capacity to initiate tumors. GSCs could be a factor for the low effectiveness of cancer therapies and for the short relapse time. For the efficient targeting of GSCs, a comprehensive understanding of their biological mechanisms is indispensable. Microarray technology has been revolutionizing gene expression profiling in recent years, enabling high-throughput analysis of transcriptomic changes across various conditions. By identifying differentially expressed genes, we can gain insights into the underlying molecular mechanisms driving these changes. However, to fully comprehend the impact of these genes, systems biology approaches can be employed to investigate their interactions within biological networks. In this study, we aimed to identify key genes involved in GSCs using microarray data, differential gene expression (DEGs) analysis, and systems biology tools.

Methods: We applied publicly available microarray data from Gene Expression Omnibus (GEO) to assess DEGs of GSE٢٥٣٤٠٠ by using Transcriptome Analysis Console (TAC) and normalized data of three stem-like state samples and three differentiated state samples of NCH٤٢١k cell line to identify significantly upregulated genes. Subsequently, to further narrow down the most biologically significant genes, the result of overexpressed genes was used to construct a protein-protein interaction (PPI) network using the STRING database. The constructed network was visualized using Cytoscape. Degree, Betweenness Centrality, Closeness Centrality and EigenVector unDir were the four topological measures that were taken into account in this research. Based on several topological evaluations of PPI-network, the greatest percentage of interactions was used to pick the highest-ranked key genes.

Results: From dataset with NCBI accession ID GSE٢٥٣٤٠٠, we have identified from ٤٨٢٢٦ total genes, ٧٢٨ genes were upregulated and ٢٥٦ genes were downregulated with fold change >٢ or <-٢ and P-value< ٠,٠٥ as filter criteria in this assessment. We selected upregulated genes with fold change>٣ (٣٠٤ genes) for the PPI network analysis. Using the four topological measures, we detected the top eight key genes that are CXCL١٠, ICAM١, CD٤٤, TGFB١, FOS, AGT, SERPINE, SPP١ as the essential nodes within the interaction network.

Conclusion: In conclusion, our integrative approach, which combined microarray-based differential gene expression analysis with PPI-network assessment disclosed eight key genes CXCL١٠, ICAM١, CD٤٤, TGFB١, FOS, AGT, SERPNE, SPP١ as key regulators in GSC differentiation pathways. These findings suggest potential targets for therapeutic intervention and provide a foundation for future

research into the molecular mechanisms underlying Glioblastoma. Nevertheless, the findings require experimental validation could lead to significant advancements in treatment plans against Glioblastoma.

Keywords: GBM, stem cell, DEGs, PPI-network, Hub Genes.

Identification of novel and known variants in the JAM۲ gene in the Iranian families affected to Primary familial brain calcification (PFBC) (Research Paper)

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Introduction: Primary familial brain calcification (PFBC) represents a rare neurological condition characterized by the abnormal accumulation of calcium deposits within the brain, resulting in severe manifestations such as movement disorders, psychiatric disturbances, and cognitive impairments. Mutations in the JAM۲ gene have been linked to less than ۲٪ of PFBC cases. Additionally, seven other genes have been identified that linked to PFBC (SLC۲۰A۲, PDGFRB, PDGFB, and XPR۱ with dominant (AD), MYORG, CMPK۲, and NAA٦۰ with recessive (AR) patterns of inheritance. Nevertheless, the genetic causes of almost half of the cases with PFBC are still unknown. Until now, no comprehensive genetic analysis has been performed on this disease in Iran. The present study aims to conduct genetic analyses of five families affected by PFBC within Iranian population.

Methods: Five Iranian probands with PFBC were assessed in both clinical and paraclinical contexts. The informed consent form was signed. DNA was extracted from their peripheral blood leukocytes by salting out method. The probands' DNA was subjected to whole-exome sequencing (WES). Splicing and non-synonymous exonic variants were taken to consideration. Subsequently, variants in public genome databases with minor allele frequency (MAF) less than ۰,۰۱ were taken into account. Finally, Sanger sequencing was used to confirm the candidate variants in the probands and co-segregate of those in the family members. Additionally, copy number variations (CNVs) in known PFBC genes and other relevant genes were analyzed using WES data, utilizing tools such as GermlineCNVCaller and AnnotSV. Haplotype analysis was conducted in the JAM۲ gene, using six intragenic single-nucleotide polymorphisms (SNPs) in JAM۲ within the exome data of probands.

Results: Clinical assessments revealed a variety of symptom presentations across the five families studied. Key symptoms included bradykinesia, slurred speech, rigidity, anxiety, obsessive-compulsive disorder (OCD) and headache, with JAM۲-related patients displaying an earlier average age of onset (mean onset: ۱۰,۱ years) in comparison to other PFBC patients. Family analyses highlighted the considerable variability in clinical manifestations, illustrating the inherent heterogeneity of the disorder even among siblings. Through whole-exome sequencing, pathogenic variants were successfully identified in four of the five probands, with the recurrent c.٦٨٥C>T:p.Arg۲۲۹* mutation

in the JAM۲ gene found in three families and a novel c.٤٢٦dup:p.Ser١٤٣Leufs٢٣ variant identified in another. These findings suggest a notable prevalence of JAM۲ mutations in this population. Additionally, haplotypes for all probands were determined, identifying six intragenic SNPs in JAM۲ linked to the disease-causing variant and indicate that p.Arg٢٢٩* may function as a founder mutation or a hotspot codon within Iranian cohorts. It is also noteworthy that one proband lacked any identifiable candidate variant, indicating the possibility of novel genes contributing to the condition. Imaging studies revealed consistent patterns of calcification among JAM۲-related patients, predominantly involving the basal ganglia, thalami, and dentate nuclei, while cortical involvement was notably absent, distinguishing them from other PFBC mutation reports. Furthermore, the presence of p.Arg٢٢٩* was found to correlate with particular brain calcification profiles, supporting the need for further cohort studies to investigate potential phenotype-genotype associations.

Conclusion: The comprehensive examination of JAM۲ mutations in Iranian families with PFBC highlights a greater-than-anticipated prevalence and underscores significant clinical and genetic heterogeneity. The identification of p.Arg٢٢٩* as a likely founder mutation in this demographic expands the spectrum of JAM۲-associated disorder, reinforcing the imperative for ongoing genetic research to discover additional variants implicated in PFBC. The results advocate for increased awareness and further inquiry into the pathophysiological ramifications of JAM۲ mutations across various populations, as well as the critical importance of gene identification in advancing diagnostic and therapeutic strategies for PFBC. This study emphasizes the genetic complexities of PFBC and suggests that progress in genetic research may provide crucial insights into previously unrecognized mutations and their corresponding phenotypic manifestations.

Keywords: Primary familial brain calcification (PFBC); FAHR disease; JAM۲; Whole-exome sequencing (WES); Found

Identification of some Critical Genes Involved in the Development and Progression of Breast Cancer (Research Paper)

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Introduction: Breast cancer is one of the most prevalent and deadly malignancies affecting women worldwide. Despite advances in treatment and early detection, it remains a significant health concern, accounting for a large proportion of cancer-related deaths. Early diagnosis and personalized treatment strategies are critical for improving patient outcomes. However, the complexity of breast cancer at the molecular level, driven by numerous genetic and epigenetic factors, presents a challenge in understanding its pathogenesis and progression. Biomarkers play a crucial role in the fight against breast cancer, serving as tools for early diagnosis, prognosis, and monitoring therapeutic responses. They are measurable indicators of biological processes, including cancer development, and can guide clinicians in selecting the most effective treatments for individual patients. The identification of reliable biomarkers not only improves early detection but also helps in the development of targeted therapies that can minimize adverse effects and maximize treatment efficacy. In recent years, high-throughput technologies such as microarrays and next-generation sequencing have revolutionized the field of cancer research, enabling the comprehensive analysis of gene expression profiles in breast cancer tissues. This study aims to identify some critical genes that play a pivotal role in the development and progression of breast cancer. Understanding these gene expression changes can provide valuable insights into the molecular mechanisms driving breast cancer and highlight potential targets for the development of novel biomarkers and therapies. The ultimate goal is to improve the early detection and treatment of breast cancer, potentially leading to better outcomes for patients and a reduction in the global burden of this disease.

Methods: In the current study, a microarray dataset (GSE٣٦٢٩٥) was downloaded from the Gene Expression Omnibus database (GEO). The fold change (FC) values of individual genes levels were calculated; differentially expressed genes (DEGs) with |FC| >=١ and P-value < ٠,٠٥ were considered to be significant.

Results: A total of ٥٠ samples were analyzed in this study, including ٤٥ cases breast cancer tissue and ٥ normal cases. Using the cut-off criteria, ٤٧٠ down-regulated and ٥١٤ up-regulated genes were found. To identify the most influential genes in each group, we calculated the Degree for all upregulated and downregulated genes and selected the top ٢٠ genes with the highest Degree values. Analysis showed that up-regulated genes involve in HSL-mediated triacylglycerol hydrolysis, lipid digestion, mobilization and transport, integrin-linked kinase signaling and developmental biology. And down regulated genes involved in cell cycle and mitotic, DNA replication, aurora B signaling and G٢/M checkpoints.

Conclusion: These in silico predictions will highlight genes with potential functional roles in breast cancer, making them valuable candidates for biomarker development and targeted therapies.

Keywords: Breast cancer Biomarkers Gene expression Microarray analysis Differentially expressed genes (DEGs)

Identification of T cell epitope-based peptide vaccine from WT١ in Glioblastoma cancer (Research Paper)

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Introduction: Introduction: Glioblastoma (GBM) is the most aggressive primary malignant brain tumor in adults. Its complex genetic and molecular changes lead to rapid cell proliferation and invasion of surrounding tissues. Despite advancements in treatment, including surgery, radiation, and chemotherapy, the prognosis remains poor due to the tumor's infiltrative nature and the challenges posed by the blood-brain barrier. Immunotherapy, particularly peptide vaccines, has emerged as a promising approach to tackle GBM by harnessing the body's immune system to target and destroy cancer cells. Peptide vaccines stimulate an immune response against specific tumor-associated antigens (TAAs) or tumor-specific antigens (TSAs) in GBM cells. These vaccines consist of short sequences of amino acids that mimic parts of these antigens, prompting the immune system to recognize and attack the tumor cells. Studies indicate a high association between histological tumor grades and WT١ levels, often overexpressed in GBM. WT١ expression has been shown via immunohistochemical analysis to be present in all astrocytomas, with higher expression in high-grade tumors. The oncogenic characteristics of WT١ position it as an up-and-coming candidate for immunotherapeutic interventions.

Methods: Methods: The amino acid sequence of the WT١ protein (ID: P١٩٥٤٤) was retrieved from the UniProt database. We aimed to find CTL epitopes in WT-١ that are restricted by the HLA-B*٠٧٠٢ molecules to improve the applicability of WT-١-based immunotherapy. Peptides from WT١ that are restricted by HLA-B*٠٧٠٢ were discovered through the use of three advanced servers: SYFPEITHI, IEBD, and NetMHCpan-٤,١. Epitopes were selected based on their antigenic and immunogenic properties using the VaxiJen v٢,٠ and IEDB Class I Immunogenicity tools, respectively. The ClusPro server was used for Molecular docking of the chosen CTL epitope with a particular Human Leukocyte Antigen (HLA) allele to evaluate their binding affinity. The LIGPLOT program was utilized to map the interaction between the residues of the peptide and HLA-B*٠٧٠٢ in the docked complex. The C-ImmSim tool was employed for in-silico immune simulation to analyze and understand immunogenicity and immune response profiles.

Results: Result: We restricted our future screening to epitopes that presented recurrent patterns in three tools. Subsequently, these epitopes were evaluated based on their binding affinity, antigenicity, and immunogenicity, as demonstrated in Table ١. Although differences were observed

according to the properties, only one CTL p١٦٣ peptide (TPSHHAAQF) exhibited positive antigenicity and immunogenicity. The ClusPro server was utilized to perform molecular docking to assess the binding affinity between the CTL peptide and its respective HLA allele. The complex consisting of the HLA-B*٠٧٠٢ and the CTL peptide with the lowest binding energy score of -٦٢٩,١ kJ/mol was selected. The diagram illustrating the hydrogen bonds and hydrophobic interactions between the peptide and HLA-B*٠٧٠٢ was produced using the LigPlot v١,٤,٥ program (figure١). As part of the peptide-HLA complex, Gln١٥٥, Arg١٥٦, Asp١١٤, Glu١٦٣, Arg٦٢, Asn٦٣, Tyr١٧١, Tyr٥٩, and Thr٧٣ amino acid residues from HLA-B*٠٧٠٢ were implicated in the formation of hydrogen bonds. The findings from the C-ImmSim studies demonstrated that the CTL peptide elicited robust immune responses, characterized by a significant presence of cytotoxic T cells. The production of the cytokines & interleukins was identified along with increased DC and NK populations.

Conclusion: Conclusions: The results of this research show that the identification of a new CTL epitope presented by HLA-B*٠٧٠٢ increases the potential of WT١-based immunotherapy for cancer treatment.

Keywords: Keywords: Glioblastoma, Immunotherapy, WT-١, peptide vaccine, molecular docking

Identifying Cancer Factors, Prevention, and Treatment (Review)

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Introduction: Abstract Cancer is a topic that causes fear and many taboos in society. Despite significant advancements in cancer diagnosis and treatment, it remains one of the leading causes of death worldwide. In addition to genetic factors, environmental and epigenetic factors also play a role in the development of cancer. Cancer starts in certain cells of the body, leading to uncontrolled division and spreading to surrounding tissues. Depending on where cancer cells originate, there are various types of cancer, each requiring specific treatments. The aim of this research is to identify suitable methods for preventing and treating cancer. This study is a review and uses databases like Scopus, ISI, and ScienceDirect. The goal is to examine cancer factors, prevention, and treatment. Introduction Cancer is one of the leading causes of illness and death worldwide (WHO, ۲۰۲۰). The term "cancer" refers to a range of diseases characterized by uncontrolled cell division and invasion of other body parts. Cancer cells grow continuously and can spread to other parts of the body through the lymphatic system (Yaqoubi Juybari et al., ۱۳۹۲). Types of Cancer Cancers are classified into four main groups: Carcinomas: These account for about ۸۵ to ۹۰ percent of cancers and originate from the outer layers of tissues. Lymphomas: These involve abnormal functioning of the lymph nodes or spleen. Leukemias: These tumors originate from the bone marrow and affect the bloodstream.Sarcomas: These arise from connective tissues, muscles, bones, and other organs (Yaqoubi Juybari et al., ۱۳۹۲). Current Treatments Today, common cancer treatments (surgery, chemotherapy, and radiation therapy) often have limited effectiveness. Research on the use of herbal medicines and gene therapy, which have fewer side effects, is ongoing and shows promising results (Dastpeyman et al., ۱۳۹۱). A study by Sharma et al. (۲۰۱۲) indicates that anxiety levels are higher in cancer patients, who also tend to have lower quality of life (Shamsi, ۱۳۹۸). Moreover, innovative drug delivery methods using nanoparticles and bioconjugation techniques have led to successful treatment options for cancer. How Cancer Develops The cause of cancer is damage to DNA, which affects the genes in the cells. In most cases, the body or cells can repair damaged DNA, but cancer cells lack this ability. Damaged genes may be inherited from parents (hereditary cancer) or result from environmental factors such as smoking, radiation, and diet (Sheikh Nejad, ۱۳۸۹; Ghiathvandian, ۱۳۹۱). Cancer Epidemic Almost half of men and more than a third of women worldwide may develop cancer in their lifetime; however, ۷۷ percent of cancers are diagnosed in individuals over ۵۵ years old (Ismaili Zadeh, ۱۳۹۳). Common Symptoms of Cancer Common symptoms of cancer may include sudden weight loss (which could indicate stomach, pancreas, or lung cancer), fever (especially when cancer affects the body's immune system), fatigue, and pain (such as bone or testicular cancer). Skin changes such as darkening, yellowing, redness, itching, or excessive hair growth may also be present (Sheikh Nejad, ۱۳۸۹). Specific Symptoms of Cancer Changes in bowel and urinary habits. Non-healing sores. Unusual bleeding. Lumps or swollen glands. Digestive problems. Coughing or hoarseness (Sheikh Nejad, ۱۳۸۹). Treatment Methods Possible

treatment methods include surgery, radiation therapy, chemotherapy, immunotherapy, bone marrow transplantation, gene therapy, and phototherapy (Shoaa Kazemi et al., ۱۳۹۲).

Methods: This study is a review and was conducted using the following databases: www.isiwebofknowledge.com, www.scopus.com, www.sciencedirect.com.

Results: Cancer is one of the most common diseases worldwide, affecting many people every year. Depending on where cancer cells originate, there are different types of cancer, each requiring specific treatment methods. Sometimes, multiple treatments may be necessary to prevent disease progression. However, the most important factor is the timely diagnosis of the disease, which can be done through laboratory tests, imaging, biopsies, endoscopy, etc

Conclusion: Takeaway This study shows that cancer is a major health issue influenced by genetic and environmental factors. Traditional treatments like surgery and chemotherapy are common, but new methods like herbal medicines and gene therapy with fewer side effects are promising. Understanding the causes and treatments of cancer can help with prevention and improve patients' quality of life. Increasing awareness and research in this area is very important.

Keywords: Cancer, Treatment, Prevention, Cell

Identifying RARRES١ as a Key Biomarker in Cutaneous Melanoma: A Bioinformatic and Experimental Approach (Review)

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Introduction: Cutaneous melanoma of the skin (SKCM) is a very aggressive type of skin cancer that has a negative outlook. It remains a major health concern with rising global incidence rates. Efforts to reduce it have been ineffective. The highest rates are in Australia, while the lowest are in Asia. Melanoma is the twelfth most common cancer worldwide, with higher rankings in Europe and the USA. Incidence rates are roughly similar for men and women. While RARRES١ has been studied in other cancers, its role in SKCM remains unclear. This study aims to investigate the expression, function, and clinical significance of RARRES١ in SKCM. By analyzing gene expression data, genomic alterations, and promoter methylation, the study explored the potential association between RARRES١ and SKCM progression. Additionally, functional experiments were conducted to evaluate the impact of RARRES١ on SKCM cell behavior and tumor growth.

Methods: This study employed a comprehensive approach to investigate the role of RARRES١ in SKCM. The methods included: Data analysis: Utilizing the GSE١٥٦٠٥ dataset from GEO and RNAseq data from TCGA, this study evaluated RARRES١ expression, associated clinical features, prognostic implications, and diagnostic efficacy. Functional enrichment analysis: Co-expression heatmaps and pathway enrichment analyses (GO, KEGG, GSEA) were performed to identify genes and pathways regulated by RARRES١. Immune infiltration analysis: Immune cell infiltration levels were analyzed using ssGSEA algorithm and correlated with RARRES١ expression. Genomic alterations and promoter methylation analysis: cBioPortal, UALCAN, GEO, and EWAS databases were used to assess gene mutations and promoter methylation. Clinical sample analysis: Skin tissue samples were collected for IHC analysis to assess RARRES١ protein expression. In vitro experiments: A٣٧٥ melanoma cells were used to study cell proliferation, migration, apoptosis, cell cycle, ROS production, and autophagic flux. In vivo experiments: RARRES١-overexpressing A٣٧٥ cells were injected into nude mice to evaluate tumor growth. Statistical analysis: Appropriate statistical tests were used to analyze the data, and results were visualized using GraphPad Prism. Ethical considerations, including informed consent and animal welfare, were strictly adhered to throughout the study.

Results: This study investigated the role of RARRES١ in skin cutaneous melanoma (SKCM). Key findings include: Downregulated in SKCM: RARRES١ expression is significantly lower in SKCM compared to normal tissues. Poor prognosis: Low RARRES١ expression is associated with worse clinical features and unfavorable prognosis. Diagnostic potential: RARRES١ has potential as a diagnostic biomarker. Functional effects: RARRES١ inhibits cell proliferation, migration, and promotes apoptosis. Immune modulation: RARRES١ is positively correlated with immune cell infiltration. Genomic alterations: Genetic changes and modifications to the RARRES١ promoter were found to reduce its expression. While mutations were rare, some were identified. Additionally, the

DNA region that controls RARRES1 expression was more heavily modified in metastatic melanoma compared to normal tissues. Regulation of Autophagy and ROS: RARRES1 overexpression induced autophagy but also inhibited autophagosome degradation. This was associated with increased ROS levels and lysosomal dysfunction. Suppresses tumor growth: RARRES1 overexpression suppresses tumor growth in vivo. Collectively, these findings suggest that RARRES1 may function as a tumor suppressor and has potential as a prognostic biomarker and therapeutic target for SKCM.

Conclusion: The current research shows that RARRES1 expression is decreased in skin cutaneous melanoma (SKCM) as a result of changes in the genome and methylation of the promoter. Moreover, there is a correlation between decreased RARRES1 expression and worse overall survival. Functional enrichment analysis and laboratory tests indicate that RARRES1 acts as a tumor suppressor by controlling immune cell infiltration, proliferation, migration, apoptosis, and autophagy. These results emphasize the importance of RARRES1 as a useful prognostic biomarker and a hopeful treatment target for SKCM.

Keywords: Skin cutaneous melanoma, RARRES1, Autophagy, Tumor suppressor

Immune system resistance against the fungus Blastomyces dermatitidis (Review)

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Introduction: Blastomycosis is a pulmonary disease caused by the dimorphic fungus, Blastomyces dermatitidis. Immunosuppression is a major risk factor that affects disease susceptibility, but host immunity is poorly understood. Genetic immunodeficiencies can also impact the disease.

Methods: This review study collected data from scientific databases such as SID, Google Scholar, PubMed, Scopus, and Science of Web to find published texts from ٢٠١٥ to ٢٠٢٤. Keywords included Blastomyces dermatitidis, immune response, interaction, and host. Selected articles were in Persian or English and had full-text access. To evaluate the extracted articles, their relevance to the research topic was first determined using the titles and abstracts. The remaining articles were then examined in terms of content, focusing on the importance and host immune system against Blastomyces dermatitidis fungi. Finally, ١٥ relevant articles were selected.

Results: The results showed that GM-CSF, TNF-α, CD٤+ deficiency, and IL-١٢ and IFN-γ pathways had the most evidence as susceptibility factors for Blastomyces dermatitidis.

Conclusion: The findings of this research can inform clinical practice to improve outcomes by better understanding host immunity and genetic susceptibility to blastomycosis.

Keywords: Blastomyces dermatitidis, immune response, interaction, host

Immunoinformatic approach for a novel protein in CAR-T cell therapy in hematological malignancies (Research Paper)

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Introduction: Cellular therapy has emerged as a key tool in the treatment of hematological malignancies. An advanced cell therapy known as chimeric antigen receptor T cell therapy (CAR T-cell therapy) has been approved by the United States Food and Drug Administration (FDA) as KYMRIAH by Novartis and YESCARTA by Gilead/Kite pharma in the year ٢٠١٧. A chimeric receptor is composed of an extracellular antigen recognition site along with some co-stimulating and signaling domains. On the whole, it turns out to be one of the most potent receptors on T cells targeting a specific type of cancer cell based on its antigenic marker. CD١٩ CAR T-cell therapy is the first clinically approved therapy for lymphoma with remarkable results in complete remission of B cell lymphoblastic leukemia up to ٩٠٪. The high rate of effectiveness of the CAR T-cell therapy against B-ALL justifies the investigation and application of this therapy for fatal diseases like all types of hematological malignancies. The most critical aspect of chimeric receptor therapy is designing and building an artificial receptor that is specific to a given type of cancer.

Methods: The in silico technique is an appropriate model to investigate the integrity and effectiveness of the engineered chimeric receptor prior to commencing in vitro experiments followed by clinical trials. This computerized experimental study aids in predicting the molecular mechanism of chimeric protein and how it interacts with both ligands. We have anticipated various features of the chimeric protein in terms of qualitative analysis (structure, protein modelling, physiological properties) and functional analysis (antigenicity, allergenicity, its receptor-ligand binding ability, involving signaling pathways). Furthermore, the reliability and validation of the binding mode of the chimeric protein against receptors were performed through a complex molecular dynamics simulation for a ١٠٠ ns timeframe in an aqueous environment.

Results: The obtained simulation study showed that CD٩٩ was a better approachable marker as compared to CD١٩ due to its better binding energy score and also binding conformations stability. The in silico results indicated that the designed antigen-binding site of the chimeric protein can recognize and bind to epitopes of CD١٩ and CD٩٩ on the surfaces of both T and B cells. Furthermore, this chimeric protein possesses the same immunogenicity as the original protein as it was synthesized through the codon bias of a mammalian expression system. Thus, the proposed model

of dual targeting anti-CD٩٩–CD١٩-CAR protein represents a universal immunotherapy intervention for hematology cancer that is both novel and successful.

Conclusion: The main purpose of this study was to construct a unique receptor with two different antigen-binding domains on T cells that can mimic the role of TCR. It will be a more advanced approach to recognize and kill that particular tumor marker bearing leukemia and lymphoma cells. Many research organizations and scientists from all over the world have started investigating and developing various models of CAR T-cell therapy. Recently, we have reported about the different forms of CAR T- cells that are in the process of development. Amongst all CAR T-cell receptors targeting dual tumor markers (Bispecific CAR T-cell or Tandem CAR T-cell) can offer extremely effective antitumor therapy for patients with B cell & T cell malignancies.

Keywords: CAR-T cell therapy, hematological malignancies, Docking and Molecular modelling, , MD simulation

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Immunoinformatic design and evaluation of a multi-epitope DNA vaccine for cross-immunization against different strains of Salmonella (Research Paper)

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Introduction: Salmonella, which can be transmitted to humans and even animals through food or water contaminated with it, causes gastroenteritis, typhoid fever and bacteremia. Control of Salmonella infection is difficult due to the emergence of antibiotic-resistant species and the effect of Its adverse effects on the immune response. Therefore, it is necessary to develop a vaccine against different strains of Salmonella.

Methods: In this study, the target antigens were identified using the VFDB server, and then their protein sequences were analyzed with the IEDB and TepiTool servers to identify B T cell epitopes. After screening, the best epitopes were selected to design the core structure of the vaccine. The ۳D structure of the vaccine was generated with the Swiss Model server and improved with The ReFOLD. Also, the three-dimensional structure of spatial B epitopes was obtained with Ellipro, and the physicochemical properties were analyzed with ProtParam and PepCalc. Next, the efficacy of the vaccine was evaluated with the HDock server and its activity in the immune system was interpreted with C-IMMSIM. Finally, the vaccine sequence was converted to DNA and then to mRNA, and the two-dimensional structure of mRNA was created with UTRdb.

Results: Designed vaccine were evaluated in terms of antigenicity, solubility, allergenicity, binding energy, tertiary structure, improved structure, spatial epitope B, physicochemical properties including stability index, aliphatic index, half-life and isoelectronic point. According to the results, final vaccine structure was confirmed.

Conclusion: In this study, for the first time, a multi-epitope vaccine DNA based on fimH, Rck, CdtB antigens was designed, which provided favorable characteristics and can potentially stimulated humoral and cellular immune system against different strains of Salmonella, although experimental studies are necessary.

Keywords: Salmonella, multi-epitope DNA vaccine, fimH, Rck, cdtB, bioinformatics tools

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Immunoinformatic design and evaluation of a multi-epitope mRNA vaccine against food-born bacterial strains including Salmonella enterica, Listeria monocytogenes, and Campylobacter jejuni

(Research Paper)

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Introduction: Food poisoning, which is known as a food-borne disease, refers to a wide range of diseases caused by the consumption of contaminated food. Pathogenic agents include bacteria, viruses, parasites, and protozoa, and bacteria play a major role in causing food poisoning. Microorganisms can be transmitted to humans through direct contamination of food or indirectly by workers and the environment, and it is also possible to transmit diseases from animals to humans and from person to person. The aim of the research is to design a multi-epitope mRNA vaccine against food-born bacterial strains including Salmonella enterica, Listeria monocytogenes, and Campylobacter jejuni, which will be more effective than existing vaccines.

Methods: In this study, the target antigens were identified using the VFDB server, and then their protein sequences were analyzed with the IEDB and TepiTool servers to identify B T cell epitopes. After screening, the best epitopes were selected to design the core structure of the vaccine. The ٣D structure of the vaccine was generated with the Swiss Model server and improved with The ReFOLD. Also, the three-dimensional structure of spatial B epitopes was obtained with Ellipro, and the physicochemical properties were analyzed with ProtParam and PepCalc. Next, the efficacy of the vaccine was evaluated with the HDock server and its activity in the immune system was interpreted with C-IMMSIM. Finally, the vaccine sequence was converted to DNA and then to mRNA, and the two-dimensional structure of mRNA was created with UTRdb.

Results: According to the results of bioinformatics analysis, the designed vaccine is high immunogenic and non-allergenic antigen that can induce immune responses against Salmonella enterica, Listeria monocytogenes, and Campylobacter jejuni which could be promising for food poisoning.

Conclusion: The designed vaccine can be used as a multi-epitope mRNA vaccine against food-born bacterial strains, although experimental studies are necessary.

Keywords: food-born bacterial strains, multi-epitope mRNA vaccine, Salmonella enterica, Listeria monocytogenes

Immunoinformatics aided design of a novel epitope-based vaccine candidate against pneumococcal surface adhesion A (PsaA) (Research Paper)

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Introduction: Streptococcus pneumoniae (pneumococcus) cause life-threatening bacterial infections such as meningitis, sepsis, and pneumonia if it invades sterile regions of the body. Moreover, pneumococcus is one of the leading causes of severe secondary infections following viral respiratory diseases such as coronavirus. Because of the boundaries of available S. pneumoniae vaccines, the development of a powerful, broad-spectrum, and cost-effective vaccine that can be effective in preventing infections caused via different pneumococcal serotypes is a significant concern of World Health Organization. Protein-based vaccine, comprising conserved pneumococcal protein antigen, can give an alternative to serotype-dependent vaccines. Pneumococcal surface adhesion A (PsaA), a highly conserved and immunogenic surface protein, can produce different levels of protection against immunological challenges with numerous pneumococcal serotypes.

Methods: In this study, the PsaA protein was considered to predict B and helper T cell epitopes using immunoinformatics tools. The immunodominant regions were selected and joined with the appropriate linker to build the final construct. Evaluation of physicochemical, antigenic and toxicity characteristics, prediction of ٣D model and structural B cell epitopes in the final model, molecular docking of the engineered construct with HLA receptor and immune response simulation were performed by computational tools.

Results: In silico outcomes indicated that the designed construct is stable, soluble, antigenic, and non-toxic. The ٣D model was constructed and refined, and Ramachandran plot, ProSA Z-score and ERRAT confirmed the quality of ٣D-model. Docking analysis showed favorable interactions between HLA and the developed construct. Finally, codon optimization was performed to enhance the expression of the vaccine in E. coli followed by in silico cloning in pET٢٨a(+) plasmid. Computational results demoneatrated that the proposed vaccine could pass the evaluations with satisfactory scores and was considered to have the potential to generate strong immune responses.

Conclusion: For the first time, this work provides a new vaccine containing the dominant epitopic regions of the PsaA antigen. Computational analysis showed valid results, however, in vitro and in vivo experiments should be performed to prove the potency of the vaccine candidate.

Keywords: Pneumococcal surface adhesion A (PsaA), Epitope-based vaccine candidate, Immunoinformatics.

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Immunotoxins: New approach for cancer target therapy (Review)

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Introduction: Cancer is recognized as a major contributor to global mortality rates. Despite the availability of diverse treatment options, numerous forms of cancer persist without a cure or develop resistance to the therapies employed. In addition, nearly all chemotherapeutic agents induce various side effects as they impact not only cancerous cells but also healthy cells. Consequently, it is essential to develop new therapeutic agents that specifically target cancer cells. Immunotoxins (ITs) offer a novel strategy in targeted cancer treatment by utilizing the precision of antibodies to transport powerful toxins directly to malignant cells. ITs are a type of fusion protein that is engineered to selectively target tumor cells, consisting of a moiety for targeting and a moiety that delivers toxicity. The targeting component typically consists of an antibody, an antibody fragment, or a ligand from the immune system, which is capable of binding to an antigen or receptor that is exclusively expressed or overexpressed in cancer cells, while remaining absent in normal cells, and the toxic agent is often a protein toxin, or its derivative, derived from animal, plant, insect, or bacterial origins. The process of receptor-mediated endocytosis is responsible for the uptake of ITs, which promote the delivery of toxic substances into the cytoplasm, and inhibit protein synthesis in targeted cells, ultimately leading to the destruction of cancer cells. This method improves the effectiveness of the therapy while reducing harm to healthy tissues. ITs development is enhanced by breakthroughs in recombinant DNA technology, which provide the means for precise targeting and contribute to better therapeutic, and combining them with other targeted therapies, including monoclonal antibodies and small molecule inhibitors, can enhance the overall efficacy of treatment. Recent clinical trials indicate that recombinant ITs can generate significant therapeutic responses in patients whose cancers are resistant to conventional treatment options. Currently, the Food and Drug Administration (FDA) has approved for human use three ITs: denileukin diftitox, tagraxofusp, and moxetumomab pasudotox, as well as the list of ITs under preclinical or clinical evaluation is expanding significantly

Methods: In this review, we will present a comprehensive overview of the targets and toxins utilized in the formulation of ITs. It will also highlight the significant advancements in applications of Pseudomonas exotoxin A (PE) protein and its derivatives in generating ITs and their role in targeted cancer therapy. Our review will be confined to investigational treatments that have entered clinical trials and remain under active clinical assessment.

Results: Although ITs exhibit significant promise, there are still challenges to overcome encompassing both off-target and on-target toxicities, human cytotoxic proteins, immunogenicity, the selection of antigen targets, the efficacy of cytosolic delivery, and targeting of solid tumors.

Conclusion: Hence, there is a need for additional research to enhance their application and tackle possible resistance mechanisms in cancer cells.

Keywords: Immunotoxin, Cancer targeted therapy, Immunogenicity

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Impact of a Missense Mutation in the Nanos۲ Gene on Spermatogenesis: An In-Silico Analysis and Implications for Male Infertility (Research Paper)

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Introduction: Male infertility is a complex condition influenced by various genetic factors, with the nanos۲ gene emerging as a critical player in spermatogenesis and reproductive health. This study presents an in-silico analysis of a specific missense mutation within the nanos۲ gene, aimed at elucidating its potential impact on protein function and its association with male infertility.

Methods: Utilizing an array of bioinformatics tools, including SIFT, PolyPhen-۲, iMutant, HOPE, and MUPro, a comprehensive assessment of the mutation's pathogenicity is conducted, structural implications, and functional consequences.

Results: The SIFT and PolyPhen-۲ analyses indicated a high likelihood of deleterious effects, suggesting that this mutation may disrupt the nanos۲ protein's stability and functionality. Structural predictions using HOPE and MUPro further supported these findings, revealing significant alterations in protein dynamics and interactions that could impair cellular processes critical for spermatogenesis.

Conclusion: These results underscore the necessity for further functional studies to validate these predictions and explore the underlying mechanisms by which nanos۲ mutations contribute to male infertility. This research highlights the utility of advanced bioinformatics tools in the identification and characterization of genetic variations linked to reproductive health, paving the way for novel diagnostic and therapeutic strategies in the field of male infertility.

Keywords: genetic variants, infertility, biomarker

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Impact of Allopurinol on Prostate Cancer Progression and Biomarker Modulation in a Phase II Clinical Trial (Research Paper)

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Introduction: Researchers have found that allopurinol, a xanthine oxidase inhibitor, may be beneficial in treating cancer preclinically. Specifically, this phase II clinical trial aims to investigate how allopurinol modulates relevant biomarkers of prostate cancer progression.

Methods: A meticulously designed randomized, double-blind, placebo-controlled trial was conducted with ٨٠ patients diagnosed with localized prostate cancer. Participants were randomly assigned to receive allopurinol (٣٠٠ mg/day) or a placebo for ٦ months. The primary endpoints, changes in prostate-specific antigen (PSA) levels and tumor volume assessed by MRI, were rigorously measured. Secondary endpoints, changes in oxidative stress markers and inflammatory cytokines, were also carefully monitored. Blood samples were collected at baseline, ٣ months, and ٦ months for biomarker analysis. Statistical analysis involved paired t-tests and ANOVA for within-group and between-group comparisons, respectively, to ensure robust findings.

Results: Of the ٨٠ participants, ٧٢ completed the study (allopurinol group, n=٣٦; placebo group, n=٣٦). The allopurinol group exhibited a significant reduction in PSA levels (mean decrease ٢,٤ ± ١,١ ng/mL) compared to the placebo group (mean decrease ٠,٨ ± ٠,٦ ng/mL, $p < ٠,٠١$). Tumor volume reduction was also significant in the allopurinol group (mean reduction ١٥,٣ ± ٣,٧٪) versus the placebo group (mean reduction ٦,٥ ± ٢,٨٪, $p < ٠,٠١$). Oxidative stress markers, such as malondialdehyde, decreased significantly in the allopurinol group (mean decrease ١,٨ ± ٠,٤ µmol/L) compared to placebo (mean decrease ٠,٥ ± ٠,٢ µmol/L, $p < ٠,٠٠١$). Inflammatory cytokines, including IL-٦, showed significant reductions in the allopurinol group (mean decrease ١,٥ ± ٠,٣ pg/mL) versus placebo (mean decrease ٠,٤ ± ٠,١ pg/mL, $p < ٠,٠١$).

Conclusion: Allopurinol's significant efficacy in reducing PSA levels, tumor volume, oxidative stress, and inflammatory markers in prostate cancer patients is a promising development. These findings suggest a potential shift in the prostate cancer management landscape, offering new hope and possibilities for improved patient outcomes. Allopurinol could emerge as a valuable adjunct therapy, enhancing the current arsenal of prostate cancer treatments.

Keywords: Allopurinol, Prostate Cancer, Phase II Trial, Biomarkers, Tumor Progression

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Impact of Long-Term Antibiotic Use on Gut Microbiota and Its Implications for Colorectal Cancer Risk (Review)

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Introduction: In terms of cancer incidence, colorectal cancer (CRC) is the second most frequent cancer in women, after breast cancer, and the third most common cancer in men, after prostate and lung cancer. It represents ٥٥٪ of CRC cases in developed regions, with Central and Eastern Europe having the highest mortality rates. Moreover, it is a multifactorial disease with an unclear primary cause. However, extensive epidemiological research has identified several risk factors, including genetic predisposition, colorectal polyps, inflammatory bowel disease, smoking, alcohol consumption, and long-term, repeated, or combined antibiotic use. Additionally, gut microbiota dysbiosis has been recognized as a potential risk factor for CRC. The purpose of this study is to examine the relationship between the frequent use of antibiotics and its effect on the intestinal microbiota and the occurrence of colorectal cancer.

Methods: The human microbiota consists of approximately ٥٠٠-١٠٠٠, distinct species of bacterial cells. The significance of this entity resides in its capacity to provide defense against pathogens, facilitate the metabolic breakdown of polysaccharides, facilitate the biosynthesis of vital vitamins, and serve a critical role in the preservation and regulation of the immune system. The gut microbiome significantly contributes to overall health maintenance and disease prevention. Also, the human intestinal tract, a nutrient-rich environment, hosts the largest microbial communities. The gut microbiota is gaining significant attention due to its influence on CRC risk through metabolites and immune interactions. Certain bacteria that produce hydrogen sulfide, acetaldehyde, and secondary bile acids can increase CRC risk. For example, the human gut microbiota functions as an essential “organ,” contributing to nourishment, regulating epithelial development, and modulating immunity. Researchers are investigating the differences in gut microbiota between CRC patients and healthy individuals, aiming to identify reliable microbial markers for CRC precursors.

Results: Accumulating evidence suggests that long-term, frequent, or combined antibiotic use can also be a risk factor for CRC. The worldwide use of antibiotics is projected to increase significantly. The use of antibiotics, even narrow-spectrum antibiotics, has solid and stable effects on the structure of the intestinal microbiota, changes the composition, and reduces the diversity of the human microbiota. Antibiotics allow colonization of pathogenic microbes and may allow colonization with carcinogenic bacteria that cause local inflammation and tumor formation. Previous epidemiological studies in humans have evaluated the possible effect of antibiotic exposure on cancer risk in the lung, breast, prostate, colon, and skin with conflicting results. In this regard,

antibiotics may be of interest because their use may seriously affect the diversity of the colonic microbiota. The administration of antibiotics has been linked to a heightened susceptibility to CRC.

Conclusion: As a result, several risk factors influence the development of CRC, with dysbiosis gut microbiota and antibiotics being particularly significant. The widespread use of antibiotics globally profoundly impacts our gut microbiota, leading to microbiome dysbiosis. Given the indispensable role of the intestinal microbiota in human health, modifications in their arrangement and composition can establish an environment conducive to the proliferation of specific pathogenic bacteria, which are known to contribute significantly to the development of colon tumors.

Keywords: Colorectal Cancer, Microbiota, Antibiotics, Dysbiosis.

Impact of Organ Donation on Grief Symptoms in Iranian Families (Research Paper)

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Introduction: Families often become the key decision-makers in determining who receives scarce, life-saving organs, especially when patients have not expressed their wishes. These decisions, made in moments of trauma and profound sadness, can ultimately determine the fate of individuals waiting for organ transplants. This study aimed to identify the factors that influence grief among donor families regarding organ donation.

Methods: This analytic cross-sectional study aimed to assess the grief scores of family members, including parents, spouses, siblings, and children, who had been through the organ donation process. Convenience sampling was used to select participants for this study. The Grief Experience Questionnaire (GEQ-٣٤) was utilized as the instrument for data collection through an online survey on the Google Forms platform. The questionnaire consisted of two parts: the first part gathered demographic information about the families of the organ donors, while the second part assessed the psychological impact of the donation (grief reaction), which participants completed themselves. Descriptive statistics and multiple linear regression were utilized to determine the factors influencing grief using SPSS software (version ١٩) with a significance level of ٠,٠٥.

Results: The donor gender was mostly male (١٥٣ (٦٨,٩٪)) with a mean age of ٣٥,٩٦ ± ١٧,٠٥ (range: ٢–٦٨) years at the time of death. The mean score of GEQ was ٩٣,٣±٢٢,٤, ranging from ٣٩ to ١٤١. The findings revealed that ٢٣ (١٠,٤٪), ١٠٠ (٤٥٪), and ٩٩ (٤٤,٦٪) of participants suffered from low, moderate, and high levels of grief, respectively. There is a significant difference between knowledge about brain death and the level of grief (P = ٠,٠٠٨). There is a significant difference between Cause of brain death. There is a significant difference between having a card (physical card, registering to get a card, donor verbal consent) and GEQ level (F: ١,٩٦, P = ٠,٠٤٥).

Conclusion: As evidenced by the obtained results, among the subscales of grief, the highest scores were related to the dimensions of guilt.

Keywords: Grief; Organ donation; Brain Death; Donor family.

Impact of Probiotic , Prebiotic and Synbiotic on Gastrointestinal Health : systematic review of clinical trials (Review)

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Introduction: The gastrointestinal system plays a pivotal role in maintaining overall health, with its balance influenced by the microbiota. Probiotics, prebiotics, and synbiotics have gained attention as potential therapeutic agents for modulating gut health. This systematic review aims to evaluate the clinical efficacy of probiotics, prebiotics, and synbiotics in improving gastrointestinal health, with a particular focus on randomized controlled trials (RCTs).

Methods: A comprehensive search was conducted using PubMed, Scopus, Google Scholar, and Medline databases to identify relevant RCTs. Our inclusion criteria encompassed clinical trials that examined the effects of probiotics, prebiotics, or synbiotics on various gastrointestinal outcomes. We identified ٢٧ RCTs, three of which were excluded due to irrelevance. The final analysis included ٢٤ trials, with ١٧ investigating probiotics, ٧ focusing on synbiotics, and ٤ evaluating prebiotics.

Results: Among the ١٧ probiotic trials, ١٥ reported positive effects on gastrointestinal health. These studies demonstrated that probiotics contributed to a reduction in respiratory infections, improved gut dysbiosis, and alleviated symptoms associated with irritable bowel syndrome (IBS). Probiotics were also shown to reduce infection rates in kidney transplant patients and mitigate the adverse effects of clindamycin use. However, two studies reported negative outcomes, emphasizing the variability in probiotic efficacy depending on strain, dosage, and patient population. The seven synbiotic trials yielded six positive results, further highlighting the potential of synbiotics in enhancing gastrointestinal health. Positive effects included a reduction in gastrointestinal infections and improvements in microbial balance. One study presented neutral results, indicating no significant impact on the gastrointestinal outcomes measured. The four prebiotic trials uniformly demonstrated positive effects, particularly in terms of reducing gastrointestinal disorders and promoting the growth of beneficial gut bacteria. These trials underscore the potential of prebiotics as a standalone intervention for improving gut health.

Conclusion: In conclusion, this systematic review reveals that the majority of RCTs support the positive effects of probiotics, prebiotics, and synbiotics on the gastrointestinal system. Probiotics, in particular, show promise in addressing various gastrointestinal conditions, while prebiotics and synbiotics contribute to maintaining gut health. Nonetheless, variability in study outcomes suggests that more research is needed to determine the optimal strains, dosages, and target populations for

these interventions. Future large-scale trials should aim to standardize treatment protocols and assess long-term benefits for a broader range of patients.

Keywords: Synbiotic ; Gastrointestinal health; clinical trials; a systematic review.

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Impact of SNPs in Implantation-Related Genes on Recurrent Implantation Failure (RIF) and Their Role in Reproductive Health (Review)

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Introduction: Recurrent implantation failure (RIF) presents a challenge in the field of reproductive medicine and impacts about ١٥٪ of women who undergo in vitro fertilization (IVF). One area of growing interest focuses on exploring the influence of nucleotide polymorphisms (SNPs) within genes associated with implantation processes that affect angiogenesis dynamics, endometrial receptivity levels and interactions between the embryo and the maternal environment. This study seeks to explore how these genetic variations impact women fertility and their role, in recurrent implantation failure through an examination of previous studies and real world results.

Methods: Information was analyzed through seven articles that examined the association between SNPs in genes related to angiogenesis (FLT١, VEGFA, KDR and FGF٢) and recurrent implantation failure. Research encompassed populations such as Korean and Polish cohorts. Genetic variations were identified through methods, like PCR RFLP with comparisons made between the allele frequencies of women and control groups. They also used haplotype analyses methods and tests such as logistic regression and chi squared.

Results: The variation in VEGFA gene (rs٦٩٩٤٧) in particular showed a heightened association with RIF risk. women with AA genotype were notably more susceptible to implantation failure (OR=٢٠٣٤, p=٠٠٠٢٣). the genetic variation, in KDR gene (rs٢٠٧١٥٥٩) was discovered to raise infertility and RIF risks among women undergoing assisted reproductive procedures. An analysis of gene interactions discovered a combined impact involving KDR (rs٢٠٧١٥٥٩) and VEGFA (rs٦٩٩٤٧). In contrast there were no connections found between the FLT and FGF gene variations and RIF. These results highlight the significance of variations within the angiogenesis pathway, in influencing recurrent implantation failure.

Conclusion: The association of recurrent implantation failure with SNPs in genes associated with angiogenesis particularly, VEGFA and KDR is very important. These SNPs associated with RIF can act as a genetic marker in the diagnosis of the condition. Although FLT١ and FGF٢ SNPs were not significantly associated, the attention on compound polymorphisms indicates the need for more studies on their mechanisms Many of these revelations are essential for further improving the results of the assisted reproductive technology by genetic targeting of the infertility treatment and The collective effect is important in revealing the complex interplay between genetics and clinical factors in the context of RIF.

Keywords: SNPs, Recurrent Implantation Failure (RIF), VEGFA, KDR, Angiogenesis

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Implementation of preventive measures based on early signs of lung cancer to reduce the risk of development (Review)

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Introduction: Lung cancer remains one of the leading causes of cancer-related deaths globally. Accounting for nearly ١,٨ million deaths annually. Despite advances in treatment, the prognosis for patients remains poor, mainly because many individuals are diagnosed at the later stages. Early diagnosis is crucial in increasing the survival rates; however, the disease is often diagnosed in the advanced stage due to non-specific or ambiguous symptoms during the early stage. Recent advancements in understanding the early signs and risk factors of lung cancer have provided opportunities for new prevention methods focused on stopping the progression of the disease. This review aims to assess the effectiveness of various potentials that can be implemented in order to identify early signs and individuals at risk. The article offers a comprehensive review of reduced risk factors in lung cancer and outlines how early intervention may have a positive impact on patients' outcomes based on the available literature.

Methods: Review of the literature was conducted by searching databases including PubMed, Scopus, and Web of Science for studies published in the last ten years (٢٠١٤–٢٠٢٤). Keywords such as "Lung Neoplasm", "Tobacco Smoking", "Early Detection of Cancer", and "Prevention" were used. Studies were selected based on their relevance to early detection, risk factor modification, and the implementation of preventive measures targeting individuals exhibiting early signs of lung cancer or belonging to high-risk groups. Studies were included if they focused on the implementation or evaluation of preventive strategies aimed at individuals with early signs of lung cancer or those at increased risk due to genetic, environmental, or behavioral factors.

Results: Tobacco use, environmental pollution, genetics, diet, and chronic obstructive pulmonary disease are some risk factors for lung cancer. There has long been an urgent need for an effective screening test to detect lung cancer early and thereby reduce mortality. Sputum cytology, chest radiography, bronchoscopies, computed tomography (CT), and low-dose computed tomography have been investigated as potential screening tests to improve survival. There has been recent advances in liquid biopsy, DNA- or RNA-based biomarkers and proteins, for lung cancer early detection which we have also discussed in this review. Individuals at increased risk of developing lung cancer can also be identified using the PLCOm٢٠١٢ model. Tobacco control and smoking prevention are the most important primary prevention measures against lung cancer. Preventing

exposure to secondhand smoke, lung carcinogens such as asbestos, arsenic, nickel, and chromium and also radon results in decreased incidence and mortality from primary lung cancers. Additionally, β-carotene supplements increase the risk of lung cancer in smokers. Thereby, smokers should also avoid β-carotene supplementation. On the other hand, there have been multiple studies in the past and a few ongoing studies to identify effective chemopreventive agents for lung cancer. Early detection and screening as well as treatment and therapy play vital roles in preventing lung cancer at early stages. Currently, the treatment options for lung cancer can be categorized into two main groups: chemotherapeutic agents and novel antibody-based therapies, commonly referred to as EGFR tyrosine kinase inhibitors.

Conclusion: Due to the increase in the incidence of lung cancer, a strong emphasis should be placed on prevention based on early signs of lung cancer. Therefore, it is necessary to enhance the efficiency of prevention and early diagnosis to reduce the risk of metastasis and development. Technological and biological advances emphasize the need to accelerate early detection research and improve cancer survival.

Keywords: Lung Neoplasm, Tobacco Smoking, Early Detection of Cancer, Prevention

Implication of gut microbiome metabolites in chronic fatigue syndrome (Review)

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Introduction: Chronic fatigue syndrome (CFS) is a long-term disorder characterized by profound fatigue, as well as various cognitive symptoms. Recent evidence suggests that the gut microbiome and its dysbiosis may be involved in the pathophysiology of CFS by affecting the regulation of metabolites related to energy metabolism, neurotransmission, oxidative reactive products, immune system dysfunction, and inflammation. This study explores the molecular mechanisms by which our microbiota contribute to the initiation or progress of the CFS.

Methods: Published literatures in Scopus, PubMed, and NCBI databases were gathered to categorize the factors affecting CFS and their relation with gut microbiota. Pre-prints, research, and review articles were utilized to conduct a comprehensive literature review. The keywords were checked for accuracy using MeSH guidline.

Results: Dysbiosis of the gut microbiome in CFS patients leads to decreased blood serum levels of essential energy-producing metabolites, such as short-chain fatty acids (SCFAs) and amino acids, while increasing fatigue-inducing factors, including lactic acid. Moreover, downregulation in hormones and neurotransmitters secretion, such as serotonin, melatonin, GABA, histamine, glutamate, stress hormones, acetylcholine, and adenosine caused by dysbiosis lead to mental fatigue. Among the main increased gut bacterial species in CFS, some Bacteroides produce glutamate and induce mental fatigue, while decreased species are SCFA-producing Lachnospiracea, Ruminococcus, Faecalibacterium, Dorea, and Anaerostipes, which impact energy metabolism. Reduced neutralization of reactive oxygen species by our microbiota or even generation of oxidative stress by-products of the microbiota leads to chronic fatigue. The overgrowth or the lower abundance of the key species leads to imbalanced metabolites in CFS.

Conclusion: Overall, this study provides a comprehensive analysis of the influencing factors and metabolites and their alternation in CFS, along with highlighting the correlation between gut microbiota dysbiosis and changes in these substances. Gut microbiota imbalances can lead to reduced blood serum metabolite levels, such as SCFAs and amino acids, which contribute to the development of CFS symptoms. Conversely, internal dysfunction may alter metabolite levels, like branched-chain amino acids (BCAAs) and oxygen, potentially affecting the composition of gastrointestinal bacteria. Furthermore, oxidative stress increases and antioxidant levels decrease in CFS patients compared to healthy individuals. An increase in reactive oxygen species (ROS) producers, such as Enterococcus faecalis within the gut microbiome, generates extracellular superoxide and hydrogen peroxide, which harm colonic epithelial cells. Various studies have shown significant decreases in levels of antioxidant compounds in the liver and gastrocnemius muscle,

including vitamin E, superoxide dismutase (SOD), glutathione peroxide (GSH-Px), and catalase (CAT), which are mainly produced by Lactobacillus, Proteobacteria, Pseudomonas, and Firmicutes. In contrast, nucleotide oxidation products like ʌ-hydroxy-deoxyguanosine (ʌ-OHdG), along with ROS such as superoxide and hydrogen peroxide, and the free radical metabolite malondialdehyde (MDA), have shown a dramatic increase. Elevated levels of lipopolysaccharides (LPS), which are inflammatory markers linked to Gram-negative bacteria enterobacteria, can increase serum immunoglobulin concentrations and contribute to fatigue. High ceramide levels from LPS breakdown can also harm gut epithelial cells, damaging the barrier and increasing gut permeability. In conditions like ME/CFS, high amounts of pro-inflammatory cytokines, sometimes produced by gut Proteobacteria, are noted. Dysbiosis and metabolic endotoxemia are significant factors in inflammation and oxidative imbalances, leading to a reduction in the tight-junction protein occludin and compromising the integrity of the intestinal barrier. While the link between inflammation and fatigue remains unclear, markers of inflammation, oxidative/nitrosative stress, and antioxidants have been proposed as potential diagnostic tools, which are linked to key cellular processes. Future research is required to elucidate the portion of the microbiota when both our cells and microbiota can produce the same metabolites. The relationship between gut microbiota dysbiosis and CFS is bidirectional as a sedentary lifestyle can lead to dysbiosis itself.

Keywords: chronic fatigue syndrome, gut microbiota, gut microbiome, Dysbiosis, metabolite

Importance of Haemophilus Influenzae Bacteria and Concerns of Drug Resistance (Review)

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Introduction: Nasopharyngeal carriage of pathogens is a significant source of transmission to other susceptible groups, notably older people. The nasopharynx is a key reservoir for bacterial pathogens that can cause upper respiratory tract infections in children. One of the most significant bacteria that colonize the nasopharynx is Haemophilus influenzae, which frequently causes sinusitis and acute otitis media (AOM). Six distinct polysaccharide capsules are available for H. influenzae, the most virulent of which is H. influenzae serotype b (Hib). Alternatively, H. influenzae can exist without a capsule (non-typeable H. influenzae). Hib was the most frequent cause of invasive H. influenzae disease in young children, including meningitis, until the Hib capsule was included in the H. influenzae vaccine and it was included in the national childhood vaccination programs in ۱۹۹۳. Through both direct and indirect (herd immunity) protection, the routine administration of Hib vaccinations resulted in a considerable drop in invasive Hib disease in all age groups. However, this also created space for an increase in non-typeable H. influenzae (NTHi) cases and non-b-serotype cases. Between ۲۰۱۷ and ۲۰۲۱, the majority (۷۶,۸٪) of invasive H. influenzae strains in Belgium were reported as non-typeable. The aim of study was Importance of Haemophilus Influenzae Bacteria and Concerns of Drug Resistance.

Methods: The present study is titled The Importance of Haemophilus Influenzae Bacteria and Concerns of Drug Resistance which was done by searching scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: According to the findings, invasive infections in children and the elderly during the same period were also found to be caused by typeable serotypes, including serotypes "f" (۹,۷٪), "b" (۵,۸٪), "a" (۲,۷٪), "e" (۱,۱٪), and "d" (۰,٤٪). These findings highlight the significance of carrying out additional studies on the prevalent H. influenzae serotypes. Two distinct methods exist for H. influenzae strains to develop antibiotic resistance: either they produce the beta-lactamase enzymes needed to hydrolyze beta-lactam antibiotics, or they develop mutations in the genes that code for the penicillin-binding protein (PBP) protein. The diversity of mutations in the ftsI gene results in several profiles that can affect the beta-lactam antibiotics differently, making macrolides and quinolones more significant alternative treatment strategies. Mutations in the ftsI gene, which encodes PBP۳, lower the binding affinity of beta-lactam antibiotics to PBP۳. One issue with treating H. influenzae with beta-lactam antibiotics is beta-lactamase-negative ampicillin-resistant strains, or BLNAR. Sequencing of the ftsI gene has revealed specific amino acid alterations that result in the BLNAR phenotype Groups I, II, III, and III-like of BLNARS are distinguished by the patterns of amino acid mutations at particular locations. In comparison to groups I and II, groups III and III-like (also known as high-BLNAR) typically have a higher ampicillin MIC (greater level of ampicillin resistance). Globally speaking, high BLNARs are changing, although more quickly in Asia than in the USA and Europe.

Conclusion: As a result of this investigation, certain serotypes for carriage (serotype "e") and the invasive group (serotypes "a" and "b") were discovered, and biotypes I, II, and III are more commonly detected in both the carriage group and the invasive group. Furthermore, the carriage (DCC, AOM) group showed higher levels of antimicrobial resistance to the drugs under analysis than the invasive group did. The ftsI gene showed a greater degree of mutation in the strains from children with AOM than in the strains from children with DCC. Given the paucity of information on the dynamics of H. influenzae that persist in a population of vaccinated children, the current study aids in laying the foundation for understanding the dynamics of H. influenzae carriage in Belgian children. Given the potential consequences for treating H. influenzae infections in light of the emergence of beta-lactam antibiotic resistance, this work offers a crucial initial understanding of the traits of circulating H. influenzae strains. Changes in the microbiology and epidemiology of H. influenzae should be closely watched since they may result in antibiotic resistance-related clinical failure.

Keywords: Haemophilus influenzae, Antimicrobial, Drug resistance

In silico analyses for potential key genes associated Hepatocellular Carcinoma (Research Paper)

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Introduction: Hepatocellular cancer (HCC) is one of the common type of liver cancer which is the third cause of death in all kind of cancers. The main reason of HCC pathogenesis is aggregation of gene mutations that caused cellular and molecular modification. It is necessary to find biomarkers with high specificity and sensitivity to screen HCC. Microarray technology is used for identify genome mechanism in liver tumorigenesis. Using data from microarray and combine them with bioinformatic approaches prepare outstanding strategy for studying comparison between gene expression in cancer and normal sample in patients. In this study, we identify key genes associated with hepatocellular carcinoma and investigate their underlying molecular mechanisms.

Methods: In the current study, two microarray dataset (GSE٣٦٣٧٦, GSE١٤٥٢٠) were downloaded from the Gene Expression Omnibus database (GEO). The fold change (FC) values of individual gene levels were calculated; differentially expressed genes (DEGs) with |FC| > ١ and P-value < ٠,٠٥ were considered to be significant. The Venn diagram was carried out for the overlapped part via Funrich software.

Results: A total of ١٧٢ overlapped upregulated genes and ١٩٣ downregulated genes were identified. To identify the most influential genes in each group, we calculated the Matthews correlation coefficient (MCC) for all upregulated and downregulated genes and selected the top ٢٠ genes with the highest MCC values. Analysis showed that up-regulated genes involve in the metabolism of lipids and lipoproteins, cholesterol biosynthesis I, mesenchymal-to-epithelial transition. Down-regulated genes mainly associate with alpha٤ beta١ integrin signaling events, Integrin family cell surface interactions, beta١ integrin cell surface interactions and p٥٣ pathway.

Conclusion: These in silico predictions will provide useful information in selecting the target genes that are likely to have functional impact on the HCC and may serve as potential diagnostic biomarkers in HCC patients.

Keywords: hepatocellular cancer; biomarker; microarray; MCC

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In silico designing of a novel epitope-based candidate vaccine targeting pneumococcal surface protein C (PspC) (Research Paper)

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Introduction: Streptococcus pneumoniae is the leading reason for invasive diseases including pneumonia and meningitis, and also secondary infections following viral respiratory diseases such as flu and COVID-۱۹. Currently, serotype-dependent vaccines, which have several insufficiency and limitations, are the only way to prevent pneumococcal infections. Hence, it is plain to need an alternative effective strategy for prevention of this organism. Protein-based vaccine involving conserved pneumococcal protein with different roles in virulence could provide an eligible alternative to existing vaccines. Pneumococcal surface protein C (PspC), an immunogenic and conserved surface protein, can produce different levels of protection against pneumococcal strains.

Methods: In this study, the protein PspC was taken to account to predict B-cell and helper T-cell epitopes using immunoinformatics tools. The epitope-rich regions were chosen and linked together with suitable linker to build the final construct. The evaluation of physicochemical properties, antigenicity, and toxicity, prediction of ۳D model and conformational B cell epitopes in the final model, molecular docking of the final construct with HLA receptor, and simulation of immune response were carried out by computational tools.

Results: The in silico results showed that the developed construct was stable, antigenic, soluble, and non-toxic. The ۳D structure was constructed and refined, and the R-plot, ProSA Z-score, and ERRAT score verified the quality of the model. The docking analysis indicated favorable interactions between HLA and the designed construct. Finally, codon adaptation was conducted to enhance the expression of the designed vaccine in E. coli followed by in silico cloning in the pET۲۸a(+)vector. The computational outcomes revealed that the suggested vaccine could pass the evaluations with satisfactory scores and could be deemed to have the potential to induce strong immune responses.

Conclusion: For the first time this work presents a novel vaccine containing the immunodominant epitope regions of PspC antigen. The computational outcomes revealed acceptable results, nevertheless, in vitro and in vivo examinations should be performed to prove the potency of the candidate vaccine.

Keywords: Pneumococcal surface protein C (PspC), Immunoinformatics, Epitope-based candidate vaccine.

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In silico identification of B and T cell epitopes for the development of a vaccine against Human T-lymphotropic virus-١ (HTLV-١) Glycoprotein ٦٢ (Research Paper)

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Introduction: Human T-cell leukemia virus type ١ (HTLV-١) is a human retrovirus that has been linked to cancer. It has been found in humans and has infected many people in the world. Over the decades, a significant effort has been to study the biological and disease-causing characteristics of HTLV-١. As a result, several experimental vaccination and treatment approaches have been developed to combat HTLV-١ infection. Although current therapies exhibit several benefits, they frequently encounter constraints, such as potentially reduced effectiveness caused by the genetic variability of HTLV-١ strains. Consequently, Additional research is needed to address these challenges and improve the effectiveness of epitope-based vaccines for HTLV-١. This immunoinformatic study examined the prediction of conformational linear B-cell and T-cell epitopes of the HTLV-١ glycoprotein ٦٢ (gp٦٢) viral protein, which plays a crucial role in virus entry, to assess their potential as vaccine candidates.

Methods: In this study, UniProt was used to retrieve all target protein amino acid sequences in FASTA format with the UniProt ID Q٨٥٦١١. The physicochemical properties of the target glycoprotein were analyzed using Expasy ProtParam. The antigenicity of each protein was evaluated utilizing the VaxiJen ٢,٠ server with a prediction threshold of ٠,٤. The target glycoprotein's ٣D structure was modeled using Phyre٢, Swissmodel, and I Tasser, popular homology modeling tools. Galaxy refine server reduced structure distortions after homology modeling to refine models. The models were then Ramachandran plotted using the RAMPAGE server to determine their quality and reliability.The models with the best results after all these analyses with high levels of coverage were extracted. The NetCTL.١,٢ server predicted the ٩-mer T cell epitopes recognized by the most common human HLA Class I supertypes: A١, A٢, A٣, A٢٤, A٢٦, B٧, B٨, B٢٧, B٣٩, B٤٤, B٥٨, and B٦٢. NetCTL.١,٢ server thresholds for Transporter Associated with Antigen Processing transport efficiency, proteasomal C-terminal cleavage, and epitope identification were ٠,٠٥, ٠,١٥, and ٠,٧٥. Immune epitope database-consensus (IEDB) was also used to identify epitopes recognized by HLA Class I alleles A-٠٢:٠١, B-٣٥:٠١, B-٥١:٠١, and B-٥٨:٠١. Net MHC II pan ٣,٢ server and IEDB NetMHCIIpan ٤,١ EL (recommended epitope predictor-٢٠٢٣,٠٩) predicted the ١٥-mer epitopes recognized by HLA Class II DRB١ alleles: ٠١:٠١, ٠٣:٠١, ٠٤:٠١, ٠٧:٠١, ٠٨:٠٣, ١٠:٠١, ١١:٠١, ١٢:٠١, ١٣:٠٢, ١٤:٠١, and ١٥:٠١.The study's HLA Class I, II epitopes should cover over ٧٠٪ of the global population. Then, overlapping epitopes with integral sequences of CTL and HTL epitopes can activate cytotoxic and helper T cells. The predicted promiscuous epitopes' antigenicity was assessed using VaxiJen server ٢,٠. We kept the antigenicity prediction threshold at ٠,٤. BCpred ٢,٠ server was employed for the identification of linear/continuous B cell epitopes. The predicted B cell epitopes

were also experimented for antigenicity. Finally, the Ellipro server predicted conformational/discontinuous B cell epitopes. To predict using the Ellipro server, the minimum score and maximum distance (Angstrom) were set to ٠,٥ and ٦ Å, respectively.

Results: Based on the computational analysis, two B cell epitopes were identified: DYSPSCCTLTIGVSSYHSKPCNP (spanning from ٢١–٤٣) and MGKFLATLILFFQFCPLILGDY (spanning from ١–٢٢). Additionally, two T-cell epitopes were discovered: LLFGYPVYV (ranging from ٢٨-٣٧) and ITWPLLPHV (ranging from ٢٧-٣٦). These epitopes were determined to be highly antigenic and immunogenic which could be highly potential to be utilized in vaccine structure.

Conclusion: In sum, this study highlights the capability of employing a bioinformatic method to discover new epitopes from gp٦٢ for the design of epitope-based vaccines. This finding presents a promising lead for the development of novel HTLV-١ vaccines although further research is necessary to confirm the effectiveness and safety of these epitopes in preclinical models and clinical trials.

Keywords: HTLV-١, Epitope-based vaccine, Gp٦٢, B cell epitopes, T- cell epitopes

In Silico Identification of Potential Key Genes as Candidate Colorectal Cancer Biomarkers (Research Paper)

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Introduction: Colorectal cancer (CRC) is a serious health problem around the world. It ranks among the top three most common cancers globally (١). CRC represents the second most prevalent cause of cancer-related mortality on a global scale. An estimated ١,٩ million new CRC diagnoses and over ٩٣٠,٠٠٠ CRC-induced deaths transpired worldwide in the year ٢٠٢٠ (٢). Data from the Iranian National Population-based Cancer Registry (INPCR) projects a significant rise in new CRC cases in Iran. Their report suggests a ٥٤,١٪ increase, from ١١,٥٥٨ cases in ٢٠١٦ to an estimated ١٧,٨١٢ cases by ٢٠٢٥ (٣). CRC encompass a spectrum of complex malignancies characterized by a heterogeneous landscape of genetic alterations and diverse molecular pathways (٤). In this study, we aim to identify the colorectal cancer's key genes and look into their underlying molecular mechanisms

Methods: In the current study, two microarray dataset (GSE٤١٢٥٨, GSE٦٨٤٦٨) were downloaded from the Gene Expression Omnibus database (GEO). The fold change (FC) values of individual gene levels were calculated; differentially expressed genes (DEGs) with |FC| > ١ and P-value < ٠,٠٥ were considered to be significant. The Venn diagram was carried out for the overlapped part via Funrich software.

Results: A total of ٢٤٤ overlapped upregulated genes and ٤٥٠ downregulated genes were identified, and ١٠ hub genes were selected for each of up and down genes. Analysis showed that up-regulated hub genes involve in the wound healing, cell motility, anti-apoptosis and immune response. Down-regulated hub genes mainly associate with spindle assembly, cell communication, signal transduction, cell growth and protein metabolism.

Conclusion: Our study suggests that UBE٢C, KIF٢٠A, MELK, NEK٢, AURKA, FGF٢, COL١A٢, IGF١, MMP٩ and ABL may be potential biomarkers and therapeutic targets for CRC.

Keywords: gastric cancer, in silico, biomarker

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In silico investigation of the single nucleotide polymorphisms (SNPs) in DNMT۳A gene as a driver gene in patients with Acute Myeloid Leukemia (Research Paper)

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Introduction: Acute myeloid leukemia (AML) is a complex hematologic malignancy characterized by the uncontrolled proliferation of myeloid progenitor cells, leading to disrupted hematopoiesis and severe clinical outcomes. One of the critical genetic alterations in AML is found in the DNA methyltransferase ۳A (DNMT۳A) gene, which is supposed to be one of the critical driver genes in AML and plays a vital role in de novo DNA methylation, crucial for regulating gene expression and maintaining genomic integrity. Disruptions in DNMT۳A, especially the R۸۸۲H hotspot mutation, are prevalent in many AML patients and are associated with poor prognoses and the establishment of a pre-leukemic state in hematopoietic stem cells. Recent advancements in high-throughput sequencing have revealed the frequency of DNMT۳A mutations and their interactions with other genetic modifications, highlighting the need for deeper understanding of their functional consequences in AML.

Methods: We identified eighteen non-synonymous single nucleotide polymorphisms (nsSNPs) in the DNMT۳A gene: ((rs۱۳۹۲۹۳۷۷۳) (Arg۷۳٦Leu/Pro/His), (rs۱٤۷۰۰۱٦۳۳) (Arg۸۸۲ Leu/Pro/His), (rs۳٦۹۷۱۳۰۸۱) (Arg٦۸۸His), (rs۳۷۷۵۷۷۵۹٤) (Arg۸۸۲Cys/Gly/Ser), (rs۵٦۸۲۰۷۹۷۸) (Arg۵۹۸Terminal point/Gly), (rs۵۸۷۷۷۵۰۷) (Leu٦٤۸Pro), (rs۵۸۷۷۷۵۰۸) (Ile۳۱۰Thr/Arg), (rs۵۸۷۷۷۵۰۹) (Met۵٤۸Thr/Lys), (rs۵۸۷۷۷۵۱۰)(Phe۹۰۲Ser), (rs۷۵۱۵٦۲۳۷٦) (Arg٦۳۵Leu/Pro/Gln), (rs۷۵٤۵۰٦۷۱۳) (Cys۵۸٦Phe/Tyr), (rs۷۵۷۸۲۳٦۷۸) (Arg۷۷۱Leu/Pro/Gln), (rs۷۵۸۸٤۵۷۷۹) (Ser۷۷۰Leu/Trp/Terminal point), (rs۷۹۷۰٤٤۹۰٤) (Gly۲۹۸Trp/Arg), (rs۱٤۱۸۰۳۹٦۸۰) (Val۷۱٦Phe/Leu/Ile), (rs۱۵۷۳۳٤۰۳۳۵) (Asp۳۳۳Asn), (rs۱۵۷۳۳٤۰٤۷۵) (Trp۳۳۰Arg), (rs۱٦۷۳۰٦۵٦۱۹) (Phe۹۰۹Cys/Ser)) using dbSNP, we analyzed these nsSNPs to determine their effect on the structure of the DNA methyltransferase ۳ alpha enzyme using Expasy and PyMOL, also stability by I-Mutant, pathogenicity and protein function through SIFT, PolyPhen-۲, and GVGD analysis.

Results: Our study examined the impact of non-synonymous single nucleotide polymorphisms (nsSNPs) on the interaction patterns and properties of the DNA methyltransferase ۳ alpha enzyme, including polar groups, hydrogen bond lengths, and hydrophobicity. The results obtained from a few prediction tools revealed significant implications of these nsSNPs on the structural and functional characteristics of the enzyme. Specifically, PolyPhen-۲ predicted a score of ۱, indicating a high likelihood of functional impact. SIFT scores were below ۰,۰۵, suggesting deleterious effects. Furthermore, GVGD classification placed the nsSNPs in class C٦۵, highlighting their potential pathogenicity. I-Mutant analysis indicated that all eighteen identified nsSNPs decrease the stability of the enzyme, leading to significant disruptions in its original function. These findings underscore

the critical role of nsSNPs in modulating the behavior and functionality of the DNA methyltransferase ٣ alpha enzyme.

Conclusion: According to in silico assays, all of the eighteen mentioned single nucleotide polymorphisms (SNPs) exhibit potential harmful effects. However, it is essential to acknowledge that in silico methods possess both advantages and limitations in predicting the impact of genetic variations. In silico analyses rely on computational algorithms to simulate biological processes, allowing for the rapid assessment of a large number of SNPs. These methods are cost-effective, time-efficient, and can provide valuable insights into the potential functional consequences of genetic variations. Despite their utility, in silico predictions are not worthy without experimental results. One of the primary limitations is the reliance on computational models, which may oversimplify the complexity of biological systems. Hence, it is important to emphasize that the predictive nature of in silico methods necessitates further confirmation of their results. Experimental validation through functional assays, such as in vitro and in vivo studies, is essential to verify the actual impact of the identified SNPs on biological processes. These experimental validations can provide comprehensive insights into the functional consequences of genetic variations and enhance our understanding of their implications for human health.

Keywords: Acute Myeloid Leukemia (AML), DNMT٣A gene, single nucleotide polymorphisms (SNPs), pathogenicity

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In Silico investigation of vitamins and their derivatives compounds as potential therapeutic agents on Helicobacter pylori using molecular docking against urease. (Research Paper)

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Introduction: Urease is an enzyme exploited by Helicobacter pylori to infect the highly acidic human stomach. Clinically used drugs are associated with many side effects; therefore, there is a need for less harmful and preferably natural compounds an alternative drug to treat Helicobacter pylori infection. The aim of this study was to investigate vitamins and their derivatives (٤٧ molecules) as urease inhibitors of H. pylori.

Methods: The crystal structures of Urease (PDB ID. ١e٩y) was obtained from the Protein Data Bank and after a cleaning with Discovery Studio ٤,١, minimized and changed to pdbqt format using MGLTools. ٤٧ FDA approved vitamins were retrieved from Selleckchem Inc web site. The ٣D structure of the ligands were retrieved from PubChem database in SDF file format and converted pdbqt format using MGLTools .Then, the ligands were evaluated as inhibitors on important residues of the urease enzyme by Autodock Vina and Autodock ٤ in pyRx program and AutoDock Vina software, and the output results were analyzed and evaluated using soft Discovery Studio software.

Results: The results of molecular docking indicated that the vitamins exhibited powerful inhibitory activity against the urease enzyme of H. pylori. The most negative binding energies are observed for the compounds; Ergosterol with Binding energy -٩,٥, Riboflavin (Vitamin B٢) with Binding energy -٩,٢, Trolox with Binding energy -٩,٠, Vitamin D٣ with Binding energy -٨,٨, Doxercalciferol with Binding energy -٨,٨, Calcipotriene with Binding energy -٨,٧, Vitamin K١ with Binding energy -٨,٠ and Folic Acid with Binding energy -٨. The results of molecular docking studies indicate that residues; His١٣٦, His١٣٨, Ala١٦٩, KCX٢١٩, His٢٢١, His٢٤٨, Asp٣٦٢ (some of which are part of the active site of the urease and also some of which are nevertheless involved in hydrogen bonding with substrate) bind to above mentioned ligands with best binding energy. Molecular Dynamic simulation showed that Trolox and Ergosterol are quite stable in binding to urease, therefore they could be valuable repurpose drugs for inhibiting urease activity of helicobacter pylori.

Conclusion: The present findings indicated the inhibitory potential of the Trolox, Ergostero, Riboflavin, Vitamin D٣, Doxercalciferol, Calcipotriene, Vitamin K١ and Folic Acid.

Keywords: elicobacter pylori, Urease, Vitamins, Molecular docking simulation

In silico molecular docking of plant-derived metabolites against BfmR of Acinetobacter baumannii

(Research Paper)

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Introduction: Acinetobacter baumannii is a multidrug resistant opportunistic pathogen, responsible for respiratory infection, pneumonia, and urinary tract infections. BfmR(RstA) is a ٣٠,٠٦ KDa protein, and a response regulator in a two-component signal transduction system (TCS). As a result, BfmR is a major controller of A. baumannii biofilm formation and an intriguing antimicrobial target. The high-resolution crystal structure of BfmR (PDB:٥E٣J) is known which provides a great opportunity for computational screening of probable inhibitors. Previous reports suggest the use of ٢٠ potential plant metabolites with antibacterial properties against OmpA, CarO, DcaP, OmpW, and PBP proteins of Acinetobacter baumannii. Here, these metabolites were docked against BmfR using PyRX software.

Methods: The methodology for the identification of novel drug candidates against A. baumannii is demonstrated below. • Refinement and quality assessment of BfmR protein. • Enlistment and collection of phytometabolite structures. • Transformation of the ٣D structure of selected metabolites into PDB. • Analyzing the binding affinity of selected metabolites using PyRX software. • Toxicity analysis

Results: Among these phytocompounds, Corilagin, Epigallocatechin gallate (EGCG), Epsilon-Viniferin, Berberine, Cucurmin, and Ellagic Acid reached the binding affinity (kcal/mol) equal to -٩, -٨,٣, -٧,٧, -٧,٥, -٧,٥- and -٧,٥ respectively. The selected hits were further analyzed for toxicity assessment using ProTox-II webserver. PROTOX prediction indicated LD٥٠ of Epigallocatechin gallate is ١٠٠٠ mg/kg with toxicity class ٤. Interestingly no hepatotoxicity, cytotoxicity, carcinogenicity, mutagenicity, or immunotoxicity were found by PROTOX as well.

Conclusion: Results suggested that Epigallocatechin gallate is a lead compound and can serve as a new drug to inhibit BfmR. To validate their inhibitory effect, EGCG can therefore be further characterized experimentally.

Keywords: Acinetobacter baumannii, BfmR, Molecular Docking, drug discovery

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Indirect Optimization of Recombinant Protein Expression Levels in the Hsp۲۷ Dicistronic SILEX System (Research Paper)

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Introduction: Design of experiments (DOE) is a statistical approach to plan, perform and interpret a large set of measurement data with a minimum number of experiments. The current study describes the optimization of a rapid screening system consisting of a dicistronic expression system containing a reporter (enhanced green fluorescent protein, eGFP), a protein model (staphylokinase, SAK) and a self-inducible system containing heat shock protein ۲۷ (Hsp۲۷).

Methods: Using RSM methodology, we indirectly identified the most effective factors on staphylokinase (SAK) expression levels among several variables, including inoculation rate, self-induction temperature and culture media, by fluorescence measurement of coupled eGFP (enhanced green fluorescent protein) expression in the dicistronic SILEX system. The expression level of SAK was measured in ۲٥ different runs for ٦ h incubation at ۹۰ rpm.

Results: The results showed that all parameters had a significant effect ($P < ۰,۰٥$) on the expression level of SAK. The optimal expression conditions were an inoculation rate of ۰,۰٥, a temperature of ۲٥°C and TB media. The analysis of variance coupled with the high value of $R^۲$ (۰,۹۱) showed that the quadratic model used for this prediction was highly significant ($p < ۰,۰٥$). Application of the optimized conditions resulted in a ~٤-fold increase in SAK expression levels (from ۱,۳ to ٥,۲ µg/ml).

Conclusion: Furthermore, the recombinant SAK with a molecular mass of ۱٦ kDa was purified by Ni-affinity chromatography and the activity was also confirmed by semi-quantitative caseinolytic assay.

Keywords: Expression, optimization, Escherichia coli, response surface methodology, green fluorescent protein

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Induced pluripotent stem cells: definition, production and their applications (Review)

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Introduction: Induced pluripotent stem cells (IPSCs) are cells that originate from adult cells that have been reprogrammed into stem cells. Therefore, these cells can differentiate into other cells. The use of this technique was done for the first time by Shinya Yamanaka and his team, who were able to reprogram mature cells and produce induced pluripotent stem cells by using specific gene vectors.

Methods: For this study we used the keyword “IPS cells” and “Stem cells” in Google Scholar database. And we just accepted review articles to our research. Finally We divided the obtained data into three categories. These categories are: 1) definition, 2) production and 3) their applications.

Results: There are different methods to create induced pluripotent stem cells, which include somatic nucleus transfer, use of specific transcription factors, micro RNA and other methods. Each of these methods has advantages and disadvantages, for example, in the use of micro RNA, specific genes can be activated, but it can be said that the interaction of this micro RNA with other parts has not been well defined yet. Induced pluripotent stem cells have various uses according to their characteristics. including use in basic research (for example, one way to study embryonic stem cells is to use these types of cells), drug screening, toxicology, disease modeling, and cell therapy.

Conclusion: Despite numerous researches on induced pluripotent stem cells, they always face challenges that we hope to overcome with more study and research.

Keywords: Induced pluripotent stem cells, IPSCs, Stem cells

Inflammatory status improved following tea consumption and combined exercise training in overweight and obese men (Research Paper)

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Introduction: One of the most important health issues in the world is obesity and its resulting inflammation, and one of the most effective ways in its prevention and treatment is physical activity. It has been shown that physical activity and drug-nutritional interventions can reduce inflammation caused by obesity. Therefore, our aim was to investigate the effect of consuming three types of tea along with combined exercise on some inflammatory indicators in overweight and obese men.

Methods: ٦٠ overweight or obese men aged ٣٠ to ٥٠ (BMI ٣٥-٢٥) were randomly assigned to four groups of training + green tea (GT+T), training + white tea (WT+T), training + Roselle tea (ST+T) and training (T) for ٨ weeks. Blood samples were measured ٤٨ hours before and ٤٨ hours after the last training session. IL-٦, TNF-alpha and Hs-CRP were measured using ELISA method. Statistical analysis was performed using ANCOVA method at a significance level of ٠,٠٥.

Results: Inflammatory markers IL٦, TNF-a, and CRP in the intervention group WT+T showed a significant reduction compared to the control group, and IL٦ in the GT+T group had a significant reduction compared to the control group. Additionally, IL٦ and CRP in the WT+T group had a more significant reduction compared to the ST+T group, and IL٦ and CRP in the WT+T group had a more significant reduction compared to the GT+T group.

Conclusion: In conclusion, the consumption of white tea with combined exercise and green tea with combined exercise significantly influenced inflammatory markers, but this was not observed in the case of Roselle tea with combined exercise. The differences in averages indicated that the effect of white tea was greater than others on the mentioned indicators.

Keywords: combined exercise training. tea. overweight. obesity

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Influence of CDKN۲A and p۱٦ Gene Expression on Human Papillomavirus (HPV) Suppression in Cervical Cells: A Comparative Analysis between HeLa and CaSki Cell Lines (Research Paper)

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Introduction: Human Papillomavirus (HPV) infection is a principal etiological factor in the development of cervical cancer. Among the various molecular players involved in HPV-associated carcinogenesis, the expression levels of CDKN۲A and p۱٦ genes have garnered significant attention. However, the precise impact of their expression on HPV suppression remains to be elucidated. This study seeks to elucidate and compare the effects of CDKN۲A and p۱٦ gene expression on HPV activity in HeLa and CaSki cervical cell lines, thereby contributing to a deeper understanding of the molecular mechanisms governing HPV regulation.

Methods: Cultured HeLa and CaSki cells were subjected to varying levels of CDKN۲A and p۱٦ gene expression manipulation using established molecular biology techniques including transfection and gene editing methodologies. The quantification of gene expression levels was performed through real-time PCR assays. Subsequent assessment of HPV activity was conducted utilizing quantitative PCR, Western blotting, and immunofluorescence techniques. Statistical analyses were employed to discern the relationship between CDKN۲A and p۱٦ expression levels and HPV suppression.

Results: Quantitative analysis revealed significant upregulation of CDKN۲A and p۱٦ gene expression in both HeLa and CaSki cells, with levels increasing from ٥۰۰ to ۱۲۰۰ copies/ng of RNA and ۳۰۰ to ۹۰۰ copies/ng of RNA, respectively. This correlated with a marked suppression of HPV activity, reducing viral load from ۲۰۰۰ to ۸۰۰ copies/ml in HeLa cells and from ۱۸۰۰ to ٤٥۰ copies/ml in CaSki cells. Statistical analysis confirmed a significant negative correlation ($p < ۰,۰٥$) between CDKN۲A/p۱٦ expression and HPV activity. These findings underscore the potential therapeutic relevance of targeting CDKN۲A and p۱٦ pathways in HPV-associated cervical carcinogenesis.

Conclusion: This study underscores the pivotal roles played by CDKN۲A and p۱٦ gene expression in modulating HPV activity within cervical cells. The observed variations in HPV suppression between HeLa and CaSki cell lines highlight potential differences in underlying regulatory mechanisms. These findings contribute to the ongoing efforts aimed at delineating the intricate molecular pathways involved in HPV-associated carcinogenesis. Moreover, they hold promise for informing the development of targeted therapeutic interventions tailored towards mitigating the burden of cervical cancer. Further investigations are warranted to unravel the nuanced interplay between CDKN۲A, p۱٦ expression, and HPV dynamics, thereby advancing our comprehension of cervical oncogenesis.

Keywords: Human Papillomavirus, Cervical Cancer, HeLa Cells, Caski Cells

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Inhibition of tau protein hyperphosphorylation in Alzheimer's disease by molecular docking method (Research Paper)

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1. School

Introduction: Alzheimer's disease is a neurodegenerative disease which imposes a heavy cost on the health system of different countries of the world. One of the pathological factors associated with Alzheimer's disease is neurofibrillary tangle that consists of accumulations of abnormally phosphorylated tau within the perikaryal cytoplasm of certain neurons. Alzheimer's disease is an undertreated disease. Currently, there are only two classes of approved drugs to treat AD, including inhibitors to cholinesterase enzyme and antagonists to N-methyl d-aspartate (NMDA), which are effective only in treating the symptoms of AD, but do not cure or prevent the disease.

Methods: The technique used in this research is molecular docking.The molecular docking approach is utilized to predict the tentative binding parameters of ligand-receptor complex. The main objective of molecular docking is to attain ligand-receptor complex with optimized conformation and with the intention of possessing less binding free energy.Bioethics importance in Bioinformatics and also having the advantage of low cost have made docking an increasingly important tool in pharmaceutical research.

Results: Inhibiting the excessive phosphorylation of Tau protein with the assistance of plant molecules which result in fewer side effects also prevents tau hyperphosphorylation and consequently Alzheimer's disease. In this research the docking of these plant molecules with tau protein will be examined utilizing The Molecular docking approach.

Conclusion: Inhibition of the binding site of phosphorus to tau protein for the purpose of preventing excessive phosphorylation will be followed

Keywords: Alzheimer, tau protein, Molecular docking

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Inhibitors as drug targets in the treatment of atherosclerosis (Research Paper)

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Introduction: Cardiovascular disease (CVD) may begin in middle age. This disease is responsible for a third of all deaths globally (٣٠٪ of men and ٢٤٪ of women). Atherosclerosis is the major cause of cardiovascular disease. Atherosclerosis is a multifactorial and complex progression. It happens when the arteries become narrow and blood flow becomes difficult in them. Atherosclerosis increases the risk of heart attack and stroke. A persistent increase in circulating low-density lipoprotein (LDL) levels in the body is one of the most important causes of the initiation and progression of atherosclerosis. Cigarette smoking, diabetes mellitus, serum cholesterol, and hypertension, are associated with risk factors for atherosclerotic disease. It is known that enzymes are involved in many pathological conditions, such as inflammation, diabetes, microbial infections, HIV, neoplastic, neglected diseases, and others. Many drug molecules are enzyme inhibitors that inhibit an aberrant human enzyme. This study aims to review inhibitors as drug targets in the treatment of atherosclerosis

Methods: To study the inhibitors as drug targets in the treatment of atherosclerosis, this article summarizes currently available articles in MEDLINE, EMBASE, Scopus, and other databases about inhibitors and drugs in atherosclerosis treatment

Results: Cholesteryl ester transfer protein (CETP) is a plasma lipid transfer protein, responsible for moving cholesterol esters and triglycerides between lipoproteins. CETP inhibitors are the best choice in the treatment of atherosclerosis. Cholesterol acyltransferases (ACATs) are other targeted proteins for enzyme inhibition in atherosclerosis. These proteins are attached to the membrane and use long-chain fatty acyl-CoA and cholesterol as substrates to form cholesterol esters. Inhibition of ACAT١ may prevent the progression of atherosclerosis. Diglyceride acyltransferase (DGAT) enzymes are involved in triglyceride synthesis. Inhibition of this enzyme may reduce the risk of atherosclerosis. Microsomal triglyceride transfer protein (MTP) is a lipid transfer protein. This protein assembles very low-density lipoproteins. The inhibition of MTTP causes a reduction in plasma triglyceride levels which thereby reduces the risk of atherosclerosis. The key enzyme in cholesterol biosynthesis is squalene synthase and inhibitors of this enzyme suppress triglyceride biosynthesis. Furthermore, Diacylglycerol acyltransferases (DGAT) are the enzymes that catalyze the final step in the assembly of TAG, and Inhibition of DGAT may reduce the risk of atherosclerosis.

Conclusion: Based on my review many inhibitors can be used as drug targets in the treatment of atherosclerosis. Inhibitors of key enzyme reactions play a major role in the selection

Keywords: Inhibitors, drug targets, treatment, atherosclerosis, enzyme

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Inhibitory Effects Of Marine Metabolites Against Some Uropathogenes and Beta-Lactamases

(Research Paper)

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Introduction: Urinary tract infection is a common disease often caused by Escherichia coli bacteria. This bacterium produces beta-lactamases that resist antibiotics. Marine actinomists can produce a wide range of metabolites, which can be used as antibiotics.

Methods: E. coli phylogenetic grouping was done using PCR on three markers yjaA, chuA, and TspE٤.C٢. ٣٠٠ Samples of patients were collected and identified by testing the diagnostic tests of E. coli. Anti biogram test was measured by using common antibiotics, and extracts of marine actinomist bacterial extract, on bacteria. ٥٠ isolates were identified and tested for sensitivity using antimicrobial agents CLSI, ٢٠٢١.

Results: ٣٢/٥٠ (٦٤ percent) of the isolates were resistant to several drugs and ١٨/٥٠ (٣٦ percent) were non-resistant. The inhibitory effect of actinomycet extract against ١٠ resistant E. coli isolates was observed. Prevalence (gene blaOXA ٤٦٪), (gene blaTEM ٦٨٪), (gene blaCTXM-IV ٦٨٪), (gene blaNDM ٢٦٪), (gene blaCTXM-II ٥٠٪), (gene blaCTXM-I ١٠٠٪) was reported in multi-antibiotic resistant samples. The phylogenetic grouping showed that E. coli's isolates consisted of group B٢ (٨٤٪), subgroup B١ (٦٪), group A (٢٪), group D (٨٪), and ٧٢٪-١٠٠٪ of the isolates were resistant to cephalosporin.

Conclusion: This resistance indicates the pressure of possible antibiotic selection in the community. Pathogen resistance factors to beta-lactam were often in the phylogenetic group B٢, and this group had the highest number of blaCTX-M and blaTEM genes in resistant isolates. Marine Actinomistasts showed great ability in inhibiting resistant isolates, so they could be used as a suitable alternative to the treatment of resistant E. coli.

Keywords: Escherichia coli, phylogenetic group, antibiotic resistance, urinary tract infection

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INLA- Based fast fully Bayesian method for brain mapping (Research Paper)

Mahboobe Maghami,[1] Azam Saffar,[2,*]

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۲.

Introduction: The brain is one of the most vital and complex organs of the human body. For centuries, researchers have sought to unravel the intricacies of its functioning. As our understanding deepens, brain mapping has emerged as an increasingly significant area of scientific inquiry. Understanding the brain is, in many ways, synonymous with understanding human behavior, cognition, and future potential. Statistical methods have proven to be indispensable tools in advancing this research. In this paper, we introduce a novel and rapid Bayesian statistical method designed to enhance the process of brain mapping. This method offers both speed and precision, providing an efficient means of advancing our understanding of the brain's structure and function.

Methods: In this paper, we present a new spatiotemporal Bayesian method for brain mapping, building upon the fast Bayesian approach developed by Masgarov. A key innovation in our method is the replacement of the traditional estimation technique with the Integrated Nested Laplace Approximation (INLA), a powerful tool for approximate Bayesian inference. INLA offers significant advantages in terms of both computational efficiency and accuracy, especially when compared to sampling-based methods such as Markov Chain Monte Carlo (MCMC). These improvements contribute to its growing popularity in Bayesian inference. We applied this model to fMRI data obtained from an auditory task and compared its performance to that of previous models, demonstrating its enhanced capability for brain mapping.

Results: The proposed method was compared with both the conventional General Linear Model (GLM) and the fast Bayesian method. Key performance metrics, including computation time, activation areas, and the False Discovery Rate (FDR), were evaluated. While the GLM was the fastest in terms of execution time, our INLA-based fast Bayesian model demonstrated superior precision and noise reduction, with only a marginal difference in speed. All three methods identified similar primary activation regions in the brain; however, our model detected a higher number of activated areas. Additionally, the INLA fast Bayesian model more effectively removed noise and irrelevant voxels, resulting in more accurate and detailed brain maps.

Conclusion: Brain mapping with modern statistical methods offers the potential for deeper and more accurate insights into brain function. While spatiotemporal statistical models generally require more computational time compared to conventional General Linear Models (GLM), they provide a more precise representation of the brain's complex dynamics. By accounting for both spatial and temporal data, these models are better suited to capture the true capacity of real-world data, ultimately leading to more reliable and nuanced findings in brain research.

Keywords: Brain mapping, fast Bayesian mode,INLA, Spatiotemporal

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Innovative Approaches for Uterine Regeneration: Stem Cells, Tissue Engineering, and Nanoparticles (Research Paper)

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Introduction: The present research has focused on the problem of tissue regeneration in the uterus to resolve such complicated conditions as uterine adhesions, endometriosis, or myometrium regarded as serious causes of infertility and chronic health problems connected with reproductive functions. Traditional treatments involving surgery and hormonal therapies alone often cannot produce long-lasting effects and can result in serious complications such as scarring, adhesions, or incomplete recovery. Advanced solutions searched for in this study include stem cell therapy, tissue engineering, and the addition of nanoparticles for treatment. The focus of this present study is on tissue regeneration in the uterus for the solution of such complicated conditions as adhesions of the uterus, endometriosis, and myometrium damage conditions, which are substantial causes of infertility and chronic problems in reproductive health. Traditional treatments, including surgery and hormonal therapies, frequently cannot provide long-lasting results and are more than often complicated by scarring, adhesions, or incomplete recovery. Advanced solutions being investigated in the present work include stem cell therapy, tissue engineering, and the addition of nanoparticles. Such a trend opens new horizons for treatment. The relevance of this investigation is an attempt for more effective therapy with less invasion that could restore normal uterine function and improve fertility.

Methods: This study focused on several ways of improving the utility of stem cells, bioengineered scaffolds, nanoparticles, and advanced aspects of tissue engineering. Notably, the involvement of stem cells, particularly of mesenchymal origin, is deemed crucial due to their well-documented abilities in regeneration and differentiation. Stem cells are also obtained from bone marrow, among other sources, such as umbilical cords, and mixed with bioengineered scaffolds to take action as support for tissue growth. The scaffolds are made to emulate the uterine environment by modeling them with decellularized uterine matrices and gelatin/polycaprolactone biofilms, which should contribute to better cell proliferation and repair. Integration of nanoparticles into these regenerative therapies, enhancing their effectiveness and potential. For instance, gold and silica nanoparticles enhance growth factor delivery and further increase the potency of stem cell therapies. They are involved in controlled release processes of key factors that further increase tissue repair angiogenesis, such as VEGF and PRP. Secondly, nanomaterials enhance scaffold biocompatibility with already available uterine tissue. The techniques of ۳D bioprinting were also studied for more complicated geometries of tissues.

Results: Several promising findings are reported in the study, the most important of which is the synergistic effect following the treatment with stem cell therapy, bioengineered scaffolds, and nanoparticles. Specifically, MSCs in combination with nanomaterials promoted tissue repair and

caused a huge enhancement in the regeneration of myometrial and endometrial layers. Similarly, MSC-loaded scaffolds exhibited better biocompatibility and integration into existing tissues due to the control of nanoparticle growth factor release and inflammation. It has been demonstrated that golden-based or silica-based nanoparticles enhance the delivery of the growth factors, thus accelerating tissue regeneration and angiogenesis of the uterine tissue. Extended-release of such factors would ensure continuous regeneration while reducing possible adverse side effects, such as excessive fibrosis or overgrowth of tissues. Nanoparticle-augmented PRP therapy shows performance, thickening the endometrium among patients with thin uterine linings and improving their implantation and conceiving abilities. Remarkably, the combination of nanoparticles with bioengineered scaffolds exhibited, in animal models, profound structural restoration of uterine tissue. Scaffolds reinforced with nanoparticles enhance cell adhesion and increase tissue performance proliferation and differentiation. It has also been noted that nanoparticles reduce recurrence in adhesions like Asherman's syndrome by modulating inflammation into long-term healing.

Conclusion: This review underlines the innovative potential of combining nanoparticles with stem cell treatment and tissue engineering in uterine regeneration. It further shows that nanoparticles enhanced growth factor delivery and efficacy in the biocompatibility and functionality of bioengineered scaffolds. This may lead to better treatment modalities for pathologies that affect uterine health by offering minimally invasive, more sustainable treatments for women affected by infertility, endometriosis, or uterine adhesions. Furthermore, nanotechnology-based regenerative medicine offers promising enhancements in the precision and efficiency of treatment. Such a review has pointed out the critical role of nanomaterials in increasing therapeutic outcomes through targeted and controlled interventions.

Keywords: uterine regeneration, stem cells, tissue engineering, nanoparticles, endometriosis

Innovative Nanoparticle-Based Strategies in Brain Tumor Treatment: Chemotherapy and Targeted Drug Delivery (Review)

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Introduction: Brain cancers are regarded as one of the most complicated and deadly cancer types. It is characterized by uncontrolled growth and abnormal cell division within the brain or spinal cord. Tumors may grow fairly rapidly and damage the delicate tissues of the brain irreparably, leading to serious neurological disabilities that critically damage the quality of life. Treatments are made more difficult by the finding of tumors in sensitive locations and the restrictions in the treatment options. This shall introduce a new dimension to treatment improvement by using nanoparticles.

Methods: The following review will outline some of the drugs used in brain tumors and the role of nanoparticles in enhancing drug delivery. Temozolomide, an alkylating chemotherapy agent used commonly for glioblastoma; inhibits DNA synthesis in tumor cells, leading to tumor atrophy. Temozolomide shows better responses when used with radiation therapy. Bevacizumab is a monoclonal antibody directed against VEGF, and its mechanism of action is inhibition of neo-angiogenesis, or the formation of new blood vessels, which subsequently slow tumor growth. Temozolomide shows improved responses when given in combination with radiation therapy. The monoclonal antibody against Vascular Endothelial Growth Factor, bevacizumab, inhibits neo-angiogenesis tumor growth. Carmustine is an alkylating agent, too, but drug delivery to the correct location with minimum systemic toxicity is achieved by placing it into the brain by localized implants. Eflornithine inhibits Ornithine Decarboxylase, an enzyme involved in cell proliferation. In this review, the efficacy of drugs in the control of tumor growth and outcomes will be discussed. This can be enhanced by nanoparticles such as lipids, biocompatible polymeric, gold, magnetic, albumin, bioactive, viral, hybrid, and light-controlled, which might improve the delivery with reduced toxic side effects of drugs.

Results: temozolomide in combination with radiation has been demonstrated to significantly increase survival from a median of ١٢,١ to ١٤,٦ months among patients with glioblastoma. However, frequent dosing and poor delivery of the drug across the brain remain challenges. Bevacizumab has shown a reduction in the volume of tumors, thus alleviating symptoms in patients who did not have any response to standard treatments; it needs close monitoring of side effects such as hypertension and bleeding. Carmustine, mainly in the form of local implants, increases the drug concentration at the position of the tumor and reduces systemic side effects, thereby improving survival in cases of high-grade glioblastoma. Eflornithine efficiently inhibits the ODC enzymes and decreases the growth of cancerous cells, thereby increasing the efficacy of treatment, more so in combination with other drugs against resistant tumors. The use of nanotechnology in

medication administration has advanced significantly. Drug release is regulated by the blood-brain barrier (BBB), which is penetrated easily by lipid nanoparticles. For instance, polymeric nanoparticles are easily manipulated to enable the targeted delivery of medications and are biocompatible. Gold nanoparticles enable targeted therapy and imaging due to their optical and thermal properties. While magnetic nanoparticles can direct drugs through the effect of external magnetic fields, light-controlled nanomaterials offer improvement by enabling better drug delivery in localization and timing with light activation.

Conclusion: The article refers to huge progress in the treatment of brain tumors, which was brought about with the introduction of novel therapeutics such as TMZ, BEV, CCNU, and EFLNTH and advanced drug delivery technologies that improved the survival of patients with high-grade glioblastoma. Temozolomide acts on DNA synthesis to prolong survival time. Bevacizumab reduces cerebral edema and clinical symptoms as it obstructs the formation of new blood vessels. The local carmustine implants provide drug concentration at the tumor site, thereby reducing systemic side effects. Eflornithine inhibits key enzymes involved in cell proliferation and enhances therapeutic outcomes. Some benefits of nanoparticles include increased localization and improved systemic toxicity with lipid nanoparticles and biocompatible polymeric nanoparticles. These magnetic and light-controlled nanoparticles provide targeted and responsive drug delivery for better treatment efficiency. However, problems still exist in poor absorption of the drug across the BBB and long-term side effects monitoring. Focusing on nanoparticle-based delivery systems and their incorporation into existing treatments is crucial to enhancing the efficacy and outcome of brain tumor therapy.

Keywords: Brain tumors, Nanoparticles, Targeted drug delivery, Chemotherapy, Blood-brain barrier

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Insight to BRCA mutation effect in breast cancer Prevention and recommended treatments (Review)

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Introduction: One of the frequent and numerous malignant tumors that affect women is breast cancer. Breast cancer develops and occurs as a result of several internal and external factors. Poor lifestyle choices, environmental factors, and social-psychological factors are all linked to its occurrence. It has been demonstrated that ٥٪ to ١٠٪ of breast cancers can be attributed to genetic mutations and family history, and ٢٠٪ to ٣٠٪ of breast cancers can be attributed to factors that may be modifiable. Breast cells are where breast cancer first develops. A collection of cancer cells known as a cancerous tumor is capable of spreading into and destroying nearby tissue. As well as spreading throughout the body, it can. Breast cells occasionally undergo changes that prevent them from growing or behaving normally. Non-cancerous breast conditions atypical hyperplasia and cysts may result from these changes. Additionally, they may result in benign tumors like intraductal papillomas.

Methods: After reaching ٢٥ years, individuals should undergo biannual or annual breast examinations by a physician. Annual breast magnetic resonance imaging or mammography is recommended for women aged ٢٥ to ٣٠, and both modalities are recommended for women over ٣٠ years old. There is now broad consensus that early detection efforts in high-risk women should primarily be based on annual contrast-enhanced breast MRI, which is by far the most sensitive test for early detection of breast cancer.

Results: The PARP family of proteins, discovered more than half a century ago, proved to have very important functions in terms of many cellular processes, including transcription, cell death, and DNA repair. Replication stress and mutations in DNA damage repair genes, which are frequently observed in cancer cells, and have led to new ideas for treatment strategies that are PARP-centered. In particular, the knowledge about the roles of PARP١ in DNA repair has led to the development of PARP inhibitors for the treatment of cancers with BRCA mutations.

Conclusion: Chemoprevention involves a variety of drugs used to prevent or delay the onset of cancer. These drugs are used as an alternative to invasive surgical procedures, such as bilateral prophylactic mastectomy, to lower a person's risk of cancer development. Selective estrogen receptor modulators (SERMs), tamoxifen and raloxifene, are commonly used in the treatment of various diseases including BC and are the only two FDA-approved compounds for primary prevention of BC. tamoxifen can reduce the risk of developing CBC by ٣٧٪-٥٨٪ in BRCA٢-mutated carriers. This trial initially demonstrated that the effectiveness of raloxifene was similar to tamoxifen in preventing invasive BC.

Keywords: ١. breast cancer(bc) ٢. BRCA١ ٣. BRCA٢ ٤. mutation ٥. PARP inhibitors

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Insight to brucellosis treatment and diagnosis (Review)

Sara Aghili Ashtiani,[١,*] Saman Hakimian,[٢]

١.
٢.

Introduction: Brucellosis can affect any organ system hearing loss in brucellosis may develope following the involvement of centural auditory pathways or avascular neural tissue due to reflex spams cause by endotoxins . the goal of the treatment brucellosis is to shorten the duration of symptoms and to prevent replase at least two drugs should be used for the treatment of brucellosis at hospital .in present study our patients were treated with antibacterial combination which is in accordance with literature because human brucellosis can affected any regimens vary.

Methods: Since ١٩٩٩ in japan have been reported .although no bacteria were isolated serum anti body detection indicated that ٤were cased by melitensis or B.abortus acquired fatigue .The study compared the BACTEC blood culture system (Becton Dickinson Diagnostic Insrument System Spark) with conventional culture methods for recovery and time to detecetion of significant isolated from normally sterile body fluids a total of ٤١٢ specimens were included in the study a significant difference was noted between the blood culture system and routine culture systemand routine culture methods for recovery of pathogenic .microorganisms that were from sterilebody fluids the most frequently isolated microorganisms recovery with both culture methods .

Results: Contact with infected animals consumptions of raw milk and ignorance regarding the disease are the major risk factors. since clinical manifestions of this disease are protein in nature Rose bengal platetest(RBPT)and serum aggulatinationtest(SAT).

Conclusion: Brucella were recovered only with blood culture system further more the mean time to detection of signification pathogens was significantly less with blood culture system than with conventional media BACTEC blood culture system was found to improve the yield of clinically significant isolated from normally sterile body fluids with reduced time to detection it maybe adanatageous for isolation of fastidiuos microorganisms such as brucella and S.pnemoniae especially from cerebrospinal and synovial fluids speciemens.

Keywords: Brucella- Bloodculture-Significant-Speciemens-Miroorganisms

Insight to colon cancer disease and treatment (Review)

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Introduction: Colon cancer (CC) stands as a formidable global health challenge, ranking as the third leading cause of cancer-related mortality. The molecular categorization of colon cancer patients remains elusive. Gene set enrichment analysis (GSEA), which investigates the dysregulated genes among tumor and normal samples, has revealed the pivotal role of epithelial-to-mesenchymal transition (EMT) in colon cancer pathogenesis. Tumor-associated macrophages are transcriptionally heterogeneous, but the spatial distribution and cell interactions that shape macrophage tissue roles remain poorly characterized. Solute carrier family (SLC) transporters are expressed in the digestive system and play important roles in maintaining physiological functions in the body. In addition, SLC transporters act as oncoproteins or tumor-suppressor proteins during the development, progression, and metastasis of various digestive system cancers. SLC٢٢A١٨, a member of the SLC٢٢ gene family, is an orphan transporter with an unknown endogenous substrate. A considerable number of colon cancer patients with local or local advanced disease suffer from QV recurrence and there is an urgent need for better prognostic biomarkers in this setting. Colorectal cancer (CRC) screening is a fundamental tool in the prevention and early detection of one of the most prevalent and lethal cancers. Over the years, screening, particularly in those settings where it is well organized, has succeeded in reducing the incidence of colon and rectal cancer and improving the prognosis related to them. Despite considerable advancements in screening technologies and strategies, the effectiveness of CRC screening programs remains less than optimal.

Methods: Since colon cancer has a high rate of shedding of tumour fragments into the blood, several research efforts are now focused on the investigation of the minimal residual disease through the detection of ctDNA to tailor the adjuvant therapy of colon cancer patients and optimize its cost/effectiveness balance. The negative prognostic impact of detectable ctDNA in patients' blood after radical surgery for colon cancer is well established. Lipidomic and proteomic analysis of membrane fractions revealed significant changes in tumor-promoting cellular pathways and cellular transporters. The oncolytic microbe can trigger pyroptotic cancer cell death, but insufficient pyroptotic response of current microbe-based biotherapeutics restricts the antitumor efficiency. Herein, we report an oral bacterial pyroptosis amplifier composed of two bacterial strains, reductive Shewanella oneidensis MR-١ (abbreviated as MR-١) and engineered Escherichia coli (E. coli) with the overexpression of pyranose oxidase, augmenting the pyroptosis effect against colon and metastatic tumors.

Results: Each bacterium is camouflaged with hyaluronic acid to survive against the harsh gastrointestinal environment and to enrich in colon tumor sites. Upon the bacteria colonizing at the tumor site, iron sucrose is orally administrated.

Conclusion: The following oral administration of Fe(Ⅲ)-contained iron sucrose leads to the intratumoral accumulation of Fe(Ⅱ) by the reduction characteristic of MR-١. Hydrogen peroxide (H O), synthesized by pyranose oxidase from E. coli, serves as the substrate for Fenton reaction to generate toxic hydroxyl radicals through Fe(Ⅱ)-H O -Fe(Ⅲ) recycling between both strains, thereby promoting immunogenic pyroptosis inside the tumor.

Keywords: cancer - colon - DNA - health - tumor - cellular

Insight to human papilloma virus and cervical cancer diagnosis and treatment (Review)

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Introduction: Human papillomavirus (HPV) infection is caused by a DNA virus of the Papillomaviridae family. Most HPV infections cause no symptoms, and ٩٠ percent of them go away on their own within two years. Some types of HPV can cause warts on the skin or mucous membranes, and some can lead to ٥٪ of cancers, including cervical, penile, vulva, vagina, anus, and oropharyngeal cancers. Developed countries have reduced this challenge by introducing structured screening programs and recently the HPV vaccine.

Methods: HPVs are one of the most common pathogens that affect humans, and there are more than ١٠٠ subtypes of HPV, which are classified into two high-risk and low-risk types depending on their oncogenic potential. Low-risk HPV subtypes include HPV-٤٢, HPV-١١, HPV-٦, HPV-٤٣, and HPV-٤٤. They are the most common non-carcinogenic subtypes and are responsible for more than ٩٠٪ of genital warts. HPV-٦ and HPV-١١ subtypes Oncogenes include HPV-١٦, HPV-١٨, HPV-٣٣, HPV-٣٥, HPV-٤٥, and HPV-٥٨, and these have the potential to cause cancer of the cervix, oropharynx, vagina, vulva, penis, and anus. Cervical cancer is the most common HPV-related cancer, and HPV-١٦ is the most common causative subtype, followed by HPV-١٨. Together, HPV-١٦ and HPV-١٨ account for approximately ٧٠٪ of all cervical cancer cases.

Results: HPV has a great tendency to infect epithelial cells of the skin and mucous membranes, and HPV infection is associated with a wide range of pathologies. HPV is the etiological factor in benign skin warts and respiratory papillomatosis in adolescents, as well as low-grade squamous intraepithelial lesions (SLE) and high-grade squamous intraepithelial lesions (SLE) are precursors of cancer and invasive carcinoma.

Conclusion: Treatment of precancerous lesions, cancers and persistent/recurrent benign lesions caused by HPV is still an incompletely resolved problem. The effectiveness of the treatment may be increased by including methods that are based on stimulation of the immune system in the fight against infection.

Keywords: Human papillomavirus (HPV), HPV vaccine, uterine cancer, genital warts and sexual contact

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Insight to human papilloma virus and treatment (Review)

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Introduction: Introduction: Human papilloma viruses(HPV) are one of the most dangerous factors of infection and considered the most common sexually transmitted disease among both males and females.they are small, non-enveloped viruses, with a doublestranded circular DNA and a simple structure and are built of only a few genes (six early and two late genes). HPV is a major public health concern with over ١٨٠ different genotypes, amongst which ٣٠–٤٠ infect human genitalia. HPV ١٦ and ١٨ genotypes cause more than ٨٠ % of cervical cancer . There are different factors that enhance chances of contracting HPV infections. Typically, HPV is transmitted through direct sexual contact or skin-to-skin contact . Pathways for HPV transmission vary across different mucosal sites per individual. They include autoinoculation within one host, direct transmission between individuals (including perinatal transmission and transmission during sexual activity), and indirect transmission through contact with hands.

Methods: Material methods: Prevalence of HPV acquisition, persistence, and infection are correlated with sexual behaviour, viral load, anatomical site, local immunity and clearance. With age, the incidence of new infections decreases, while persistence increases.

Results: Results: HPV infection can be acquired in utero via the placenta or umbilical cord blood, parentally or through breast milk or during vaginal delivery, at caesarean section. Perinatal transmission of LR-HPV to neonates at birth has been confirmed to be associated with recurrent respiratory papillomatosis (RRP) development.

Conclusion: Conclusion: Our main analysis supported the association of systemic HIV infection, immunosuppressive medications ,smoking ,and young age at first pregnancy,, number of sexual partners with increased risk for worse HPV and cervical disease outcome .

Keywords: Human papillomvirus ;Treatment ; Disease ; Ovary

Insight to the effect of PCOS on infertility (Review)

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Introduction: Polycystic ovary syndrome (PCOS) is one of the most common hormonal and genetic disorders in women; was first described by Stein and Leventhal in ١٩٣٥, and the incidence of the syndrome is estimated at ١٥-٢٠٪ of women in the world of reproductive age, (١٥-٢٠٪) of women in the world of reproductive age (١٢-٤٥) years. It is the leading cause of infertility. Whether it is primary or secondary in women. About ٢٦٪ of women with cysts are within primary infertility, ١٤٪ of them are within secondary infertility, ٣٠٪ include a regular menstrual cycle, ٥٠٪ suffer from infrequent menstruation, and ٢٠٪ suffer from amenorrhea. Polycystic ovary syndrome causes depression and anxiety in infertile women. Endometrial disorder can be an additional factor that causes infertility and frequent implantation failure and frequent abortion in women with PCOS and infertility. Ketogenic diet can be effective in improving the fertility of women with PCOS, and OMT improves fertility by activating the cholinergic anti-inflammatory pathway, and acupuncture induces ovulation by affecting follicles, and finally, yoga improves metabolic efficiency and... It increases fertility. Cultural and social expectations make Omani women feel anxious and stressed, and they always fear losing their husbands. Omani women always feel guilty for not giving their husband children.

Methods: Endometrial disorder can be an additional factor that causes infertility and frequent implantation failure and frequent abortion in women with PCOS and infertility. Ketogenic diet can be effective in improving the fertility of women with PCOS, and OMT improves fertility by activating the cholinergic anti-inflammatory pathway, and acupuncture induces ovulation by affecting follicles, and finally, yoga improves metabolic efficiency and... It increases fertility. Cultural and social expectations make Omani women feel anxious and stressed, and they always fear losing their husbands. Omani women always feel guilty for not giving their husband children. We found that women with a PCOS reported comparable rates of anxiety and depressive symptoms to women with other infertility diagnoses. Yet, women with a PCOS reported slightly lower body appreciation scores. Vitamin E can increase ovulation and pregnancy rates in women with PCOS and resistant to clomiphene citrate By improving oxidative stress and reducing the exogenous dose of HMG.

Results: Research has shown that PFASs may act as endocrine disrupting chemicals(EDCs) and pose potential risks to reproductive health and development. Studies showed that high pre-IVF BMI in women withPCOS was associated with lower pregnancy and live birth rates. Furthermore, a highpre-IVF BMI in women with PCOS significantly increased the risk of miscarriage, GDM,gestational hypertension and caesarean section. In every woman with PCOS, age is inversely correlated with AMH, but BMI has no relationship with AMH and only causes ovulation disorder.

Conclusion: High levels of homocysteine are more common among women with PCOS. In polycystic ovary syndrome, one of the main causes of infertility is Anovulation, which is used to induce ovulation with letrozole and clomiphene citrate tablets. Probable explanations include reduced progesterone levels, prolonged exposure to estrogen, higher levels of free insulin, insulin like growth factor-\, androgens, and luteinizing hormone (LH), which can lead to aberrant endometrial cellular proliferation and receptivity. Endometrial disorder can be an additional factor that causes infertility and frequent implantation failure and frequent abortions in women with PCOS and infertile. according to the multivariable adjusted logistic regression analysis and QGC, PFOA in follicular fluid correlated with aheightened risk of PCOS. PFOA might play a direct role in the occurrence of PCOS. These discoveries have increased our understanding of the harmful effects of PFOA exposure and raised concerns about the impact of exposure to long-carbon-chain PFCAs on reproductive health.

Keywords: PCOS infertility pregnancy ovulation

Integration of synthetic biology and quantum computing as a new frontier in precision oncology

(Review)

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Introduction: The domain of cancer treatment has been characterized by remarkable progress alongside enduring difficulties. Even with advancements in specific therapies, the complicated dynamics of cancer biology and the diverse ways patients react remain considerable challenges. Precision oncology aims to customize treatments based on the unique traits of each patient's cancer, presenting a promising option. Nonetheless, the present methods in precision oncology often face obstacles stemming from the intricate molecular and cellular relationships at play, compounded by the shortcomings of current computational models that struggle to accurately forecast individual responses to treatment. This article explores the promising possibilities of integrating synthetic biology with quantum computing as a new pathway in precision oncology. Synthetic biology emphasizes the creation and arrangement of novel biological components, devices, and systems, and holds great promise for crafting highly tailored treatments that can adapt as cancer evolves. On the other hand, quantum computing can rapidly handle and scrutinize vast biological datasets with remarkable precision. This makes it an essential asset in tackling the computational challenges encountered by current cancer treatment approaches. The fusion of these two advanced technologies could transform the realm of precision oncology, leading to the development of more efficient and tailored cancer treatments.

Methods: Integrating synthetic biology with quantum computing in precision oncology involves multiple crucial phases. Initially, synthetic biology methods are employed to create customized genetic circuits and cellular frameworks specifically aimed at cancer cells. These systems can be programmed to react to the distinct molecular characteristics of various cancer types, facilitating highly targeted treatments. For instance, synthetic gene circuits might be designed to trigger therapeutic genes when certain cancer markers are present, ensuring that the treatment focuses on the cancerous tissue while reducing harm to healthy cells. At the same time, quantum computing plays a vital role in analyzing the extensive datasets produced by these synthetic biology systems. Traditional computing approaches often struggle with the intricate nature and scale of biological information, especially when simulating the complex interactions that occur both within and among cells. In contrast, quantum computers can handle this data more effectively by utilizing quantum bits (qubits), which enable the simultaneous processing of multiple possibilities. This feature is crucial for accurately modeling the fluid behavior of cancer cells and forecasting their responses to different treatment strategies. To assess the effectiveness of this integrated method, experimental cancer models are employed. Here, synthetic biology constructs are introduced into cancerous cells, and

their behavior is observed through simulations enhanced by quantum technology. These models serve to refine the designs of synthetic biology and improve the quantum algorithms used for data processing. Through ongoing testing and enhancement, the collaborative approach of synthetic biology and quantum computing is consistently advanced, ensuring it can effectively achieve the intended therapeutic results.

Results: Preliminary results from the merge of synthetic biology and quantum computing in targeted cancer treatment are very encouraging. The synthetic biology frameworks have shown they can effectively hone in on cancer cells by recognizing their distinct genetic and molecular characteristics. These frameworks have proven capable of distinguishing between malignant and healthy cells, which minimizes the chance of collateral damage often seen in traditional treatments. Furthermore, the integration of quantum computing has greatly improved the speed and precision of data analysis, facilitating immediate modifications to treatment plans based on the most current biological findings. In experimental models, this combined strategy has fostered the creation of more efficient personalized therapies. For example, in studies involving aggressive cancers that usually resist standard therapies, the partnership of synthetic biology and quantum computing has yielded better treatment results, such as slower tumor progression and higher survival rates. Additionally, this method has sped up the drug discovery timeline, enabling the swift identification of promising therapeutic agents for further testing in clinical environments.

Conclusion: The fusion of synthetic biology with quantum computing marks a significant leap forward in the realm of precise cancer treatment, unlocking fresh possibilities for crafting highly tailored therapies for patients. This joint approach addresses critical challenges in cancer research, including the complex aspects of cancer biology and the pressing need for improved predictive models. Preliminary results suggest that this partnership not only boosts the precision and efficacy of cancer therapies but also accelerates the discovery of new treatment options. As these technologies advance, additional studies are essential to connect their theoretical possibilities with real-world applications. This involves creating more sophisticated quantum algorithms specifically designed for oncology's requirements, along with developing scalable synthetic biology frameworks that can be consistently implemented in clinical environments. In the end, the effective merging of these pioneering technologies has the potential to revolutionize cancer care, resulting in more potent and customized therapies that improve patient results and lessen the societal impact of cancer.

Keywords: synthetic biology, quantum computing, precision oncology, cancer treatment

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Interaction Studies Between Myricetin and papain-like Protease of Infectious Bronchitis Virus

(Research Paper)

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Introduction: The infectious bronchitis virus (IBV) is the cause of avian infectious bronchitis, an acute contact respiratory infectious disease that affects poultry. Controlling avian infectious bronchitis due to the continuous emergence of new serotypes and variants by vaccination is difficult. IBV causes severe economic losses in the poultry industry worldwide. IBV encodes a nonstructural protein called papain-like protease (PLpro). It plays a key role in viral replication and blocking host immune response. Myricetin is a flavonoid found in tea, berries, fruits, wine, and herbs and has been reported to exhibit antiviral, antimicrobial, anticancer, and antiplatelet effects. In this article, we investigate the interaction between myricetin and papain-like protease of infectious bronchitis virus.

Methods: First, the Discovery Studio software version ۳,۵ was installed on the laptop CPU Intel coreiV ۹۷۵۰H – RAM ۱٦GBytes DDR٤ – Graphics GTX ۱٦٥۰. ۲. In the second stage, various articles were used to obtain the desired protein code. The most frequently used code in the articles was selected as the protein code, and then the enzyme code was entered into the search section of the PDB site to download the desired protein. The code for the desired compound was entered on the PubChem website to obtain the suitable ligand, and its ۳D structure was downloaded in SDF format. Since the Discovery Studio software did not support this format, the SDF file was converted to PDB format. The ligand and protein were docked to form a ligand-protein complex using the Auto Dock Vina, version ۱,۰,۵. Using the Discovery Studio program, the different kinds of hydrogen bonds that were created in the ligand-protein complex were analyzed.

Results: The protein (code ٤X۲Z) and the ligand (code ٥۲۸۱٦۷۲ myricetin) were selected for interaction analysis and examination. After completing the docking process, the study was carried out using Discovery Studio ۳,۵ software, and four hydrogen bonds were identified, involving the following amino acids: ALA۱۰٦, ASN۱٥٥, THR۲۹۱ and SER۱۰٥.

Conclusion: The compound under investigation formed a ligand-protein complex with the Papain-like protease enzyme by creating four hydrogen bonds. It should be noted that the above studies were bioinformatics-based. To confirm the results and for further investigation, it is necessary to examine the inhibitory effects of the compound myricetin on the Papain-like protease enzyme under in vitro conditions.

Keywords: Infectious bronchitis virus, Myricetin, Papain-like protease, Enzyme, Ligand-protein

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Intracellular Delivery of Diphtheria Toxin Elicits Anti-angiogenic Response in Cells Overexpressing Vascular Endothelial Growth Factor Receptor ٢ (Research Paper)

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Introduction: The vascular endothelial growth factor receptors, namely VEGFR١ and VEGFR٢, constitute tyrosine kinase receptors prominently expressed on both endothelial cells and tumor vessels, significantly influencing the intricate process of angiogenesis. In this study, a trimeric arrangement of the VEGFR١ and VEGFR٢ binding peptide (VGB٣) was strategically incorporated through genetic fusion into the truncated diphtheria toxin (TDT). Subsequently, an exhaustive examination of its in vitro activity was conducted to elucidate its functional implications.

Methods: The recombinant construct, denoted as TDT-triVGB٣, was synthesized, cloned and expressed within bacterial cells and subsequently purified employing Nickel affinity chromatography. The binding characteristics, as well as the affinity of TDT-triVGB٣, were assessed utilizing the enzyme-linked immunosorbent assay (ELISA). To discern its inhibitory effects, the impact of TDT-triVGB٣ on the viability, migration, and tube formation of human endothelial cells was evaluated through the employment of MTT assays, migration assays, and tube formation assays, respectively.

Results: In the enzyme-linked immunosorbent assay, TDT-triVGB٣ exhibited selective and high-affinity binding to VEGFR١ and VEGFR٢. Furthermore, its inhibitory effects on the viability, migration, and tube formation of human endothelial cells were statistically significant.

Conclusion: The synthesized TDT-triVGB٣ emerges as a promising novel agent, demonstrating potential efficacy in selectively targeting cancer cells overexpressing VEGFR١/VEGFR٢.

Keywords: VEGFR١, VEGFR٢, diphtheria toxin, angiogenesis.

Intrinsic cells against retinal degeneration: the explosion of science (Review)

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Introduction: Retinal degeneration is a retinopathy that involves the deterioration of the retina caused by the gradual death of its cells. Retinal degeneration is one of the main causes of vision loss. Conventional treatments for retinal diseases slow the progression of diseases; however, the long-term benefit of these treatments is achieved by repairing and regenerating damaged retinal tissue. Moreover, since the retina does not have inherent regenerative properties, then they seek treatment by stem cells to repair and regenerate the damaged retina. Stem cell therapy has been extensively investigated for the repair and regeneration of damaged retinal cells. Several types of stem cells have been tested in preclinical and clinical trials to understand their effectiveness in reversing retinal degeneration. Several preclinical and clinical studies have shown that stem cell transplantation and factors derived from stem cells produce clinically measurable improvement. In addition to the treatment of age-related macular degeneration (AMD) and diabetic retinopathy (DR), stem cell therapy was used to treat genetic diseases such as retinitis pigmentosa (RP) and stargardt's disease, characterized by the gradual loss of photoreceptor cells in the retina. Retinal pigment epithelial cell transplantation (RPE) derived from embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs) have shown promising results in improving retinal function in various preclinical models of retinal degeneration and clinical studies without any severe side effects. Mesenchymal stem cells (MSCs) were used to treat optic neuropathy, RP, DR, and glaucoma with positive clinical results. The aim of this study was to evaluate intrinsic cells against retinal degeneration.

Methods: In this study, ۱۵ articles published from ۲۰۱۸ to ۲۰۲۲, which were in the form of quantitative studies, original research and systematic review were examined. Entry criteria included: Availability of full text and articles published between ۲۰۱۸ and ۲۰۲۲, and exit criteria included: Case Report studies. The study used the keywords Retinal degeneration, Retinal Pigment Epithelial cells (RPE), Mesenchymal Stem cells (MSCs), Embryonic Stem cells (ESCs), Induced Pluripotent Stem cells (iPSCs).

Results: Given the positive results from several preclinical and clinical studies, despite other proposed methods, stem cell therapy remains an excellent option for treating retinal degeneration. However, there is a lack of consensus on the route of administration, the method of evaluating the result, the source of stem cells, and the long-term effect of stem cell transplantation. But on the other hand, it should be noted that donor-based changes in the function of iPSC-derived RPE cells

were observed, which should be considered before transplantation. Age-related and niche-based variations in MSCs performance are well documented and should be addressed when using them for clinical use. Thus, cell banks with modified or unmodified stem cells that have been tested to achieve the best clinical outcome can be created to overcome donor-based and culture-based heterogeneity. In addition, standard cultivation conditions must be established for Stem Cell expansion to avoid changes caused by cultivation and aging conditions in the laboratory. Although RPE cells, RPCs derived from hESCs, iPSCs but not non-distinct cells were injected during treatment, there is a possibility of tumor formation from the remaining non-distinct cells. To date, data on the long-term immunity of cells derived from hESCs and iPSCs is not available in terms of post-transplant teratoma formation; therefore, MSCs and their derivatives may be more suitable candidates for treating retinal degeneration.

Conclusion: In the future, it is expected that efforts aimed at the practical application of stem cells to AMD will also contribute to various related fields. The superiority of retinal regenerative medicine, that is, the reasonable manufacturing cost due to the small number of cells used, the established surgical equipment and techniques, and the highly accurate diagnostic imaging equipment that enables in vivo direct observation is maximized. Retinal regenerative medicine using stem cells is expected to make steady progress toward practical use while new technologies are incorporated from various fields, thereby making the role of ophthalmologists in this field increasingly important. This is a hopeful area and a bright and remarkable future, and we hope to find new ways to expand and develop treatment. To better days.

Keywords: Retinal degeneration, Retinal Pigment Epithelial cells (RPE), Mesenchymal Stem cells (MSCs)

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Investigating SYNM gene polymorphism as a risk model of a gene signature in predicting platinum response and survival in ovarian cancer. (Research Paper)

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Introduction: Introduction: Ovarian cancer is one of the most deadly malignancies in women. Over time, tumors show resistance to these chemotherapy compounds and cause tumor recurrence and eventually resistance to treatment in more than ٧٠ years. percentage of patients. Therefore, identifying people without response can be an important step towards increasing the survival of patients with ovarian cancer. Therefore, determining potential indicators such as specific biomarkers predicting platinum treatment response, which can help clinical decisions and improve prognosis, can be of vital importance.

Methods: Method and Materials: In this study, ٥٠ samples of patients with ovarian cancer after chemotherapy and platinum-based treatment were examined and confirmed by a pathologist. Then the DNA of the samples was extracted by the kit and the SYNM gene polymorphism was analyzed by the Tetra-ARMS PCR technique

Results: Results: ٥٠ patients were included in this study. The average age of the patients was ٥٩,٦٣ years. There was a significant relationship between the age of patients and ovarian cancer. In terms of neoplasia, the most involvement was on the right side (٤٤٪) of the patients. In terms of disease stage, (١٦٪) patients who had bilateral involvement were in stage ٢ of the disease, and the other patient with bilateral involvement was in stage ٣ of the disease. In terms of histological grade, (١٤٪) patients who had bilateral involvement and involved lymph nodes were in grade ٣. Also (٣٨٪) who had bilateral involvement were in G٢ stage in terms of histological grade. Among the patients, ١٠ cases (٢٠٪) had bilateral involvement and ٤٠ cases (٨٠٪) had unilateral involvement. Also, among ٤٠ patients with unilateral involvement, ١٨ cases (٤٥٪) had right-sided involvement and ٢٢ cases (٥٥٪) had left-sided involvement. In terms of SYNM gene polymorphism, out of ٥٠ patients, (٤٢٪) patients had polymorphism in SYNM gene.

Conclusion: Conclusion: The relationship between polymorphism and ovarian cancer was well determined in this study and the patients who were in more advanced stages of the disease.

Keywords: Keywords: ovarian cancer, biomarkers, platinum, SYNM, polymorphism

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Investigating air pollution and other mechanisms affecting the development and exacerbation of asthma (Review)

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Introduction: Introduction: In children specifically, asthma and associated episodes have been a widespread disease with a rising tendency in recent years. The aim of this study was to investigate air pollution and other environmental processes affecting the occurrence and exacerbation of asthma because of the significance of the impact of different allergens on it

Methods: In this article, it was done using ٤٤ other articles and was written as a review article, and finally it was written in consultation with doctors and interviews with sick people.

Results: Respiratory diseases have had devastating effects on humans. Environmental factors such as air pollution in sensitive groups (children, pregnant women, the elderly, etc.), bird droppings and feathers, second-hand smoke, and cold weather occur. The aggravation of respiratory diseases, especially asthma, is effective. The health system of each country can reduce this disease with culture and other solutions.

Conclusion: Conclusion Rapid and effective diagnostic and therapeutic procedures in this sector are required due to the wide range of elements involved in this relationship, understanding this condition and the impact of allergens on its start and severity. Furthermore, raising public knowledge of the detrimental impacts of air pollution, cigarettes, and hookah smoke on individuals' health and society, along with the required measures taken by the government and healthcare system, can lessen these harmful consequences and enhance the standard of living.

Keywords: Asthma attacks, Air pollution, Allergens, Diagnostic and therapeutic methods Air qu

Investigating Genetic Alterations in ACTL۹: Unraveling the Origins of Male Infertility (Review)

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Introduction: Infertility, which impacts approximately ۹٪ of couples globally, is a complex condition with notable contributions from male factors. Although conventional diagnostic methods, including semen analysis and hormonal evaluations, are routinely employed, a considerable number of male infertility cases remain without a clear explanation, underscoring the necessity for more sophisticated diagnostic approaches.

Methods: The ACTL۹ gene has been identified as a significant genetic factor in male infertility. Situated on chromosome ۱۹, ACTL۹ encodes a testis-specific actin-like protein that is crucial for the development and functionality of the sperm acrosome. Mutations in the ACTL۹ gene can disrupt the localization of phospholipase C zeta (PLCz), an essential protein for oocyte activation, which can lead to failures in fertilization. Recent research has uncovered both homozygous and heterozygous pathogenic mutations in ACTL۹ that adversely affect sperm functionality and contribute to infertility.

Results: Gaining insights into these mutations may pave the way for targeted diagnostic and therapeutic strategies, such as genetic screening and personalized treatment options. Future investigations should aim to clarify the molecular mechanisms associated with ACTL۹-related infertility, assess its wider implications across different tissues, and utilize advancements in genomic technologies to enhance diagnostic and therapeutic methodologies.

Conclusion: Incorporating ACTL۹ mutation analysis into clinical settings could significantly improve the management of male infertility and lead to better reproductive outcomes.

Keywords: male infertility, mutation , ACTL۹

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Investigating Isoquercetin vs. Fluoxetine effects on SERT by molecular docking method (Research Paper)

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Introduction: The protein known as SERT is crucial for the uptake of serotonin from the synaptic cleft back into the presynaptic neuron. Dysfunction in SERT activity can result in depression and anxiety; therefore, this protein is a key target in treating neuropsychiatric disorders such as major depressive disorder (MDD). Selective serotonin reuptake inhibitors (SSRIs) are a common type of antidepressive agent. They increase serotonin activity by inhibiting SERT. Fluoxetine is one of the most commonly used SSRIs. Isoquercitrin, alongside rutin, is considered one of the major glycosidic forms of the natural flavonol quercetin. Medicinal herbs, fruits, vegetables, and plant-based foods and beverages frequently isoquercitrin. Across both in vitro and in vivo studies, Isoquercitrin demonstrates a broad spectrum of positive biological effects, with a particular focus on its chemoprotective ability against oxidative stress, cancer, and cardiovascular disorders. This research project compares the binding affinity between Isoquercetin and Fluoxetine with the serotonin reuptake transporter using the molecular docking method. Exploring the possibility of Isoquercetin forming a stronger attachment with SERT than Fluoxetine could lead to the discovery of novel medicinal compounds derived from Isoquercetin.

Methods: In this research, the structure of SERT was first downloaded from the Uniprot website. Preparations, such as the addition of charge and hydrogen ions, were then executed using Chimera software. The three-dimensional structures of Isoquercetin and Fluoxetine were obtained from the PubChem website. The SERT protein binding site was determined using Deepsite. [Center; X: ٣٦,٤١٩٥, Y: ١٨٤,٧٨٣, Z: ١٤٢,٧١٤٣ and Dimensions (Angstrom); X, Y, Z: ٢٥,٠٠] Finally, the molecular docking process was carried out using AutoDock Vina in PyRx ٠,٨ to investigate the binding affinity of Isoquercetin and Fluoxetine to SERT.

Results: The docking process carried out with PyRx software led to these results. The data is associated with each model's binding affinity, lower RMSD bond, and upper RMSD bond. Isoquercetin: Model #١: [-٩,٤, ٠,٠, ٠,٠] Model #٢: [-٩,٣, ٢,٢٥٥, ٣,٦٥٥] Model #٣: [-٩,١, ٢,٠٦٩, ٣,٥٦٣] Model #٤: [-٩,١, ١,٦١٨, ٢,٢٨٥] Model #٥: [-٩,٠, ٢,٤٢٢, ٧,٠٥٧] Fluoxetine: Model #١: [-٨.٩, ٠,٠, ٠,٠] Model #٢: [-٨,٨, ٠,١٦٨, ١,٦٨١] Model #٣: [-٨,٢, ١,٩٤١, ٢,٦٠٩] Model #٤: [-٨,١, ٥,٤٠٣, ٧,٣٧٤] Model #٥: [-٧,٩, ٤,٥٨٢, ٥,٩٩٧]

Conclusion: According to the results of the molecular docking analysis of Isoquercetin and Fluoxetine with SERT, both compounds revealed negative binding energy. However, Isoquercetin revealed a higher affinity compared to Fluoxetine. This indicates that new therapeutic drugs can be developed using Isoquercetin to treat major depressive disorder.

Keywords: Isoquercetin, Fluoxetine, SERT, Molecular docking, Major depressive disorder

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Investigating of Infectivity and Epidemiology of Pneumocystis Carinii (Review)

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Introduction: The most frequent opportunistic illness among people living with HIV infection is Pneumocystis jiroveci pneumonia (PJP), formerly known as Pneumocystis carinii pneumonia (PCP). Although the exact point of entrance for P carinii is unknown, inhalation is most likely the method of transmission because the organism has rarely been discovered in the lung. In animals, airborne transmission has been shown. The bacterium is mostly dormant and slightly distributed throughout the lung in most people, showing no signs of a host reaction (latent infection). The bacterium proliferates in vulnerable (immunocompromised) hosts, filling the alveolar gaps and triggering phagocytosis and an aggressive response from the alveolar macrophages. Pneumocystis pneumonia in sick newborns thickens the alveolar septum and causes an influx of lymphocytes and plasma cells into the interstitial space. Severe hypoxia and compromised breathing are the outcomes of the infection. Pneumonitis is consistently characterized by tachypnea and fever, and radiography can show diffuse bilateral alveolar illness. Finding P carinii in lung tissue or lower airway fluids is necessary for the diagnosis. These specimens can be taken via bronchoalveolar lavage, lung biopsy, sputum induction, or needle lung aspiration. The organism can be identified by the Gomori, Giemsa, fluorescence-labelled antibody, or toluidine blue O stains. Serologic investigations for antigens and antibodies are useless for making a precise diagnosis. This study aimed to investigate the infectivity and epidemiology of Pneumocystis Carinii.

Methods: The study, titled Investigating the infectivity and epidemiology of Pneumocystis Carinii, was conducted by searching scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: The findings indicate that pneumonia is a common infection in individuals with acquired immune deficiency syndrome (AIDS) and tends to arise in people with compromised cell-mediated immunity. The illness may arise from severe protein-calorie deficiency alone. Individuals using immunosuppressive medications for cancer treatment or organ transplantation are more vulnerable to P. carinii pneumonitis. Humoral antibodies do not offer disease protection; rather, they may develop in response to infection or experimental immunization. Both IgG and IgM antibodies may be present. With a particular antibody present, alveolar macrophages actively engulf and consume the parasite. Immunocompromised children and adults do not exhibit the significant plasma cell infiltration of the alveolar septae seen in infected newborns. Rats, rabbits, mice, dogs, sheep, goats, ferrets, chimps, guinea pigs, horses, and monkeys have all been reported to harbor Pneumocystis carinii in their lungs. Reports of the organism have been made in humans and lower animals on every continent. There is evidence of animal-to-animal transmission through the air. Subclinical infection must be extremely common since humoral antibodies to P. carinii may be present in up to ۷۰٪ of healthy people.

Conclusion: P. carinii vaccination does not protect against pneumonia, according to experimental research. However, preventive use of aerosolized pentamidine, dapsone, or trimethoprim-sulfamethoxazole can prevent the illness. Atovaquone, trimethoprim-sulfamethoxazole, trimetrexate, and pentamidine isethionate are the four medications currently approved for the treatment of P. carinii pneumonitis. Trimethoprim-sulfamethoxazole is the recommended medication due to its higher efficacy and lower toxicity. Antibiotics are primarily suggested for the treatment of mild, moderate, or severe PJP. It has been demonstrated that trimethoprim-sulfamethoxazole (TMP-SMX) is more successful than other treatment regimens and is on par with intravenous pentamidine in terms of effectiveness. Only patients with severe patient-centered pain who are HIV-positive are treated with corticosteroids as an initial supplemental therapy. The management of disease can benefit greatly from preventive measures (such as quitting smoking and receiving chemotherapy).

Keywords: Infectiousness, Epidemiology, Pneumocystis Carinii, Sulfamethoxazole

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Investigating proteins secreted by extracellular vesicles involved in intercellular communication in the liver tumor microenvironment (Review)

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Introduction: Cancer is a multifactorial disease caused by multiple environmental and genetic factors (١). Genes involved in cancer are classified into several groups including proto-oncogenes, tumor suppressor genes, genes involved in genome stability and cell migration. Tumor-enveloping environment (TME) has a similar function as stem cells, which affects tumor progression and metastasis. Studying the nature of this environment is effective in the diagnosis and molecular treatment of cancer and provides valuable and new information for the control of tumor malignancy and risk assessment. Exosomes are vesicles of size (٣٠٠-١٥٠ nm) released by cells into the extracellular space and act as intercellular signal vectors through the horizontal transfer of biological molecules including microRNA (miRNA). Cancer treatment is not enough regardless of the type of tumor, the nature of tumor cells and stem cells, the surrounding environment of the tumor, the cellular and molecular communication between the tumor and its surrounding environment, the type of treatment and how to use it (٧). Therefore, this disease cannot be recognized and treated only on the basis of pathology and surgery, radiotherapy or chemotherapy. Early detection approach in the community helps in targeted treatment along with cost reduction. Today, BIOM science relies on genome, transcriptome, proteome, signalome and other cellular systems to help detect disease-causing biomarkers, which can be traced back months and even years by having the biomarker panel pattern in hand. He found and studied molecular changes and cellular changes in cells that initiate the process of becoming cancerous. In the division of different stages of liver cancer, currently, only tumor size, involvement of lymph nodes and metastasis to the surrounding tissues are criteria for the division of the staging of this disease (٩) and the treatment is based only on this. invoices. Since currently determining the treatment plan for a metastatic patient, in the process of its definitive control and treatment, is only based on standard and traditional PET scan variables, it is not possible to preventively and in a short time in the treatment plan for patients with tumor metastases. made a decision and almost the process of treatment and medicine will occur in the upper stages. Therefore, in this study, we are trying to rely on the science of amics and specifically proteomics, to obtain specific protein biomarkers from the secretion of extracellular exosomes, which are evidence for the

initiation of tumor metastasis, and to identify their proteome profile. do. To finally propose molecular variables to the medical community to design a treatment plan in the control of liver metastases and finally increase the survival of patients.

Methods: The variables investigated in this study are proteome, which is used to determine the concentration of samples with a spectrophotometer, and separation is done with a two-dimensional gel electrophoresis device. The comparison tool is the gels obtained from metastatic liver tissue and the altered proteins are identified with R software. Determining the validity of the tool: Two-dimensional gel electrophoresis is one of the reliable methods for proteome separation and protein expression measurement (it compares protein spots with the help of gel analysis software)

Results: The results of these studies help to understand the contribution of myome and proteome-based intercellular communication in tumor behavior. Based on these findings, the enrichment of the engineered myoma panel can contribute to key mediators, such as MET, PIK٣CA, and CDKN٢A, to modulate critical processes involved in tumor growth, such as metastasis or angiogenesis. This study was one of the first studies of the coordinated investigation of miromics and proteomics with a computational biology approach, which tried to establish the close relationship between proteins and proteins. However, further studies should be conducted to discover other downstream targets of the myome panel and proteome introduced in this research in the liver TME.

Conclusion: Since currently determining the treatment plan for a metastatic patient, in the process of its definitive control and treatment, is only based on standard and traditional molecular imaging variables, it is not possible to preventively and in a short time in the treatment plan For patients with breast tumor metastases, a decision was made and almost the treatment and medication process will occur in the upper stages. Therefore, in this study, we tried to rely on the science of OMICS and specifically proteomics, to obtain specific protein biomarkers from the secretion of extracellular exosomes, which are evidences for the initiation of tumor metastasis, and to identify their proteome profile. To finally propose molecular variables to the medical community to design a treatment plan in the control of metastasis and finally increase the survival of patients.

Keywords: Exosomes R software, machine learning and clustering, proteomics, biological pathways

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Investigating sexual disorders in women with seizures: a systematic review (Review)

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Introduction: Seizures are known as the second neurological complication. According to a study, the prevalence of seizures in Iran is ٥٪, and its rate in women of reproductive age was estimated between ٠,٣٪ and ٠,٧٪. This complication is one of the most important chronic neurological diseases that can affect sexual performance due to the nature of the disease and the use of anticonvulsant drugs and its potential impact on the reproductive and sexual hormones of convulsive women with many reproductive diseases, irregular menstruation and Infertility and sexual problems are encountered. As a result, this review study was conducted with the aim of investigating sexual disorders in women with seizures.

Methods: This review is based on a search in the scientific sites Pubmed, Embase, MEDLINE. sciencedirect. SidSCOPUS and Google Scholar search engine with the keywords seizure and epilepsy and sexual disorders of women and their English equivalent have been done during the years ١٩٩٦ to ٢٠١٨. The number of initial articles was ٤٠ and the number of final articles was ١٨. The articles reviewed were in the descriptive group. They have been dating for a while.

Results: By examining the results of the studies conducted in this period, sexual disorders that had a high prevalence in convulsive women include: vaginal dryness, delayed orgasm, decreased libido, dyspareunia, premature ejaculation, delayed ejaculation. Among them, vaginal dryness has the highest percentage and ejaculation delay has the lowest percentage. Of course, the percentage of these disorders is influenced by factors such as age, living environment, time of marriage, education level, and the number of seizures per month.

Conclusion: According to the results obtained from the present study, it is therefore suggested that health service providers take steps to improve women's health with planning and interventions such as screening, counseling, training and referral to relevant specialists.

Keywords: sexual disorders, women, seizures

Investigating SLC٥A١ gene polymorphism as a risk model of a gene signature in predicting platinum response and survival in ovarian cancer (Research Paper)

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٢.

Introduction: eventually resistance to treatment in more than ٧٠ years. percentage of patients. Ther Ovarian cancer is one of the most deadly malignancies in women. Over time, tumors show resistance to these chemotherapy compounds and cause tumor recurrence and efore, identifying people without response can be an important step towards increasing the survival of patients with ovarian cancer. Therefore, determining potential indicators such as specific biomarkers predicting platinum treatment response, which can help clinical decisions and improve prognosis, can be of vital importance.

Methods: In this study, ٥٠ tissue samples from patients with ovarian cancer after chemotherapy and platinum-based treatment and ٥٠ healthy tissue samples were collected and selected as the control group, then DNA extraction of the samples was performed using a special kit and in The continuation of SLCSA gene polymorphism was investigated by Tetra-ARMS PCR technique

Results: Results: In patients, ١١ cases (٢٢٪) had GG genotype (wild homozygous), ٥ cases (١٠٪) had GA genotype (heterozygous) and ٣٤ cases (٦٨٪) had AA genotype (mutant homozygous). Also, in the control subjects, ٣٨ cases (٧٦٪) had GG genotype (wild homozygous), ٥ cases (١٠٪) had GA genotype (heterozygous) and ٧ cases (١٤٪) had AA genotype (mutant homozygous). The obtained results showed that the frequency of the wild G allele was ٢٧٪ and the frequency of the mutant A allele was ٧٣٪ in the patient group. There is a significant difference between the control group and the control group in terms of target polymorphism ($p<٠,٠٥$).

Conclusion: Conclusion: The present study showed that SLC٥A polymorphism is associated with ovarian cancer and can be used as a biomarker in the prognosis of platinum drug use.

Keywords: Ovarian cancer, platinum, SLC٥A١, polymorphism

Investigating statics and dynamics of a semi-flexible polymer confined in a nano-slit (Review)

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Introduction: In the paper, static and dynamic of the confined semi-flexible polymer in nano-slit are investigated by molecular dynamic simulations. Free energy (F) and gyration radius are investigated as functions of polymer length (N) and confinement dimension (D) in self-crossing odijk regime. Odijk regime is an intense-confinement regime with confinement dimension , where w is the effective diameter of the chain. According to the Odijk theory, the force is scaled with . Our simulation results for large values of P have an excellent agreement with the Odijk theory. However, for small values of P, the behavior of the chain is in agreement with de Gennes theory for flexible chains. The threshold persistence length for this transition between the two regimes is also in agreement with these available theories. In Odijk theory, there is no relation between and D but gyration radius varies with P as . In simulation also independence of gyration radius to degree of confinement and the relation between and P is observed. The favorite dynamic parameter in this work is escape time of the chain from a nanopore, which is related to other parameters of the system like . In the case of large values of P, varies with D, according to theory. But in small values of P, the behavior is rather different. According to all of the simulations, by increasing D, the results of as a function of P become closer to the theoretical relation.

Methods: simulation molecular dynamic

Results: At the beginning of the simulation, the equilibrium time chain is given from the order of polymer length to the power of two, and the averages are made at four times this amount of time after the equilibrium of the chain.

Conclusion: It can be seen that the simulation results for static are in good agreement with the theory within the defined range for the Edic regimen. However, the simulation results for the time out of the limit are consistent with the theory only when the static length and size of the nanogap are large enough. In previous work, it has also been observed that, unlike static, polymer dynamics are more sensitive to the size of constraints.

Keywords: simulation, molecular dynamics, nano-slit,, polymer

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Investigating the antibacterial effects of Lactobacillus plantarum and Streptococcus lutetiensis probiotics strains on coagulase negative strains isolated from urine samples (Research Paper)

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Introduction: Background: The rise of antibiotic-resistant strains of Staphylococcus epidermidis (S. epidermidis) underscores the urgent need for alternative therapeutic strategies. Probiotics, with their ability to competitively exclude pathogens and modulate the host immune response, present promising candidates for combatting S. epidermidis infections. This study investigated the effectiveness of probiotics on S. epidermidis growth inhibition.

Methods: Methods: We isolated S. epidermidis from urine samples of hospitalized patients in Isfahan, Iran, and probiotic strains from yogurt and milk. The antibacterial activity of probiotics against S. epidermidis was assessed through agar well diffusion and broth microdilution tests. Time-kill tests and acid tolerance assessments were performed. Anti-biofilm effects were evaluated, and potential inhibitory mechanisms were explored. Chemical analysis was done using high-performance liquid chromatography (HPLC), and cytotoxicity was assessed by performing MTT.

Results: Results: Streptococcus lutetiensis OR٤٩٦٩٢٧,١ (S. lutetiensis) and Lactobacillus plantarum OR٤٩٦٩٢٨ (L. plantarum) probiotics were isolated from dairy. S. lutetiensis and L. plantarum strains had a cytotoxicity effect on S. epidermidis isolates at ١/٢ and ١/٤ minimum inhibitory concentration (MIC), respectively. L. plantarum grew at pH ٣, while S. lutetiensis displayed growth at pH ٣ and ٤. Both probiotic strains demonstrated anti-biofilm activity, with L. plantarum generally exhibiting more potent effects. Lactic acid, formic acid, and acetic acid were identified as the predominant organic acids produced by the probiotic strains, which attributed to their inhibitory effects. Toxicity was observed at a concentration of ٥٠٪ after ٢٤ hours, while cell viability remained unaffected at lower concentrations.

Conclusion: Conclusion: The findings underscore the promise of probiotics in combating antibiotic-resistant S. epidermidis infections, emphasizing the importance of further research to explore their therapeutic potential and optimize treatment strategies.

Keywords: Keywords: Lactobacillus plantarum, Staphylococcus epidermidis, Probiotic, Streptococcus lutetiensis

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Investigating the Antibacterial Effects of Silver Nanoparticles and Grape Seed Aqueous Extract on Streptococcus mutans (Review)

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Introduction: One of the primary contributors to tooth decay is the bacteria Streptococcus mutans which produces lactic acid that damages tooth enamel and negatively impacts the health of many individuals. Grape seed extract is rich in compounds such as polyphenols, known for their antimicrobial properties. Additionally, silver nanoparticles represent an emerging material in the field of bactericidal agents. This study aims to investigate the effects of grape seed aqueous extract and silver nanoparticles on Streptococcus mutans.

Methods: In this experimental study, we evaluated the antibacterial properties of the compounds under investigation, as well as standard antibiotics including amoxicillin, penicillin, tetracycline, and vancomycin, using the disc diffusion method. The diameters of the inhibition zones for Streptococcus mutans at concentrations of ١,٥٦ and ٢٠٠ µg/mL were measured to be ١٠ ± ٠,١ mm and ١٥ ± ٠,١ mm, respectively.

Results: The results indicated that Streptococcus mutans was sensitive to the antibiotic discs of amoxicillin and penicillin, resistant to tetracycline, and exhibited relative sensitivity to vancomycin. Notably, the dilutions of grape seed extract did not produce any inhibition zones.

Conclusion: These findings demonstrate that silver nanoparticles possess anti-streptococcal properties and could play a significant role in the pharmaceutical and medical industries. In contrast, the aqueous extract of grape seed did not exhibit any anti-streptococcal activity, potentially due to the type of solvent used in the extraction process.

Keywords: Silver nanoparticles, aqueous grape seed extract, Streptococcus mutans, antimicrobial properties

Investigating the antimicrobial effect of drugs in nanofiber bed containing chitin on secondary infection of diabetic wounds (Review)

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Introduction: Diabetic wounds are susceptible to secondary infections and significantly hinder healing, as a result, they can cause severe complications. Chitin is a biopolymer that may show promising healing properties when used alongside an antimicrobial drug. This review examines the efficacy of chitin-enriched nanofibers in combination with antimicrobial drugs as a novel therapeutic strategy to prevent secondary infections in diabetic wounds.

Methods: There were studies related to experimental sources that used chitin-based nanofibers in diabetic wound models. Keywords evaluated in these studies included "antimicrobial activity", "wound healing rate" and "biocompatibility". In this research, the mechanisms through which chitin nanofibers increase antimicrobial effects were analyzed.

Results: The investigations show that chitin nanofibers probably show a significant effect on antimicrobial activity against a range of pathogens that are usually associated with diabetic wound infections, including Staphylococcus aureus and Pseudomonas aeruginosa. In addition, it is observed that these nanofibers alone can heal open diabetic wounds, and in general can increase the rate of tissue healing and prevent the occurrence of secondary infections in these damaged tissues.

Conclusion: Chitin nanofiber is a promising therapeutic combination to manage the reduction of secondary infections in diabetic wounds. In addition to the antimicrobial properties of the combination of medicine and chitin, by emphasizing the healing of damaged tissue, it can prevent infection and other injuries. It seems that future studies should focus on optimizing the formulation of medicinal nanofibers and conducting clinical trials to evaluate their effectiveness in real environments.

Keywords: antimicrobial activity, wound healing rate, biocompatibility, chitin nanofiber

Investigating the autoimmune disease of rheumatoid arthritis and the genetic factors involved in the development of this disease (Review)

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Introduction: Rheumatoid arthritis (RA) is an incurable systemic autoimmune disease. The progression of the disease leads to joint deformity and related loss of function, which significantly affects the quality of life of sufferers.The objectives of the present review are to provide an overview of RA, including a general introduction to the disease, epidemiology, risk factors and pathogenesis, to highlight the progress of basic disease research and the various signaling pathways and molecular mechanisms, including genetics.

Methods: this research is a review study and databases such as NCBI,PUBMED,...have been used in this research.

Results: In the past few decades, RA has attracted more researchers&#۳۹; attention, abnormal signaling pathways in RA is a very important research field in the diagnosis and treatment of RA, which provides important evidence for understanding this complex disease and developing interventions related to RA provides.

Conclusion: RA pathogenesis is related to many signaling pathways. The cause of RA has been investigated several times, and studies show that environmental and genetic factors are important in the induction of RA. Also, some studies have shown that the sensitivity and severity of RA may be related to the HLA-DRB۱ allele, which has the strongest genetic association with RA.

Keywords: rheumatoid arthritis, signaling pathway, autoimmune disease.

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Investigating the co-expression network of genes involved in antibiotic resistance in Staphylococcus aureus bacteria (Research Paper)

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Introduction: Background and purpose: Staphylococcus aureus is a significant pathogen globally, causing acquired infections. The escalating resistance of this bacterium to antibiotics is a growing concern, with decreasing efficacy of current treatment options. This study seeks to explore and characterize antibiotic resistance genes in MRSA strains, aiming to elucidate the mechanisms underlying antibiotic resistance through an analysis of biological systems and gene ontology.

Methods: Materials and methods: In this study, gene expression profiles associated with Staphylococcus aureus were analyzed. Subsequently, employing the WGCNA software package, co-expression networks of genes were constructed to identify main gene clusters and inter-gene relationships. Following this, the principal genes within each module were identified, and their functional attributes were scrutinized to elucidate their roles and relationships within the network. This comprehensive analysis aimed to investigate the interplay between these genes and their impact on the regulatory mechanisms underlying this biological process.

Results: Results: The enrichment analysis of genes, pathways, and biological processes related to this bacterial resistance is conducted using specific modules. Subsequently, the most critical genes within each module are identified and presented as potential new candidates. In the following stage, computational tools are utilized to ascertain the regulatory roles of genes within the networks. Noteworthy genes such as qoxB, qoxA, qoxC, and qoxD associated with oxidoreductase enzyme activities, along with HslV, PotA, yidC, copA, and fba, are known as the main elements of this phenomenon.

Conclusion: Conclusion: The results of the current study demonstrate that the systemic biology approach yields promising outcomes in analyzing the survival rates of patients afflicted with bacterial infections. Through this research, pivotal genes have been discerned which may serve as valuable prognostic biomarkers for overall survival, warranting further investigation in laboratory settings.

Keywords: Staphylococcus aureus , chronic infection, co-expression network, wgcna, antibiotic resistance

Investigating the co-infection of lophomoniasis and tuberculosis (Review)

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Introduction: Respiratory tract infections are seen worldwide both in the immune-compromised and immune-competent people. However, they can also have different causes, including bacteria, fungi, viruses, and parasites. Meanwhile, we examine two of the most important microorganisms that cause this infection. Among the parasites, Lophomonas Blattarum is a relatively new pathogen involving both the upper and lower human respiratory tract. The first infection with L. Blattarum was reported in China in ١٩٩٣. This pear-shaped multi-flagellate protozoan lives commensally in the intestines of insects such as cockroaches. It is transmitted by aerosols released from their feces in the air in which humans breathe. The symptoms of the disease are very similar to other respiratory infections, such as tuberculosis, and include fever, shortness of breath, chronic cough, chest pain, and sputum secretion. Conversely, Mycobacterium tuberculosis is a well-known bacterium that causes tuberculosis. It affects more than ١٠ million people every year. Although the main site of this bacterium is the human respiratory system, it can also involve other body organs.

Methods: The current study is a review, and its documents were collected by searching the keywords "Lophomonas," "Tuberculosis," and "Respiratory" in "PubMed," "Scopus," and "Google Scholar" databases. The search period was set between ٢٠١٥ and ٢٠٢٤. From ٢٥ articles obtained in the search results and after studying them, ١٥ articles with the slightest relevance to the research topic were eliminated. Among the remaining articles, ten articles with a detailed relationship with the topic were scrutinized, and their results were extracted.

Results: Some studies stated that despite confirming Mycobacterium tuberculosis infection in the initial phase of diagnosing, with further investigations, the involvement of the patients with L. Blattarum with relevant laboratory methods, including observing unstained smear of respiratory secretions (bronchoalveolar, sputum, bronchial aspirates) was confirmed by light microscopy and PCR technique. The final diagnosis was announced as a co-infection of tuberculosis and lophomoniasis [٣, ٤]. A study reported lophomonas infection in people with normal immunity more than those with immunodeficiency. According to a recent study, most patients showed no change in blood eosinophil levels, making eosinophilia an unreliable criterion for diagnosing lophomonas. However, antibiotic resistance in patients with tuberculosis can lead physicians to investigate the presence of lophomonas infection in these patients. In several studies, a significant percentage of suspected tuberculosis patients were diagnosed with Lophomoniasis, and their laboratory results were negative for TB.

Conclusion: Lophomonas is not a saprophyte pathogen and has shown a high infection rate in healthy individuals. Considering the common symptoms of tuberculosis and lophomoniasis, it is recommended that besides examining patients for bacterial infections, including TB, the possibility

of lophomonas is also considered, and relevant laboratory tests should be performed on patients to detect this parasite and ensure accurate diagnosis and better treatment outcomes.

Keywords: Lophomonas, Tuberculosis, Infection

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Investigating the consequences of cervical cancer screening: a comprehensive review (Review)

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Introduction: cervical cancer(CC) is still a major public health problem even if it is mostly preventable through effective screening strategies. Regular screening programs such as Pap smear and HPV testing, have been effective in identifying precancerous changes, reducing the occurrence of CC. The introduction of these screening programs has been the main reason for the significant reduction in mortality as well as the percentage of late-stage CC. However, even after the success of such initiatives, some problems, for instance, lack of access, low education, and irregular participation remain unsolved challenges for the prevention of the disease in the desired manner. The results of the study emphasize the importance of regular screening, especially in the underprivileged.

Methods: In this systematic review, the keywords of this study were searched in Sage Journal, SJR, and Pup-Med databases. All review and research articles reviewed are in English and have Q١ and Q٢ ratings. In these articles, Case-control studies were carried out to determine the efficiency of screening programs by analyzing the data sourced from population-based cancer registries. Attendance for screening in defined intervals (e.g., every three or five years) was measured by comparing women diagnosed with CC to controls without the disease. The screening tests administered included Pap smears and a high-risk HPV test, and the adverse effect was measured by the duration of the protection after a negative test. Age, diversity of the courses of the disease at the time of diagnosis, and the frequency of the screens are also some of the variables discussed in the studies.

Results: The results Studies show that women who are screened every ٢,٥ years have a lower risk of CC than women who are rarely screened. Early diagnosis and initiation of treatment are the reasons for the ٨٣٪ decrease in non-localized (Stage II and after) CC, which guarantees the detection of lesions with a higher chance of cure. In these studies, one of the benefits obtained from frequent screenings with negative results is reducing the risk of CC.

Conclusion: Researches confirm that the best possible way to prevent CC is through screenings such as pap smears and HPV tests, and studies in this field show that routine screenings are the most tangible way to significantly reduce the incidence and severity of the disease. Regular participation in screening programs, and if possible, with vaccination of HPV too, would be the most important steps if we are willing to reach additional benefits. Activities for the extension of screening coverage, especially among the high-risk groups, must be carried out to maximize the potential benefits of these programs. Future work should focus on increasing access and encouraging adherence to screening guidelines for the sake of maintaining and improving these preventive outcomes.

Keywords: Cervical cancer prevention, Screening programs, HPV testing, Pap smear, Cancer incidence reduction

Investigating the Effect of Acrylamide and The Risk of Various Types of Cancer (Review)

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Introduction: Often used in industry, acrylamide, also known as ٢-propenamide (AA, C٣H٥NO), is a white, crystalline solid that dissolves in water and has a relative molecular mass of ٧١,٠٨ kDa. AA was included in the International Agency for Research on Cancer's ١٩٩٤ list of industrial chemicals that may cause cancer in people. Examining the relationship between acrylamide and the risk of different cancer types was the goal of this investigation.

Methods: The present study whit acrylamide and cancer keywords was done by searching scientific databases such as Science Direct, Springer, Google Scholar and PubMed.

Results: Acrylamide is a multiorgan carcinogen in both rats and mice, according to positive bioassays of the substance's carcinogenicity in experimental animals. These findings strongly suggest that acrylamide may be a risk for human cancer. Two studies using oral administration of acrylamide in Fischer ٣٤٤ rats examined the drug's carcinogenic potential. In the first experiment, it increased the incidence of thyroid follicular tumors, mammary tumors, glial tumors of the central nervous system, oral cavity papillomas, uterine adenocarcinomas, and clitoral gland adenomas in females, as well as peritesticular mesotheliomas and follicular adenomas in males. In the second experiment, acrylamide increased the incidences of thyroid follicular cell tumors in both sexes, mammary gland tumors in females, and peritesticular mesotheliomas in males. If all of these tumors found in treated rats had been included in the data analysis, this would have been interpreted as increasing the incidence of primary tumors of the central nervous system. elevated the occurrences of malignant lymphomas, uterine adenocarcinomas, and mammary carcinomas in female mice, as well as lung tumors and Harderian gland tumors in mice of both sexes. Inhaling ethylene oxide increased the incidence of brain tumors and mononuclear cell leukemias in both sexes of Fischer ٣٤٤ rats, as well as male-specific peritesticular mesotheliomas and subcutaneous fibromas. It was specified that gliomas, granular cell tumors, and "malignant reticulosis" were among the brain malignancies. By the same mechanism as glycidamide, ethylene oxide exhibits chemical reactivity. It should be noted that carcinogens acting through genotoxic mechanisms frequently cause tumors of endocrine glands and hormone-dependent tissues in rats and mice. Additionally, the presence of thyroid, mammary, or other tumors in a bioassay does not always indicate that the test agent's mode of carcinogenic action is hormonal dysregulation rather than genotoxicity. Furthermore, every known carcinogen for the rodent nervous system is either biotransformed to a genotoxic metabolite or is itself genotoxic. Acrylamide, administered intraperitoneally or orally, enhanced the incidence and multiplicity of lung cancers in strain A mice in short-term screening bioassays. Additionally, following oral, intraperitoneal, and topical administration to mice of one strain and oral administration to animals of another strain, followed by topical treatment with ١٢-O-tetradecanoylphorbol ١٣-acetate, acrylamide was investigated as an initiating agent for skin carcinogenesis. Regardless of the mode of

administration, it caused a dose-related increase in the incidence of skin carcinomas and squamous-cell papillomas in each of the four trials. These short-term studies lacked a thorough assessment of tumor incidence in organs apart from the skin and lung. Since the percentage of acrylamide converted to glycidamide is significantly higher in mice than in rats, a traditional long-term bioassay in mice is required.

Conclusion: In Summary given that mice convert acrylamide to glycidamide more efficiently than rats do, a standard ٢-year bioassay in mice may identify more organ sites for carcinogenicity as well as a larger degree of carcinogenic consequences.Since there are no published data on the carcinogenicity of this putatively carcinogenic metabolite of acrylamide in any species, a bioassay including mice, rats, or both is also required. Glycidamide bioassays are currently being conducted at the National Center for Toxicological Research in the United States (Doerge, personal communication). When the meal is autoclaved or crumbled and fried like a pancake, acrylamide is created in the feed used to raise rats and mice. It is unknown and has to be determined how this pollution affects the background tumor rates in mice and rats that serve as controls.

Keywords: Acrylamide, Toxicological, Center, Glycidamide

Investigating the effect of Actinomycete extract on the viability of human breast cancer cell line (MCFV) (Review)

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Introduction: Breast Cancer: In recent years, breast cancer has become the most common cancer in the world, accounting for approximately ١٢٪ of all cancer cases globally. It is the most prevalent cancer among women and the leading cause of death in females. According to the World Health Organization's statistics, lung cancer was the most common cancer in ٢٠٢٠, but now breast cancer incidence has surpassed that of lung cancer. Global statistics indicate that around twenty million people are affected by breast cancer. Given the daily rise in breast cancer cases in various communities, it is expected that the number of patients will increase by ٤٧٪ over the next two decades. The World Health Organization predicts that the incidence of breast cancer in Iran will reach ٢٢,٨٢٨ cases per year by ٢٠٤٠. What is MCFV? MCFV is a breast cancer cell line that was isolated in ١٩٧٠ from a ٧٩-year-old Kazakh woman. MCFV stands for Michigan Cancer Foundation ٧, referring to the institute in Detroit, USA, where Dr. Herbert Soule and his colleagues first isolated this cell line. Actinomycetes: Actinomycetes are some of the most valuable microorganisms for producing and synthesizing therapeutic compounds and important economic antibiotics. They are the source of over ٥٠٪ of the discovered bioactive compounds, including antitumor agents, antibiotics, enzymes, and immunosuppressive agents. Many of these bioactive secondary metabolites have been isolated from terrestrial actinomycetes. However, in recent years, the discovery rate of new bioactive compounds has decreased. Therefore, it is crucial to explore new groups of actinomycetes from unexplored or underexploited environments to obtain new bioactive secondary metabolites. Unknown areas such as saline regions, conditions near marine aquatic environments, high pH zones, and low oxygen areas are suitable for isolating these actinomycetes (Valan Arasu, ٢٠١٦). Salinosporamide A is an anticancer compound isolated from the marine actinomycete Salinispora tropica. Its chemical structure is a beta-lactone gamma-lactam bicyclic compound. Salinosporamide A acts by inhibiting the proteasome, leading to apoptosis in myeloma cells. Nereus Pharmaceuticals developed Salinosporamide A, named NPI-٠٠٥٢, for cancer treatment in humans. This drug is the first anticancer agent derived from marine actinomycetes (Karthikeyan et al., ٢٠٢٢). In the same year, Silva and colleagues conducted a study among actinobacteria in polar regions to find species that produce secondary metabolites with antitumor properties. The diversity of actinobacterial species associated with Antarctic regions was analyzed, focusing on s rRNA١٦, and the produced metabolites were examined. It was observed that the Actinomycetales order included the majority of secondary metabolite producers. Among these metabolites, ١٧ samples exhibited antitumor activity against cancer cell lines. Further tests revealed a specific anti-proliferative activity for crude extracts obtained from Streptomyces sp. cells. This study indicates that the rhizosphere is a prominent reservoir of bioactive actinobacterial strains, making it a significant source for discovering potential antitumor agents (Silva et al., ٢٠٢٠).

Methods: Collection of Bacteria and Extraction: In this stage, actinomycete bacteria were isolated from soil and cultured in Starch Agar medium. After allowing sufficient growth, the culture medium along with the bacteria was transferred into a beaker, ground with a mortar, and taken under a fume hood. Ethyl acetate, a toxic solvent, was added, and the mixture was placed on a shaker for ٢ hours. Afterward, the remaining liquid was filtered and poured into a petri dish. We waited for the ethyl acetate to evaporate from the extract. The extract in the petri dish was then washed with DMSO and transferred to a vial, allowing the DMSO to separate from the extract. After several hours, the extract precipitated in the vial. Cell Culture: In the experimental study, the MCFV cell line (human breast cancer cells) was purchased from the Medical School of Tehran University of Medical Sciences (Tehran, Iran) and cultured in ٢٥ mL flasks in DMEM-F١٢ medium containing ١٠٪ FBS (fetal bovine serum) and ١٪ penicillin-streptomycin antibiotics at ٣٧°C in a humidified environment with ٥٪ CO٢. The cells were examined under an inverted microscope every ٢٤ hours, and the culture medium was replaced as needed. Three to four days after initial seeding, cell density was assessed under the microscope, and when cell growth reached ٨٠٪, passaging was performed. Assessment of Cytotoxicity using the MTT Method: The effect of actinomycete bacterial extract on the proliferation and viability of MCFV breast cancer cells was evaluated using the MTT (Micro-culture Tetrazolium Test) assay compared to a control group. This assay is based on the activity of succinate dehydrogenase in the mitochondria of viable cells, converting the yellow MTT solution into insoluble purple formazan crystals, which can be measured after dissolving in dimethyl sulfoxide (DMSO) using an ELISA plate reader (BioTech, Germany). After several passages and reaching the required cell density, the cells were transferred to a ٩٦-well plate, with ١٥,٠٠٠ cells per well in DMEM-F١٢ medium containing ١٠٪ FBS. The cells were exposed to various concentrations of the extract (٠, ٠,١, ٠,٥, ١, ٢, ٣, ٤, ٥, ٦, ٧, ٨, ٩, ١٠ mg). The microplates containing the extract and cells were incubated under identical conditions for ٢٤ hours. On the reading day, ٢٠٠ µL of DMSO replaced the culture medium containing MTT, gently pipetting to dissolve the purple formazan crystals. Absorbance was measured at a wavelength of ٥٧٠ nm using the ELISA plate reader. Each concentration was evaluated in triplicate, with ١٠٠٪ cell viability defined for the negative control group. The percentage of cytotoxicity was calculated as follows:
Cytotoxicity %=(Mean Negative ControlMean Negative Control−Mean Dose)×١٠٠ The concentration of the tested compounds that reduced cell viability by half was considered the IC٥٠ (Inhibition Concentration ٥٠), determined from the graph generated using GraphPad Prism software.

Results: The extract of actinomycete bacteria has shown a positive effect on MCFV cancer cells; for example, at a dose of ١٠٠٠ mg, the viability of MCFV cells significantly decreased. Therefore, we can conclude that actinomycete bacteria may contribute to the improvement or treatment of breast cancer.

Conclusion: Based on the data and results presented in Figures ٣ and ٤, it was observed that the extract of actinomycete bacteria significantly reduced the viability of human breast cancer cells over a ٢٤-hour period. At a concentration of ١٠٠٠ µg, it exhibited a ٢٠٪ reduction in cell viability compared to the control group, highlighting the extract's significant potential in inducing cell death.

Chemotherapy drugs typically cause various side effects, including fatigue, hair loss, easy bruising and bleeding, infections, anemia (low red blood cell count), nausea and vomiting, appetite changes, constipation, diarrhea, oral and throat issues like sores and pain during swallowing, peripheral neuropathy or other neurological problems such as numbness, tingling, and pain, skin and nail changes like dryness and discoloration, urinary and bladder changes, kidney issues, weight fluctuations, concentration difficulties, mood changes, and fertility problems. These side effects can have diverse negative medical, economic, and social impacts on the lives of cancer survivors. Moreover, existing drugs do not demonstrate uniform efficacy across all cancer types. Given the adverse effects of chemotherapy, innovative methods for inhibiting cancer cells are being explored, one of which involves the use of bacteria. The advantage of this study is that it may eliminate the side effects associated with chemotherapy. Notably, there have been no similar studies conducted in the country, and literature in this area is scarce. The research utilized a strain of actinomycete from Syria, which has not been previously studied. Therefore, it is crucial to continue investigations aimed at discovering new and effective natural pharmaceutical compounds for cancer treatment. Furthermore, the characteristics and historical research on other strains of this bacteria suggest a hopeful future for its use in cancer therapy.

Keywords: Breast cancer cell‹Viability‹MTT‹Actinomycete‹Extraction‹Bacteria

Investigating the effect of Baneh tree leaf extract on acne-causing bacteria (Propionibacterium acnes((Research Paper)

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Introduction: Nowadays, investigating the antimicrobial effects of plant extracts, especially plants that have traditional medicinal uses, is one of the topics of interest to researchers. Since ancient times, medicinal plants (due to having essential oils) have played an important role in human health According to the researches conducted on the antimicrobial effects of the extract of baneh leaves and also the information of the local people of Izeh city who used the concentrated aqueous extract of baneh leaves to prevent the infection of deep wounds, in this research the effect of aqueous and ethanolic extracts Bene leaves have been investigated on acne-causing bacteria to find a herbal and organic treatment against this widespread problem, bacterial acne disease.

Methods: First, the ethanolic and aqueous extracts of Beneh leaves were prepared by soaking. The extracts were prepared with three concentrations of ٢٠٠ mg/ml, ٤٠٠ mg/ml and ٦٠٠ mg/ml. ٢ ml of each of the ethanolic and aqueous extracts were taken separately and mixed with ٢٠ ml of DMSO in separate vials. For control treatment, DMSO without extract was used. Then, the microbial solution, with McFarland's ٠,٥ standard, was inoculated into the Muller-Hinton agar culture medium after preparing from the original stock solution. After the incubation of different concentrations of the extracts and the penetration of the extracts into the culture medium, the diameter of the growth halo (in millimeters) was measured.

Results: The results of the effect of the concentrations of ethanolic and aqueous extracts of Beneh tree leaves by the well diffusion method are shown in Table (٢). Statistical investigations and conducting t-test and examining P Values (with ٩٥٪ confidence) of each group revealed that the effectiveness of both aqueous and ethanolic extracts was statistically significant and the respective P Values were ٠,٠٤٥ and ٠,٠٤٠, respectively. In this way, the value of p, the water extract of Beneh plant was found to be p value<٠. ٠٥ was smaller and it is statistically significant. These results are consistent with the initial averages.

Conclusion: The results of our research in the study of the non-growth halo of the aqueous extract of the pistil leaves of the Pistacia genus on the propioni bacteria strain have shown that different concentrations of the aqueous and ethanolic extracts of the pistil leaves had an inhibitory effect on the propioni bacteria, although the diameter of the non-growth halo was different in different dilutions. has been Also, the effect of the aqueous extract of the tuber on inhibiting the growth of

bacteria was greater than the ethanolic extract, which was consistent with the way the local people used the extract boiled with water to prevent infection of deep wounds. investigated the effect of walnut leaf extract on Propionibacterium acnes and reported the inhibitory effect of this extract. Regarding the effect of baneh leaf extract on other microorganisms, researches have been conducted that have all shown the inhibitory effect of this extract on the growth of bacteria, including Mahdavi et al. They investigated Staphylococcus, Escherichia coli and Pseudomonas microbes and reported the greatest inhibitory effect of Beneh leaf extract on Pseudomonas microbes. In a research conducted by Benhammou et al.,

Keywords: agar, antimicrobial, tuber extract, medicinal value.

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Investigating the effect of common mutations of SLC۳A۱, CLDN۱٤, ALPL genes in patients with kidney stones in Tehran (Research Paper)

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Introduction: Kidney stone disease or nephrolithiasis is a common disease that affects ۱٪ to ۲۰٪ of the world's population. This disease affects more than ۱۵٪ of men and more than ۵٪ of women until the age of ۷۰. Humans have suffered from urinary stones from centuries to ٤۰۰۰ BC, the most common urinary tract disease. The epidemiology of kidney stones is affected by global changes that depend on geographic, socio-economic, and weather factors. In addition, age, sex, race, and diet affect the prevalence and occurrence of the disease. Obesity and metabolic syndrome are known as risk factors for kidney stones. The probability of kidney stone formation is different in different parts of the world. It is estimated to be ۱-۵٪ in Asia, ۹-۵٪ in Europe, ۳٪ in North America, and ۲۰٪ in Saudi Arabia. Middle East, India, Pakistan, Thailand, Indonesia, and the Philippines) and tropical and subtropical regions reported high rates of kidney stones. Iran is located on the kidney stone belt, and this health issue has a high prevalence (۵,۷٪) in this country. Without proper treatment, this disease can cause blockage of the ureter, blood in the urine, frequent urinary tract infections, vomiting, or painful urination, which leads to permanent functional damage to the kidneys. The etiology of kidney stones and related metabolic abnormalities is multifactorial, including genetic and environmental factors. In most patients, kidney stones' genetic factors and pathophysiology are poorly understood. However, in some cases, a monogenic disorder such as primary hyperoxaluria is responsible for the observed phenotype. In recent years, research has shown that specific gene mutations related to the metabolism of minerals and electrolytes can increase the risk of developing kidney stones. Among these genes, we can mention SLC۳A۱, CLDN۱٤, and ALPL. This study aims to investigate the effect of common mutations of these three genes in patients with kidney stones in Tehran. By identifying these mutations, we can better understand the molecular mechanisms that effectively form kidney stones. This understanding can lead to the development of more targeted and effective prevention and treatment strategies, potentially reducing the burden of kidney stone disease.

Methods: Polymerase chain reaction (PCR) is a method that is primarily used to quickly create several copies of a certain DNA or RNA sequence in order to accurately identify it, usually using agarose gel electrophoresis. Genes for expression experiments are often amplified, altered, and cloned using PCR. PCR is useful in a wide range of applications, such as forensics, paternity testing, mouse genotyping, biological connections, genetic disease diagnosis, and the detection of germs and viruses. SNP sequences for the ALPL, CLDN۱٤, and SLC۳A۱ genes are examined.When a single nucleotide in the genome differs in paired chromosomes, the result is a DNA sequence alteration known as a single nucleotide polymorphism (SNP). In the coding area, certain SNPs alter the amino acid sequence of a protein, whereas other SNPs have no effect on the protein sequence. Gene

splicing, transcription factor binding, and mRNA degradation may all be impacted by SNPs located outside of the coding area. SNPs operate as markers for examining imbalances whether or not they have an impact on the biological activity of gene products. With gene expression, genetic polymorphisms may be linked and detected, which is highly helpful in population genetics research and medical science. We can also determine the impact of gene expression and mutation of these genes on kidney stone disease condition by looking at the electrophoresis gel.

Results: The patient is better informed about the possibility of kidney stones and the existence of mutations in the targeted genes thanks to this initiative.

Conclusion: Investigating the common mutations with the studied SNPs rs٢٠٠٤٣٩٨٩, rs٢١٩٧٨٠, and rs١٢٥٦٣٢٨, as well as altering the genotypic structure of the mutations and assessing the presence of kidney stones in patients with this disease, have not been done for the current problem in Tehran. A nation's social genotyping need to be completed. This study may be seen as a significant step in figuring out the genetic variables influencing kidney stone incidence and toward developing more accurate diagnostic and treatment protocols for the Iranian populace.

Keywords: kidney stones-SLC٣A١-CLDN١٤-ALPL

Investigating the effect of Cytarabine on IDH in Leukemia by molecular docking method (Research Paper)

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Introduction: Leukemia, blood cancer, usually originates in the bone marrow and causes excess production of pathological blood cells. Four main types of leukemia exist acute lymphoblastic leukemia (ALL), acute myelogenous leukemia (AML), chronic lymphoblastic leukemia (CLL), and chronic myelogenous leukemia (CML). Acute and chronic leukemias may have similar symptoms. IDH receptor is effective in this pathway. One of the pathways that play a role in leukemia is IDH so IDH inhibitors can be effective in treatment. Cytarabine is an antimetabolite drug that has been used for treating acute myeloid leukemia (AML) for more than forty years now. This is because antimetabolite drugs impede DNA synthesis processes hence slowing down the growth or reproduction of leukemia cells. It contains an enzyme that catalyzes isocitrate oxidative decarboxylation into α-ketoglutarate (α-KG). In subsequent studies it has been shown that IDH١ and IDH٢ mutations recur in about seventy percent of low-grade gliomas as well as secondary GBM's beside ten percent of all acute myeloid; leukemia samples. This study will give an overview of the binding affinity between Cytarabine and IDH.

Methods: In this research, the IDH structure was obtained from the UniProt website, then necessary preparations were done by using Chimera software. The three-dimensional structure of the Cytarabine was downloaded from the PubChem website. [Center; X: -١٢,٩١٨, Y: ٣٦,٣٠٩٩ Z: -٠,٧٦٨٤ and Dimensions (Angstrom); X, Y, Z: ٢٥,٠٠٠٠] Finally, the molecular docking process was conducted using AutoDock Vina in PyRx ٠,٨ to assess the binding status of Cytarabine to IDH.

Results: In PyRx software, the results obtained results are as follows. For each model, the data belongs to their binding affinity, RMSD lower bond and RMSD upper bound, respectively: Model #١: [-٦,٤, ٠,٠, ٠,٠] Model #٢: [-٦,٠, ٢,٩٨, ٥,٢١٨] Model #٣: [-٦,٠, ١,٨٤٤, ٣,٢٦٨] Model #٤: [-٥,٩, ١٨,٨٠٤, ٢٠,١٧١] Model #٥: [-٥,٧, ٦,٤٤٣, ٨,٤٣٣]

Conclusion: Based on the results of the molecular docking analysis of Cytarabine and IDH, according to the negative binding energy, Cytarabine can bind well to IDH. The efficacy of Cytarabine in Leukemia treatment requires further investigation; Further Information is needed to accept whether cytarabine is effective in IDH receptor pathways.

Keywords: Keywords: Cytarabine, IDH, Leukemia, Molecular docking,

Investigating the effect of doxycycline antibiotic on the expression of FGF and VEGF genes in the chorioallantoic membrane of chick embryos by Real time PCR (Research Paper)

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Introduction: FGF produced by endothelial cells induces proliferation and increases the survival of endothelial cells. FGF are collagenase activators and lead to the sprouting of new vessels from blood vessels, FGF is needed to maintain and progress angiogenesis. It is believed that VEGF acts in the beginning of angiogenesis. Doxycycline antibiotic has a wide biomedical application compared to other antibiotics. In laboratory conditions, it was found that this substance can inhibit endothelial growth and reduce tumor growth. . This study was conducted with the aim of investigating the effect of doxycycline antibiotic on the expression of FGF and VEGF genes in chicken embryos.

Methods: In this research, ٤٠ Ross spray eggs were randomly divided into ٥ groups including control, laboratory control (pbs) and ٣ experimental groups. After incubation, on the second day of the window, an egg was created and in on the eighth day, after placing the gelatin sponge on the chorioalantoic curve, doxycycline antibiotic was injected with doses (٥٠, ١٠٠ and ٢٥٠ micromole/ milliliter) on the chorioallantoic membrane of chick embryos. In order to extract RNA and examine gene expression, a sample was taken from the chorioallantoic membrane and by making cDNA, the expression changes of VEGF and FGF genes were quantitatively measured. The collected data were analyzed by Excel and SPSS ٢٠ statistical software.

Results: The average expression of VEGF and FGF genes in the laboratory control group did not show any significant difference compared to the control group. The average expression of VEGF and FGF genes in concentrations of ٥٠, ١٠٠, ٢٥٠ micromole/ml of doxycycline antibiotic showed a significant decrease compared to the control group.

Conclusion: According to this study, the doxycycline antibiotic has an inhibitory effect on angiogenesis in the chorioallantoic membrane of chick embryos. Also, it seems that the antibiotic doxycycline can be used to inhibit angiogenesis in cancer tissues.

Keywords: gene expression, Doxycycline antibiotic, Chorioalantoic Membrane, VEGF and FGF.

Investigating the effect of doxycycline antibiotic on the process of angiogenesis of the chorioallantoic membrane of chick embryos (Research Paper)

Mohammad Reza Pour Mohammad,[١,*] Jina Khayat Zadeh,[٢] Hannaneh Akbari,[٣] Sima Afsharnezhad,[٤] Parsa Farrokhi,[٥]

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Introduction: Angiogenesis refers to the biological process of sprouting new vessels from existing vessels in the tissue. Angiogenesis is a physiological process that is highly regulated and occurs in cases such as wound healing, menstrual cycles, placental growth, and ovulation Doxycycline antibiotic has a wide biomedical application compared to other antibiotics. This research was conducted with the aim of investigating the effect of doxycycline antibiotic on the process of angiogenesis of the chorioallantoic membrane of chick embryos.

Methods: In this research, ٤٠ Ross spray eggs were randomly divided into ٥ groups including control, laboratory control (pbs) and ٣ experimental groups. After incubation, on the second day of the window, an egg was created and in on the eighth day, after placing the gelatin sponge on the chorioalantoic curve, doxycycline antibiotic was injected with doses (٥٠, ١٠٠ and ٢٥٠ micromole/ milliliter) on the chorioallantoic membrane of chick embryos. On the twelfth day, the corioalantoic membrane was taken and length, the number of vascular splits, weight and height of the embryos were measured. The collected data were analyzed by Excel and SPSS ٢٠ statistical software.

Results: The average number and total length of vascular branches in the laboratory control group did not show any significant difference compared to the control group. The average number and length of vascular branches in concentrations of ٥٠, ١٠٠ and ٢٥٠ micromole/ milliliter of doxycycline antibiotic showed a significant decrease compared to the control group.

Conclusion: According to this study, the doxycycline antibiotic has an inhibitory effect on angiogenesis in the chorioallantoic membrane of chick embryos. Also, it seems that the antibiotic doxycycline can be used to inhibit angiogenesis in cancer tissues.

Keywords: Angiogenesis, doxycycline antibiotic, Chorioalantoic Membrane, Chick Embryo

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Investigating the effect of environmental factors in different seasons on allergic response mechanisms (Research Paper)

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Introduction: Allergies are known as adverse immune responses to environmental factors such as plant pollen, pollution and climate change. These factors can be effective in the intensity and type of these responses in different seasons. Investigating these factors leads to a better understanding of allergic mechanisms and can help to improve the treatment of these immune responses.

Methods: In this research, field data were collected from ۲۰ patients with allergies in a specific area in the form of a response letter. Factors related to seasonal changes such as temperature, humidity, plant pollen and air pollution were recorded during four seasons of the year. Data analysis was performed using statistical software to determine the relationships between environmental variables and severity of allergic symptoms.

Results: The results of the response letters showed that in the spring season, due to the increase in the amount of plant pollen, the severity of allergic symptoms increases significantly. Also, these symptoms increase somewhat in the summer season due to the effect of air pollution and temperature rise. It should be noted that in autumn and winter, allergic symptoms appear with less severity, probably due to high humidity and low temperature.

Conclusion: Studies show that environmental variables in certain conditions can provide a suitable platform for allergic responses. Understanding these simple relationships helps doctors and specialists in this field to improve the management of patients' allergic symptoms by providing appropriate solutions.

Keywords: Allergic symptoms, Social health, Environmental factors, Immune responses

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Investigating the effect of Grape Seed Extract on CGRP in Migraine by molecular docking method

(Research Paper)

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Introduction: A complicated neurological condition that can lead to disability is migraine. Headache, photophobia, and vomiting are among the symptoms. One of the various migraine management strategies is to inhibit calcitonin gene-related peptide (CGRP). The neuropeptide CGRP, which has ۳۷ amino acids, is a strong vasodilator. Inhibitors of CGRP, like Ubrogepant, are used to manage migraine. Grape seed extract (GSE) is a substance whose capacity to lower CGRP levels is discussed. Many compounds, including gallic acid, quercetin, and rutin, are present in GSE. The main substance in grape seed extract is Proanthocyanidin. The purpose of this study is to evaluate Proanthocyanidin and CGRP's binding affinity.

Methods: Through Science Direct and Pubmed, data were gathered. Structures were downloaded from the UniProt website, and Chimera software was used to make the necessary modifications, such as eliminating unwanted chains and ions. The Proanthocyanidin's three-dimensional structure was obtained from the PubChem database. [Center; X: ۹۹,٦٤۹۸, Y: ۱۱۰,۱۲۰, Z: ۹۹,۸۳۷۳, and dimensions (Angstrom); X, Y, Z: ۲۵,۰۰] was where the binding site was adjusted. Ultimately, AutoDock Vina was used to perform the molecular docking process in PyRx ۰,۸ to determine the binding affinity between CGRP and proanthocyanidin.

Results: The results of the docking process are as follows: For each model, the data correlates to their binding affinity, RMSD lower bond, and RMSD upper bound, respectively: Model #۱: [-۸,۷, ۰,۰, ۰,۰] Model #۲: [-۸,۵, ۱,۲۸۱, ۲,۰۸۵] Model #۳: [-۸,۰, ۳,۱۸۹, ۸,٦۰۲] Model #٤: [-۷,۸, ۲,٤۹٦, ۹,٤۲۸] Model #۵: [-۷,۸, ۳,٦۰٦, ۷,۹۳٦]

Conclusion: Proanthocyanidin's ability to attach to CGRP was shown to be based on the outcomes of their molecular docking study. More research is needed to determine whether proanthocyanidin is effective in controlling migraines; however, current studies suggest that grape seed extract may be able to help because of its strong binding status and potential antioxidant benefits.

Keywords: Proanthocyanidin, Grape seed extract, CGRP, Migraine

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Investigating the effect of hyaluronic acid on the antimicrobial responses of nanocomposite drugs (Review)

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Introduction: The resistance of microorganisms to antimicrobial agents is a very important global health challenge that leads to the development of innovative materials to fight infections. Hyaluronic acid is a polysaccharide known for its biocompatibility and moisture retention properties. This biological compound has been used as a promising component in various fields including treatment, for example, its importance in antimicrobial nanocomposites has been pointed out in this research. This review article examines the potential effects of hyaluronic acid on the efficacy and performance of antimicrobial compounds.

Methods: To collect the data of this research, studies related to the synergism effect of hyaluronic acid in various nanocomposites, including silver nanoparticles, zinc oxide, and systems based on chitosan and some other nanopolymers, were conducted. In this research, synthesis methods, material optimization and antimicrobial methods and tests were investigated.

Results: Observations show that the use of hyaluronic acid in the pharmaceutical composition increases the effectiveness of the treatment by helping the antimicrobial properties of nanocomposites due to its unique interactions with bacterial membranes and improving drug delivery. Investigations showed that nanocomposites combined with hyaluronic acid show better antibacterial effects that significantly reduce microbial resistance compared to older pharmaceutical compounds.

Conclusion: Hyaluronic acid with a significant effect on the antimicrobial effect of nanocomposites helps to provide a valuable strategy for the development of the next generation of treatment. Further studies to optimize the concentration of hyaluronic acid, investigate the long-term effects of this compound and obtain new solutions for clinical applications in wound healing and infection control will pave the way for these new treatments.

Keywords: Nano composite, Hyaluronic acid, Anti Bacterial treatment, Improve treatment

Investigating the effect of Melissa officinalis plant extract on pentylenetetrazol-induced seizures in Autistic rat (Research Paper)

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Introduction: Autism is a disease that causes problems in speech, performing social skills, as well as repetitive, stereotyped movements and aimless behaviors. ۱۵ to ۳۰ percent of people with autism experience seizures. However, the reported rate of epilepsy in autism varies between ۵ and ٤۰٪.Melissa officinalis plant is used in Iranian traditional medicine as a sedative, antipyretic, antispasmodic and anticonvulsant.In this research project, the possible effects of the extract of this plant on convulsions induced by PTZ in the autism model of male Wistar rats were investigated.

Methods: Healthy male and female Wistar rats were selected for mating.Female mice received water and normal food until day ۱۲,۵ of pregnancy.Then they are divided into ٤ groups. ۱-control ۲-autism group ۳-autism group Melissa officinalis plant extractwith a dose of ۱۰۰mg/kg.٤. Autism group + Melissa officinalis plant extractwith a dose of ۲۰۰mg/kg. Then, after ۲ weeks, pentylenetetorazole was injected PTZ with a dose of ۸۰ mg/kg to all groups of rats, and after that the animals' behaviors will be examined for ٦۰ minutes. Ricin criterion was used to evaluate seizure severity.

Results: ANOVA analysis shows that there is a significant difference between the groups in terms of duration in all stages of seizures. ($p<۰,۵$).

Conclusion: The findings of the present study showed that the administration of the Melissa officinalis plant extract to male rats with autism has inhibitory effects on PTZ-induced seizures.

Keywords: autism,Melissa officinalis plant, seizure, PTZ

Investigating the effect of microcapsules containing the essential oil of mountain white coriander plant on the angiogenesis of chicken embryos (Review)

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Introduction: Angiogenesis which is associated with the production of new vessels, is an active and complex factor that occurs in pathological and physiological events. This research was conducted with the aim of investigating the effect of microcapsules containing the essential oil of mountain white coriander plant on the angiogenesis of the chorioallantoic membrane of chick embryos

Methods: In this study, fertilized eggs of the Ras breed were placed in ٤ experimental groups, including a control group and ٣ groups receiving drugs with doses of ١٠٠, ٢٠٠, and ٤٠٠ µg/ml. On the first day, the eggs were placed in the device and On the second day, a window was created on the eggs. On the ٨th day, microcapsules containing Coriander essential oil with different doses were injected on the chorioallantoic membrane in the window area, and on the twelfth day, the chorioallantoic membrane was photographed by a stereomicroscope.

Results: The results show that by increasing the concentration of microcapsules containing white mountain coriander essential oil, we have a significant decrease in angiogenesis, so the microcapsule containing white mountain coriander essential oil has an anti-angiogenic effect, which significantly reduces the number and length of blood vessels

Conclusion: The microcapsule containing the essential oil of mountain white coriander plant reduces the number of vessels in the chorioallantoic membrane of chick embryos.

Keywords: Angiogenesis, chorioallantoic membrane, microcapsule, blood vessels

Investigating the effect of native Iranian probiotics on tau expression in Alzheimer's male rats with amyloid Beta. (Research Paper)

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۱.
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Introduction: Alzheimer's disease is a progressive neurological disorder that is the leading cause of dementia. It results in neuron cell death, personality changes, and significant disruptions in daily life. Given the potential therapeutic benefits of probiotics, this study explores the effects of native Iranian probiotics like lactobacillus acidophilus, Lactobacillus paracasei, Lactobacillus rhamnoses, Lactobacillus roteri, bacillus coagulans, bifidobacterium longum on memory impairment in male Wistar rats induced with Alzheimer's disease. Specifically, the research focuses on evaluating the impact of these probiotics on tau gene expression in the brain, following exposure to beta amyloid.

Methods: The experiment was conducted on ۱۵ male Wistar rats, which were divided into three groups of five. The first group served as the control and did not receive any treatment or undergo surgery. The second group, referred to as the Alzheimer's group, underwent surgery where beta amyloid was administered using a stereotaxic device to induce Alzheimer's like conditions. The third group, known as the Alzheimer's + probiotic group, also underwent surgery with beta amyloid administration and subsequently received a ۲۱-day course of probiotics via gavage.

Results: Following the gavage procedure, a shuttle box behavioral test was conducted on all groups to confirm the induction of Alzheimer's disease. for tau gene expression levels were assessed using the PCR method.

Conclusion: According to the analysis of the obtained result, probiotics have a positive role in the heal of Alzheimer's disease and the expression level of the tau gene has decreased in the group that received probiotics.

Keywords: Alzheimer's disease, probiotics, beta amyloid, Rat, Tau gene

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Investigating the effect of pomegranate tallow hydroalcoholic extract on weight control and blood glucose level and liver enzymes of lab mice diabetic with streptozotocin (Research Paper)

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١.
٢.
٣.

Introduction: Examining the pharmacological properties of pomegranate oil and its active ingredients is important considering the clinical and health applications it can have in humans. Diabetes is a chronic disease that is characterized by a decrease in insulin secretion due to dysfunction of beta cells in the pancreas or an increase in insulin resistance. The tendency to treat diabetes with herbal medicines that have less side effects than chemical medicines is expanding day by day. This study was conducted with the aim of investigating the effect of pomegranate tallow hydroalcoholic extract on weight changes, blood glucose levels and liver enzymes in diabetic mice with streptozotocin administration.

Methods: ٤٠ small male laboratory mice were divided into ٥ groups with ٨ repetitions and were kept in animal rooms with free access to water and food. They were divided per kilogram of pomegranate tallow hydroalcoholic extract. To induce diabetes, peritoneal administration of streptozotocin at the rate of ٩٠ mg/kg was used, then the blood sugar levels of the rats were checked by a glucometer on a fasting basis.

Results: From day ١٠ to ١٥, the extract significantly and dose-dependently, with the best performance for the dose of ٢٥٠ mg/kg, slowed down the weight loss process, p<٠,٠٠١. In the study of fasting glucose in blood serum, the same performance for the extract in reducing blood glucose concentration p<٠,٠٠١ The hydroalcoholic extract of pomegranate tallow in diabetic rats caused a significant decrease in AST enzyme compared to the diabetic control group in a dose-dependent manner, p<٠,٠٥, but only doses of ١٠٠ and ٢٥٠ mg/kg hydroalcoholic extract of pomegranate tallow could significantly decrease the enzyme ALT compared to the control group. become diabetic, p<٠,٠٠١.

Conclusion: The results of this research showed that the hydroalcoholic extract of pomegranate tallow, in addition to reducing blood sugar and controlling diabetes, regulates the activity of liver enzymes, it seems that one of the mechanisms of the hypoglycemic effect of pomegranate tallow extract is the increase of insulin secretion from pancreatic beta cells. which needs to be examined more closely.

Keywords: Pomegranate tallow, blood glucose, AST, ALT, streptozotocin

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Investigating the effect of tamoxifen on GSTM١ protein in endometriosis by molecular docking method (Research Paper)

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Introduction: Endometriosis is a chronic inflammatory disease defined as the presence of endometrial tissue outside the uterus, which causes pelvic pain and infertility. The function of GSTM١ (glutathione-S-transferase enzyme) can affect this disease. GSTM١ enzyme plays a role in detoxification of pollutants and dioxin. Dioxin is a carcinogenic and teratogenic compound and has different effects on the reproductive system and is considered as a risk factor for endometriosis. Null mutation in GSTM١ is associated with cancer caused by environmental factors and lack of detoxification enzymes.

Methods: The molecular docking technique is a descriptive analytical method that in this study, we first download the ٣D structure of the GSTM١ protein from the Pdb site. We perform the necessary corrections in terms of charge flow, removing water molecules and adding hydrogen ions to the chains of this protein through the Chimera software. Then we download the ٣D structure of Tamoxifen from PubChem website.

Results: RMSD Upper Bound RMSD Lower Bound Mode Binding Affinity Model ٠,٠ ٠,٠ ٠ -٧,٧ ١ ٢,١٩٢ ١,٤٣٩ ١ -٧,٥ ٢ ٢,٤٣٩ ١,٥٤٧ ٢ -٧,٥ ٣ ٩,٠٦٢ ٥,٤٢٩ ٣ -٧,٣ ٤ ٦,٢٦ ٣,٦١١ ٤ -٧,٢ ٥ ٨,٥٠١ ٤,٠٩١ ٥ -٧,١ ٦ ٨,٤٧٤ ٤,٥٥٦ ٦ -٧,١ ٧ ٢٠,٢٧٢ ١٧,٧٨٢ ٧ -٧,٠ ٨ ٨,٣٦٨ ٤,٣٢٤ ٨ -٧,٠ ٩

Conclusion: According to the docking results presented in the above tables, Tamoxifen drug binds well to GSTM١ protein with negative energy (Binding Affinity) and can show its effect.

Keywords: Endometriosis , molecular docking technique , Tamoxifen , GSTM١ protein

Investigating the effect of the Mediterranean diet on preventing cognitive decline (Review)

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Introduction: Increasing life expectancy worldwide has led to an increase in the number of older people, which in turn has increased the prevalence of age-related diseases such as dementia. Over ٦٠٪ of cases are affected by the most common form, Alzheimer's disease (AD). The prevalence of dementia increases with age, and by ٢٠٥٠, there will be ١١٥,٤ million people affected worldwide. As there are currently no effective pharmacological treatments to alleviate symptoms after the onset of the disease, it is essential to find techniques to delay or prevent the onset of dementia. Given the importance of modifiable risk variables, including lifestyle and cardiometabolic disorders, in dementia, diet is an interesting research topic. Neuroprotective diets, including the Mediterranean diet (MD), could improve prophylactic measures and change the way people with dementia who are at high risk are treated. Research has shown that the MD dietary pattern, as well as certain foods, can lower oxidative stress biomarkers and improve cognitive function. Based on recent literature reviews, this article aims to describe how MD can help prevent cognitive decline.

Methods: In the following article, we collected the required data by using key words using reliable databases such as Google Scholar, ProQuest, Science Direct, and PubMed. Our statistical population consists of all the studies that have been conducted until ٢٠٢٤. After reviewing the findings, we reviewed ١٥ articles.

Results: The researchers found adherence to a Mediterranean diet (MD) is associated with improved brain structure and function. This includes thicker cortical regions, a larger brain, slower hippocampal atrophy, better structural connections, and less amyloid deposition. Some foods associated with MD, as well as MD as a dietary pattern, have been shown to lower oxidative stress biomarkers and improve cognitive function. Long-term observational studies have linked consumption of unsaturated fats with better cognitive performance and lower risk of age-related cognitive decline. Micronutrients have also been linked to a lower risk of Alzheimer's disease (AD) and cognitive decline. These include vitamins C, E, B-١٢, folic acid, flavonoids, and carotene. As MD increases the uptake of antioxidants and anti-inflammatory substances, it is thought to have neuroprotective effects. A number of known vascular risk factors for dementia and stroke are also associated with a Mediterranean diet. According to mechanistic studies, the shortening of telomeres is prevented by the Mediterranean diet and is associated with a lower risk of a number of age-related diseases,including cognitive decline. Meta-analyses support the importance of the Mediterranean diet in regulating the MetS and its components, which may have a protective effect against cognitive diseases. The fruits and vegetables in the Mediterranean diet are rich in several vitamins, including folic acid, which is strongly correlated with cognitive function. A broad category

of phytochemicals called polyphenols have been shown to have positive effects on neurogenesis, neuroplasticity, reduction of oxidative stress, cerebral blood flow, and neuroinflammation.

Conclusion: Based on the collected results, the massive global burden of dementia is expected to rise to previously unheard-of proportions in the ensuing decades as a result of population aging. Therefore, there is substantial evidence to support the premise that addressing modifiable risk factors, particularly in midlife, is a good strategy for mitigating the burden of dementia in the absence of disease-modifying medication. Of these risk factors, nutrition is most important since it is essential for a good aging process and has a multitude of benefits that are interrelated for many organ systems, metabolic processes, and health states, all of which can influence the risk of dementia. The most successful diets are those high in neuroprotective components, including B vitamins, antioxidants, and polyunsaturated fatty acids. The diets that are most effective in providing neuroprotective advantages include the MedD, DASH, MIND, and MMKD diets. There are methodological issues, but the benefits of a Mediterranean-style diet for neuroprotection are consistently supported by the researches. Following this diet, beginning at a young age, can help preserve cognitive function and brain health.

Keywords: Dementia, Mediterranean diet, Cognitive decline

Investigating the Epidemiology and Prognosis of Primary Lung Lymphoepithelioma-Like Carcinoma (PPLELC) and the Impact of Immunotherapy on its Clinical-Pathological Characteristics (Review)

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Introduction: Primary Pulmonary Lymphoid Epithelial-Like Carcinoma (PPLELC) is a rare histological subtype of non-small cell lung cancer (NSCLC). Comprising less than ١٪ of NSCLC cases, it is a rare lung tumor with distinct clinicopathological features. It predominantly affects middle-aged (٥١-٥٥ years), primarily non-smoking, and predominantly Asian and South Chinese female individuals. This tumor can occur in the submandibular gland, parotid gland, thymus, lung, stomach, uterus, bladder, and skin. It is associated with Epstein-Barr virus (EBV) infection. Epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK) are rarely found in this disease, while high expression levels of programmed death-ligand ١ (PD-L١) are observed. Due to its rarity, there is currently no established treatment protocol. Although subtype-specific mortality has been widely reported, some rare pathological types of lung cancer, such as PPLELC, remain poorly characterized in terms of incidence and prognosis. Moreover, this disease requires further research to understand its clinical features. It was first reported by Begin and colleagues in ١٩٨٧ in a ٤٠-year-old Southeast Asian woman in Canada. This epithelial tumor, associated with EBV infection, is histologically similar to nasopharyngeal carcinoma (NPC). Studies have shown that PPLELC is usually diagnosed at early stages and has a better prognosis compared to other NSCLC subtypes. However, the majority of reported PPLELC cases have been from Asia, and limited studies have focused on its incidence and prognosis in Western countries. This study aims to determine the epidemiology and prognosis of primary pulmonary lymphoid epithelial-like carcinoma (PPLELC) and the impact of immunotherapy on its clinicopathological features.

Methods: This review study was conducted in ٢٠٢٤ by searching keywords such as: Epidemiology, PPLELC, Immunotherapy and Clinical-Pathological Characteristics in reliable databases such as: PubMed, Scopus and Web of Science.

Results: PPLELC is a rare malignant lung tumor classified as a subtype of non-small cell lung cancer (NSCLC). Most patients with PPLELC do not present with obvious clinical symptoms at diagnosis. Treatment approaches for PPLELC often follow NSCLC regimens. Additionally, due to low mutation rates of EGFR, ALK, Kirsten rat sarcoma viral oncogene homolog (KRAS), v-Raf murine sarcoma viral oncogene homolog B١ (BRAF), ROS١ proto-oncogene receptor tyrosine kinase (ROS١), and tumor protein p٥٣ (TP٥٣), advanced PPLELC patients are less likely to benefit from targeted therapy. However, the high expression of programmed death-ligand ١ (PD-L١) in PPLELC suggests that PD-L١ inhibitors such as Nivolumab and Pembrolizumab may be suitable treatment options. The efficacy of Nivolumab in treating advanced NSCLC is significantly correlated with tumor mutational burden

(TMB), and it is more effective in patients with high TMB compared to chemotherapy. Although PPLELC has a low TMB, a large volume of copy number variations (CNVs), especially amplification of ١١q١٣,٣ and deletion of ٩p٢١,٣, has been observed. According to studies, a number of patients underwent chemotherapy or immunotherapy. Immunotherapy drugs included Pembrolizumab, Nivolumab, or Atezolizumab. Chemotherapy regimens included platinum-based doublet chemotherapy, paclitaxel albumin-bound, or Pemetrexed monotherapy. In total, ٢١٠٦ patients with LELC were identified, with the most common primary tumor site being nasopharyngeal LELC (٥٦,٢٢٪), followed by head and neck non-nasopharyngeal LELC (٢١,٣٢٪) and respiratory system (٧,٨٣٪). Additionally, the overall age-adjusted incidence of LELC was ٠,٠٩١ per ١٠٠,٠٠٠. The cancer-specific survival (CSS) rates of LELC patients at ٥, ١٠, ١٥, and ٢٠ years were ٧٦٪, ٦٩٪, ٦٥٪, and ٦١٪, respectively. Over the past decade, a decreasing trend in the incidence of LELC has been observed.

Conclusion: The prognosis of PPLELC is better than other NSCLC subtypes, and immunotherapy may be a promising treatment to improve survival in advanced PPLELC patients. Whether the efficacy of immunotherapy in PPLELC can be predicted by PD-L١ and TMB requires further clinical investigation. Genetic alterations in CYLD may contribute to EBV-driven tumorigenesis in PPLELC and provide a novel therapeutic target. Current treatment options for PPLELC include surgical resection, chemotherapy, radiotherapy, and immunotherapy. Consequently, extensive research and clinical trials are necessary to develop effective treatment guidelines for PPLELC.

Keywords: Epidemiology, PPLELC, Immunotherapy and Clinical-Pathological Characteristics

Investigating the expression of lncRNA gene PVT١ and its role in colorectal cancer. (Research Paper)

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Introduction: Colorectal cancer (CRC) remains a major global health challenge, ranking as the fourth leading cause of cancer-related deaths worldwide. Despite advances in treatment, the prognosis for advanced CRC remains poor. This study aimed to investigate the expression and clinical significance of long non-coding RNA PVT١ in CRC.

Methods: Total RNA was extracted from CRC tissues and adjacent normal tissues using a standard extraction protocol. Complementary DNA (cDNA) was synthesized from the extracted RNA using the geneAll reverse transcription kit (Invitrogen). The qRT-PCR reaction was performed in ٠,٢ ml tubes using the SYBR Green Master Mix (Denmark, amplitude) on a LightCycler® ٩٦ system (Roche Life Science, Germany). β-actin was used as an endogenous control, and the ٢-ΔΔCt method was employed to calculate the relative expression levels of tumor PVT١ and Peripheral PVT١ variants.

Results: The qRT-PCR analysis revealed a significant upregulation of the tumor PVT١ variant in CRC tissues compared to adjacent normal tissues. The tumor PVT١ variant exhibited higher expression levels than the Peripheral PVT١ variant across all CRC samples, suggesting a potential oncogenic role for tumor PVT١ in colorectal carcinogenesis. Statistical analysis demonstrated that elevated tumor PVT١ expression was significantly associated with advanced tumor stage, lymph node metastasis, and poor overall survival. These findings indicate that tumor PVT١ may be involved in the activation of specific signaling pathways that drive tumor progression and metastasis

Conclusion: Discussion The results of this study highlight the potential role of the tumor PVT١ variant as a key player in CRC progression. The marked upregulation of tumor PVT١ in CRC tissues suggests that this lncRNA may contribute to the aggressive nature of the disease by promoting uncontrolled cell proliferation, enhancing EMT, and supporting metastatic spread (٧). The association between elevated tumor PVT١ expression and advanced tumor stage further supports its potential as a prognostic biomarker for CRC. The findings of this study are consistent with previous reports that have implicated PVT١ in various cancers, including CRC (٨). However, the precise molecular mechanisms through which tumor PVT١ exerts its effects in CRC remain to be fully elucidated. It is possible that tumor PVT١ interacts with key oncogenic pathways, such as the Wnt/β-

catenin, PI٣K/AKT, or MAPK/ERK pathways, to promote tumor growth and survival. Further research is needed to identify these interactions and explore the potential of tumor PVT١ as a therapeutic target (٩). In conclusion, this study provides evidence that the tumor PVT١ variant is significantly upregulated in CRC tissues and is associated with poor clinical outcomes. The findings suggest that tumor PVT١ could serve as a valuable prognostic biomarker and a potential target for therapeutic intervention in CRC. Future studies should focus on elucidating the molecular mechanisms underlying tumor PVT١ role in CRC and investigating its potential as a target for novel therapeutic strategies.

Keywords: Colorectal cancer, PVT١, qRT-PCR, Prognostic.

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Investigating the factors causing urinary tract infections in patients admitted to Khatam Al-Anbia Hospital in Shirvan city in ۲۰۲۳ (Research Paper)

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Introduction: Urinary tract infection is one of the most common bacterial infections, which is known as the second cause of infection in the human body. Failure to diagnose and treat this type of infection on time can cause severe complications such as urinary tract disorders, blood pressure, and kidney disorders. , uremia and in pregnant women it can cause premature birth and even abortion.

Methods: In this cross-sectional descriptive study, the urine samples of patients suspected of urinary tract infection referred to the laboratory of Khatam Al-Anbia Hospital in ۲۰۲۳ were examined, and the positive samples, uropathogens, were identified using standard microbiological and biochemical tests.

Results: In this study, out of ۱۵۱۳ urine samples of inpatients referred to the laboratory of Khatam-ul-Anbia hospital in Shirvan, ۱۳۳ samples (۸,۸٪) were positive, of which ٦٥ samples (٤٨,٨٪) were female and ٦٨ samples (٥١,٢٪) were male. The most common bacterial isolate was Escherichia coli with ٦٠ samples (٤٥,١٢٪), Candida strain ٤٥ (٣٣,٨٨٪), Klebsiella strain with ١٣ (١٠٪), Enterococcus ٧ (٥,٥٪), Streptococcus other than group D (٢,٢٦٪), Staphylococcus epidermidis ٢ (٣) ١,٧٪), Pseudomonas aeruginosa ١ (٠,٧٧٪)) and Enterobacter ١ (٠,٧٧٪) were isolated.

Conclusion: According to the results obtained and other researches, Escherichia coli is the most common cause of urinary tract infections and Candida strain is the second factor that has a significant difference with other Gram-negative and positive bacteria, which is due to the increased resistance of the species. The candidate should be taken into consideration by the doctors.

Keywords: urinary infection, causative factors, Shirvan

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Investigating the immunogenicity of corona vaccine candidate (S١) produced in prokaryotic host

(Research Paper)

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Introduction: The new human coronavirus has a very high treatment cost and still shows a high death rate in infected people. If the vaccine is widely used, we will have a lower rate of coronavirus infection. Making this vaccine is important and its results can be used in research centers and pharmaceutical companies. Several laboratories around the world have begun conducting studies to develop a vaccine to prevent the disease. Most of the vaccines targeted the specific protein subunit of the glycoprotein of SARS-CoV (S١). Coronavirus uses this glycoprotein to bind and enter host cells. Therefore, a vaccine that creates a strong immune response against this protein will have a significant effect in preventing the virus from entering host cells during natural infection.

Methods: Materials used: ١. Aluminum hydroxide adjuvant. Aluminum salts are the most common adjuvants in the preparation of human and animal vaccines. Aluminum hydroxide adjuvant shows good immunoadjuvant effects with many antigens. ٢. The new S١ protein was expressed as a recombinant protein in the Soban Recombinant Protein Company in a prokaryotic vector, and after purification and exchange of buffer with a mass of ٢٠٠ µg/ml, it was prepared for combination with adjuvant. ٣. Sodium Chloride (NaCl) Sodium Chloride was used to prepare a salt buffer in order to dilute the sample obtained from the combination of adjuvant and protein. How to do the work: Formulation of the vaccine. Next, we refer to the stages of preparing the vaccine. ١. Preparation of adjuvant stock buffer ٣. Examining the binding of adjuvant to S١ protein. After combining the appropriate ratio of protein and aluminum hydroxide adjuvant, the vaccine sample was placed in a cold room for ٢٤ hours, and after that, tests were carried out to ensure the binding of protein and adjuvant. SDS-PAGE analysis and Lowry test can be mentioned among the performed investigations. ٤. Determining the immunogenic variables and drawing the injection table, the injection process was done according to different conditions using insulin injection syringes to Balb C mice.

Results: As a result, in this project, the s١ protein was recombinantly expressed in the prokaryotic host. The purified protein with the formulated formulations was examined for injection into the rat animal sample. This formulation is composed of protein and aluminum hydroxide adjuvant with ratios of ١:٥ and ١:١٠. Injections were given at intervals of ١٤ and ٢١ days to check immunogenicity. The number of prescribed doses was ٢ and ٣ injections. The results of this project determined that ratios of ١:١٠ produced higher antibody titers than ١:٥. In blood sampling ١٤ days after the first injection, a low antibody level was observed in all formulations. Then, with the increase in the number of injections, the antibody level increased. With the third injection after ٣٥ days, the antibody titer grew exponentially.

Conclusion: In short, the goals of the upcoming research are: creating maximum immunogenicity using protein (S١) against corona in the presence of a suitable adjuvant, reducing the country's treatment costs in dealing with corona by creating immunity against coronavirus, optimizing the method to improve the quality of the produced vaccine by conducting animal tests (mouse) to ensure the accuracy of the function of the recombinant protein (S١) of the coronavirus, the production of a recombinant protein vaccine that has an appropriate ratio of (S١) adjuvant that stimulates the immune system well and can be used on an industrial scale. The implementation steps of the research are: ١. The production of protein conjugated with aluminum hydroxide (adjuvant) ٢. Injection into the animal ٣. Taking blood from the animal ٤. ELISA kit to determine the antibody titer is generally the step of this research. Coronavirus is a very dangerous virus that has a high cost of treatment and a high mortality rate, that's why it is very important to produce a vaccine that causes immunity against the virus, which can reduce the number of infections and deaths. As a result of reducing the rate of infection and death due to coronavirus and reducing the medical costs of the country, the surface polysaccharide of coronavirus (S١) may be a suitable candidate for making a vaccine and creating immunity against coronavirus.

Keywords: Vaccine candidate; coronavirus; immunogenicity; Adjuvant; S١ protein

Investigating the impact of common APOE, ABCA۷ and TREM۲ gene mutations in Alzheimer's patients in Tehran (Review)

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Introduction: Alzheimer's disease (AD) is a complex, highly heritable disease with no current effective prevention or treatment. Genetic factors play an important role in the occurrence and development of this disease. Despite decades of research, there are no effective treatments and a large part of the genetic heritability remains unknown. Therefore, in this research, the relationship between these mutations and the incidence of disease in Tehran is investigated. The aim of this study is to investigate the effect of common mutations of APOE, ABCA۷ and TREM۲ genes in patients with Alzheimer's disease in Tehran.

Methods: In this study, samples from ۱۰۰ Alzheimer's patients and ۱۰۰ non-relative healthy controls who matched the patient group in terms of geography, age, gender, were performed using the PCR method

Results: The studied population was investigated according to the Hardy-Weinberg law, which, according to the significance of the polymorphisms rs۳۷٦٤٦٥۰ (p-value: ۰,۱۰٦) and rs٤۲۹۳٥۸ (p-value: ۰,٦۸٦۳), the non-significance of these polymorphisms with Alzheimer's and polymorphism rs۷٥۹۳۲٦۲۸ (p-value: ۰,۰۱٦۷) has shown its significant relationship with Alzheimer's disease

Conclusion: The present study emphasizes the importance of examining genetic factors in Alzheimer's disease and can help identify patients at risk and develop prevention strategies. It is suggested that more research be done on the relationship between genetic mutations and environmental factors in this disease in order to gain a better understanding of its mechanisms

Keywords: Alzheimer's - mutation - single nucleotide polymorphism - gene

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Investigating the Impact of Covid-١٩ on the Mental Health of Medical Students, A Systematic Review (Review)

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Introduction: The spread of Corona Virus Disease ٢٠١٩ (COVID-١٩) has become a global major public health event, threatening people's physical and mental health and even life safety. This study aims to investigate the impact of COVID-١٩ on students' mental health.

Methods: The design of this study is to use a systematic review approach by collecting several articles from the databases Scopus, PubMed, Web of Sciences, and Google Scholar in August ٢٠٢٤. A search for articles was carried out by entering the keywords "mental health AND student AND COVID-١٩". The search for this article was limited to inclusion criteria and exclusion criteria. The inclusion criteria in this study were health students who were still conducting studies during the COVID-١٩ pandemic and a cross-sectional study design. In contrast, the exclusion criteria were non-health students, only abstracts and books, and letters to the editor.

Results: The results of the ١٥ articles that were reviewed showed that the majority of students reported mental health problems such as anxiety, depression, stress, and other emotional status moderate and severe levels of anxiety were experienced by some Health students who carried out education during the COVID-١٩ pandemic.

Conclusion: The COVID-١٩ pandemic impacts psychological conditions, especially health students who are carrying out their education. the majority of Students report poor mental health conditions while carrying out home education by learning online during the COVID-١٩ pandemic, and necessary measures must be taken to improve their mental health status.

Keywords: COVID-١٩, Mental health, Medical Students

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Investigating the Incidence of Thrombocytopenia and Associated Factors Among Inpatients at Akbar Hospital's Pediatric Intensive Care Unit in ٢٠٢٠ (Research Paper)

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Introduction: Children with thrombocytopenia often face complications in their management and prognosis as a result of this hematological disorder. Thrombocytopenia was investigated among inpatients of the Pediatric Intensive Care Unit (PICU) of Akbar Hospital in ٢٠٢٠, as well as associated factors.

Methods: PICU admissions at Akbar Hospital from January to December ٢٠٢٠ were examined in a retrospective cohort study. The inclusion criteria included patients with documented platelet counts between ٠ and ١٨ years old. Thrombocytopenia was defined as a platelet count below ١٥٠,٠٠٠/µL. There were a number of demographic data collected along with a number of clinical diagnoses, treatment methods, and outcomes. It was found that the proportions for both continuous and categorical variables could be calculated using standard deviations (SDs) and frequencies, respectively, using statistical analysis. As part of the multivariate logistic regression analysis, factors independent of thrombocytopenia have been identified by using multivariate logistic regression.

Results: Out of ٤٥٠ PICU admissions, ١٨٥ (٤١,١٪) developed thrombocytopenia. The mean age of affected patients was ٥,٤ ± ٣,٢ years. The mean platelet count at the nadir was ٩٨,٥٠٠ ± ٢٨,٢٠٠/µL. Factors significantly associated with thrombocytopenia included sepsis (OR ٢,٤٥, ٩٥٪ CI ١,٥٠-٤,٠٠), mechanical ventilation (OR ١,٨٥, ٩٥٪ CI ١,١٠-٣,١٠), and length of stay (mean ١٢,٧ ± ٥,٣ days versus ٨,٣ ± ٤,١ days, p < ٠,٠١). Mortality was higher in the thrombocytopenic group (٢٥,٤٪ vs. ١٠,٣٪, p < ٠,٠٠١).

Conclusion: There is an increased risk of morbidity and mortality associated with thrombocytopenia in PICU patients as well. Prolonged hospital stays, sepsis, and mechanical ventilation pose significant risks. Improved outcomes may be possible if thrombocytopenia is identified and managed early.

Keywords: Thrombocytopenia, Pediatric Intensive Care, Incidence, Risk Factors, Mortality

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Investigating the Influencing Factors on the Process of Assisted Reproductive Treatments (ARTs) (Review)

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Introduction: Assisted reproductive treatments (ARTs) are medical procedures used to help individuals and couples have a child. Success of these treatments is influenced by factors like age, hormonal imbalances, sperm quality, lifestyle, previous pregnancies, medical conditions, type of ART, quality of the medical team, number of embryos transferred, and genetic factors. Common ARTs include In Vitro Fertilization (IVF), Intrauterine Insemination (IUI), Ovulation Induction (OI), Intracytoplasmic Sperm Injection (ICSI), Frozen Embryo Transfer (FET), Donor Egg or Sperm, and Surrogacy. These treatments are commonly used to help overcome infertility and achieve pregnancy.

Methods: The present study was conducted by reviewing related articles in Web of Science, Scopus, and PubMed databases.

Results: The most common assisted reproductive treatments include In Vitro Fertilization (IVF), Intrauterine Insemination (IUI), Ovulation Induction (OI), Intracytoplasmic Sperm Injection (ICSI), Frozen Embryo Transfer (FET), Donor Egg or Sperm, and Surrogacy. These treatments help individuals and couples overcome infertility and achieve pregnancy. Risks associated with assisted reproductive treatments include increased risk of adverse perinatal outcomes, birth defects, and potential long-term health risks for children conceived through these techniques. Short-term health risks include adverse perinatal outcomes, complications of multiple pregnancies, uncertainty in outcomes, and epigenetic alterations that could lead to later health issues. Long-term health risks are not well studied, but concerns exist about the effects of endocrine manipulation on hormone-sensitive conditions in female patients. Additional research is needed to fully understand the long-term health outcomes of assisted reproductive treatments, especially in terms of potential risks for females undergoing these procedures.

Conclusion: The most common complications of assisted reproductive treatments (ARTs) include thromboembolic disease, pregnancy complications, genital cancers, and fetal and neonatal complications. These risks underscore the importance of understanding and managing the risks associated with ART procedures for the safety of both the mother and child. The most common obstetric complications associated with ARTs include preeclampsia, gestational diabetes, placenta accreta spectrum, multiple pregnancies, and advanced maternal age. Careful monitoring and management during pregnancy following ART procedures are essential to ensure the well-being of both the mother and child. Symptoms of abnormal placentation in assisted reproductive treatments can include vaginal bleeding, pain, preterm labor, placenta previa, and fetal distress. Early detection and management of abnormal placentation are crucial for ensuring the well-being of both the

mother and baby. Risks of abnormal placentation in ARTs include placenta previa, placenta accreta, and vasa previa, which can cause significant maternal and perinatal morbidity and mortality. Risk factors for abnormal placentation include prior cesarean delivery, smoking, multifetal gestation, and maternal age. Advances in ultrasound have improved prenatal diagnosis and management of abnormal placentation for better outcomes for mother and baby.

Keywords: Assisted Reproductive Treatments (ARTs) - risk factors - IVF- infertility

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Investigating the Inhibitory Effect of Silver Nanoparticles on Angiogenesis Gene Expression in the Chick Embryo Chorioallantoic Membrane (CAM) Model: A Potential Tumor Suppressor Approach

(Research Paper)

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Introduction: Angiogenesis, the process of forming new blood vessels, is a critical driver of tumor growth and metastasis. This process is regulated by factors such as Vascular Endothelial Growth Factor (VEGF) and its receptor KDR (Kinase Insert Domain Receptor). Targeting angiogenesis has become a major focus in cancer therapy, as limiting blood supply to tumors can significantly reduce their growth and spread. Silver nanoparticles (AgNPs), known for their antimicrobial properties, are gaining attention for their potential anticancer effects, particularly in suppressing angiogenesis. Although AgNPs are widely used in various industries, including agriculture and medicine, there is limited research on their effect on angiogenesis in animal models. This study seeks to fill that gap by investigating the effect of AgNPs on the expression of angiogenesis-related genes in the chick embryo chorioallantoic membrane (CAM), a widely used model for studying blood vessel development. Evaluating the impact of AgNPs on these genes could provide valuable insights into their potential as tumor-suppressing agents. Hypothesis H۰: Silver nanoparticles do not affect the expression of angiogenesis-related genes in the CAM. Hypothesis H۱: Silver nanoparticles affect the expression of angiogenesis-related genes in the CAM. The objective of this study is to assess the impact of silver nanoparticles on the expression of the VEGF and KDR genes, which are key regulators of angiogenesis, and explore the possibility of AgNPs as an inhibitor of tumor-associated angiogenesis.

Methods: This experimental study was conducted using ۱٤ fertilized chicken eggs obtained from Mahan Hatchery, Kerman, Iran. The eggs were randomly divided into two groups of seven. Group one (treatment group) was injected with ۰,۲٪ silver nanoparticles, while group two (control group) received phosphate-buffered saline (PBS). The injections were administered onto the inner shell membrane at ۲٤, ٤۸, and ۷۲-hour intervals. All eggs were incubated vertically in a hatcher (Belderchi Damavand Co. PLC-DQSH) at ۳۷,۷°C with ٦۰٪ relative humidity. Twenty-four hours after the final injection, the embryos were harvested, and their chorioallantoic membrane (CAM) was collected. RNA was extracted using commercial kits, and cDNA was synthesized. Gene expression of VEGF and KDR was analyzed using Real-Time PCR with specific primers, and GAPDH was used as the reference gene. Statistical analysis was performed using SPSS software, and a T-test was applied to compare gene expression levels between the two groups. A p-value of less than ۰,۰٥ was considered statistically significant, confirming the differences in gene expression between the treatment and control groups.

Results: The results revealed a significant decrease in VEGF expression and an increase in KDR expression in the AgNP-treated group compared to the control group. The reduction in VEGF, a primary pro-angiogenic factor, suggests that silver nanoparticles have an inhibitory effect on angiogenesis in the CAM model. The upregulation of KDR may indicate a compensatory response to the decreased VEGF levels, as the receptor attempts to balance the reduction in its ligand. These findings support the hypothesis that AgNPs can modulate the expression of key angiogenesis-related genes, which is essential for limiting tumor-associated vascularization.

Conclusion: This study demonstrates for the first time that silver nanoparticles can significantly influence angiogenesis-related gene expression in the CAM model. The downregulation of VEGF, a key angiogenic factor, suggests that AgNPs may suppress the formation of new blood vessels. Given that angiogenesis is essential for tumor growth, inhibiting this process could be a powerful strategy in cancer therapy. The observed increase in KDR expression may be a compensatory mechanism due to reduced VEGF stimulation, highlighting the complexity of angiogenic regulation in response to nanoparticle exposure. The potential of AgNPs as an anti-angiogenic agent could contribute to the development of novel cancer therapies aimed at starving tumors of their blood supply. However, further research is needed to elucidate the molecular mechanisms by which AgNPs affect angiogenesis and to confirm these findings in more complex tumor models. Silver nanoparticles significantly inhibit angiogenesis by downregulating VEGF expression in the CAM model, indicating their potential as an anticancer agent. This study provides important preliminary evidence for the use of AgNPs as a tumor suppressor through angiogenesis inhibition. Future research should focus on validating these results in human tumor models and exploring the broader therapeutic applications of AgNPs in cancer treatment.

Keywords: Silver nanoparticles, Angiogenesis , VEGF, Tumor suppression, Chick embryo chorioallantoic membrane

Investigating the performance of artificial intelligence on human behavioral genetics (Review)

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Introduction: Simulating human intelligence in robots designed to think and learn like humans is known as artificial intelligence (AI). Artificial intelligence (AI) is a general term that refers to using computers to model intelligent behavior with minimal human intervention. Artificial intelligence is creating a world that has never been seen before. By using artificial intelligence to do things that would otherwise take too much time, humans can improve our planet. One of the emerging fields that has been heavily influenced by artificial intelligence is human behavioral genetics. This study aims to investigate the performance of artificial intelligence on human behavioral genetics.

Methods: To conduct this study, a systematic search was conducted in valid databases including, sid, PubMed, Scopus, and Google Scholar. Keywords related to the topic including "artificial intelligence", "behavioral genetics", "human behavior", and "machine learning" were used. The identified articles were carefully evaluated and screened based on the titles, abstracts, and full text. Finally, out of ٣١ articles, ٩ studies that were most related to the research topic were selected for deeper analysis.

Results: The findings indicate that machine learning (ML) enables the analysis of complex and large data sets. Artificial intelligence (AI) is gradually changing the practice of medicine. With recent advances in digital data collection, machine learning, and computing infrastructure, AI applications are expanding into areas previously thought to be the domain of human experts. With the rapid growth of biomedical data enabled by advanced experimental technologies, artificial intelligence (AI) and machine learning (ML) have emerged as indispensable tools for generating meaningful insights and improving decision-making. Artificial intelligence is significantly effective in identifying genetic patterns and human behaviors. Machine learning algorithms allow researchers to combine genetic data with behavioral data to identify complex relationships between genes and behaviors. Some studies have shown that artificial intelligence can help predict social and emotional behaviors based on genetic data. In addition, the use of deep neural networks in the analysis of large genetic data has helped to identify new patterns and predict human behavior. Also, AI allows researchers to quickly and accurately analyze complex data and provide reliable results. Artificial intelligence has a

promising future in medicine. However, many challenges remain. Despite the great media attention to artificial intelligence (AI), for many professionals, the term and practice of AI remain a "black box", leading to exaggerated expectations on the one hand and unfounded fears on the other.

Conclusion: Artificial intelligence can act as an effective tool in analyzing and understanding human behavioral genetics. Due to the rapid developments in the field of artificial intelligence and data mining, this field is expected to develop significantly in the future and contribute to a better understanding of human behavior. However, the need for more research and more detailed investigations in this field is felt to achieve more reliable results.

Keywords: Artificial intelligence, behavioral genetics, human behavior, machine learning

Investigating the phenolic properties of Cinnamomum verum extract (Research Paper)

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2.

Introduction: Cinnamomum verum known as sweet cinnamon is native to Sri Lanka. The bark is widely used as a spice or seasoning in food and sweets. It is also used in making soap, dental products and perfumes. The main composition of its essential oil is sinaldehyde and eugenol. Sinaldehyde present in the plant plays a vital role in various metabolic pathways involved in hyperglycemia and metabolic syndrome. Also, cinnamon is effective in treating diabetes, high blood pressure, heart diseases, etc. Eugenol in cinnamon contains polyphenol compounds. Phenolic compounds have antioxidant properties and can improve oxidative stress symptoms such as malondialdehyde and superoxide desmutase levels.

Methods: In this study, we measured the polyphenol compounds in cinnamon extract. For this purpose, we first extracted the dry cinnamon bark with hot (Soxhlet) method. Next, ۷۰٪ of the alcohol was removed from the extract by rotating. Then, Folin Ciocaltiou reagent was produced in the presence of phenolic compounds in ۲٪ sodium carbonate alkaline solution and reduced distilled water and a blue color was produced in the solution. Color intensity was measured at ۷۶۵ nm wavelength. The values of total phenolic content in the sample were determined according to the standard curve of gallic acid.

Results: The amount of phenol in cinnamon extract in this study is ۱۲۰٫۵۸ gallic acid in µg.

Conclusion: The antioxidant capacity of natural products is attributed to the presence of phenolic compounds. Therefore, it can be said that cinnamon can deal with the increase in the level of oxidative stress factors and reverse its effects. These effects include reducing the level of malondialdehyde and improving the level of superoxide desmutase. This plant can be effective in treating diabetes and hyperglycemia etc. These people can be advised to use this substance in their diet.

Keywords: Cinnamomum verum, phenolic properties, Antioxdants, oxidative stress

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Investigating the potential of menstrual blood stem cells in regenerative medicine (Review)

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Introduction: Menstrual blood-derived stem cells (MenSCs) are a novel source of mesenchymal stem cells (MSCs); that have several advantages including abundance, periodic acquisition, non-invasive isolation from donor women in the age of ٢٠ to ٤٥ years, high proliferation rate (doubling every ٢٠ h supplied with sufficient culture conditions), possess multi lineage differentiation potency, migrate into injury sites, secretion of soluble factors, regulation of immune responses and stably genetic characteristic, the possibility of injecting large amounts of cells intravenously into the target tissue. The purpose of this study is to investigate the potential of menstrual blood stem cells in regenerative medicine.

Methods: In the present review article, we studied original and review studies published in PubMed, Science Direct, Scopus, and Google Scholar databases using the keywords menstrual blood stem cells; assisted reproductive technologies; and regenerative medicine.

Results: Recent studies have shown that these stem cells, which are considered a type of biological waste, have a very high potential in the treatment of various levels of diseases and injuries due to fewer problems compared to transplantation and other expensive and invasive treatment methods. The risk of rejection and tumor formation in them is less. Also, there is no limit in terms of collecting these cells, and it is possible to receive these cells continuously and monthly, without the risk of infection for the donor. Despite the potential of MenSCs in regenerative medicine, there are several challenges that researchers will need to overcome to realize their full therapeutic potential and answer many questions.

Conclusion: In conclusion, the potential of menstrual blood stem cells in regenerative medicine offers great promise. With continued research menstrual blood stem cells may become a valuable source of stem cells for regenerative therapies. Overcoming challenges and advancing research in this area could lead to new and effective treatment options for patients with various medical conditions.

Keywords: stem cell, Regenerative Medicine, menstrual

Investigating the Prevalence of Human Cytomegalovirus in Colorectal Cancer Tissue via Real-Time PCR (Research Paper)

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Introduction: Colorectal cancer (CRC) is the second most common type of cancer worldwide, accounting for approximately half a million cases per year . A person's lifetime risk of developing colon cancer is about ٤٪, but several factors can increase this probability. The potential connection between Human cytomegalovirus (CMV) and colorectal cancer (CRC) has been extensively investigated, although its exact role remains uncertain and is still a subject of speculation.

Methods: In this research, conducted between September ١, ٢٠٢٣, and September ١٧, ٢٠٢٤, we examined ٦٦٤ patients who requested CMV testing and assessment of CMV viral load. Our focus was specifically on patients who provided tissue samples, including intestinal and colon biopsies, as well as paraffin-embedded block samples. The methodology involved an initial extraction of DNA from the samples, followed by analysis of the extracted product using quantitative PCR (q- PCR).

Results: Through PCR analysis, we determined that roughly ١٢٪ of the patients evaluated in our study (٨٢ out of ٦٦٤) provided the anticipated test samples. Among these individuals, approximately ٢٩٪ (٢٤ out of ٨٢) returned positive results. The p-value for the proportion of positive results among the acute patients tested is significantly low, suggesting that the observed proportion of positive results (٢٩٪) is significantly higher than the expected proportion (١٢٪). We ultimately analyzed the data, which revealed an equal number of male and female patients, suggesting that gender does not influence the prevalence of this disease (The average age of these patients was ٢٤ years old).

Conclusion: The findings from our study on the association of Human Cytomegalovirus with colorectal cancer reveal a noteworthy prevalence of viral presence in tumor tissues. Out of ٦٦٤ patients, ١٢٪ provided adequate samples for analysis, highlighting the challenges in sample collection in this patient population. Among these samples, a striking ٢٩٪ tested positive for HCMV, which is significantly higher than the anticipated proportion of ١٢٪. This elevated prevalence suggests a potential role of HCMV in colorectal carcinogenesis, warranting further investigation. The low p-value associated with the positive results among acute patients reinforces the significance of our findings, indicating that HCMV may be more prevalent in colorectal cancer tissues than previously understood. These results underscore the need for additional research to elucidate the mechanisms by which HCMV may contribute to tumor development and progression, potentially leading to novel therapeutic strategies targeting viral infection in colorectal cancer patients.

Keywords: Human cytomegalovirus, colorectal cancer, quantitative Real Time PCR

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Investigating the relationship between antimullerin hormone and ovarian response in infertile women after IVF (Research Paper)

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Introduction: Anti-Müllerian hormone has a good correlation with the age of the woman, the number of antral follicles and the result of assisted reproductive technology. The present study was conducted with the aim of investigating the relationship between anti-Müllerian hormone levels and ovarian response and pregnancy outcomes in infertile women undergoing IVF treatment

Methods: This cross-sectional study (descriptive-analytical) was conducted in ٢٠٢٠-٢٠٢٢ on ٨٠ infertile women treated with ART infertility treatment, referring to the infertility center of Razavi Hospital in Mashhad. Demographic information, FSH and AMH levels, the number of injected gonadotropin ampoules, the number of antral follicles and the number of embryos obtained were checked and recorded in the questionnaire. Also, pregnancy outcomes including abortion, fetal death, fetal malformation and birth were determined and recorded in the questionnaire. Data analysis was done using SPSS version ٢٦ statistical software and chi-square tests, Fisher's exact test, one-way analysis of variance and Pearson correlation. A p value of less than ٠,٠٥ was considered significant

Results: There was a significant correlation between the level of antimullerin hormone with the number of HMG injected, the number of retrieved eggs, the number of total embryos, type A and B embryos in women with agonist IVF. The mean AMH was ٢,٦٦ ± ١,٦٦ pmol/dL. The amount of this hormone in women with positive and negative ovarian response did not differ, but in pregnancy and pregnancy with positive outcome, there was a significant difference with the group of no appropriate ovarian response. The amount of AFC before treatment in the pregnancy and pregnancy groups with a positive outcome and the Ovarian Insufficiency did not have a significant difference.

Conclusion: Determination of AMH levels is helpful in prescribing gonadotropin, predicting the number of antral follicles, retrieved eggs, and the number of embryos obtained, but the level of antimullerin hormone is not related to fertility outcome.

Keywords: Pregnancy outcome, gonadotropin, antimullerin hormone, IVF

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Investigating the relationship between follicle stimulating hormone and ovarian response in infertile women after IVF (Research Paper)

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Introduction: Infertility and low fertility rate in the ectopic fertilization cycle can be due to the condition and level of hormonal levels caused by ovulation stimulation methods, which in cases of reduced ovarian reserve, the follicular response to gonadotropin stimulation is also reduced and few eggs will be produced. The present study aimed to investigate the predictive effect of follicle stimulating hormone (FSH) and number of antral follicles in infertile women before IVF on ovarian response and pregnancy success rate.

Methods: This cross-sectional study (descriptive-analytical) was conducted in ۲۰۲۰-۲۰۲۲ on ۸۰ infertile women treated with ART infertility treatment, referring to the infertility center of Razavi Hospital in Mashhad. First, the levels of AMH, FSH, CBC, LFT, TFT, Ur, Cr, and Prolactin were measured and vaginal ultrasound was done to determine the number of antral follicles (AFC) and the number of gonadotropin ampoules needed was determined and recorded in the file. On the ۲۰th to ۲۱st day of the cycle, the patients were subjected to imitation transfer and GnRH ampoules were injected. By visiting again on the second day of menstruation, gonadotropin was injected. From the ٦th day of injection onwards, ultrasound was performed every other day to see at least ۲ follicles of ۱۷ to ۱۸ mm. ۵ to ۱۰ thousand hCG units were injected depending on the number of follicles, and then ۳٦ to ٤۰ hours later, ovulation was first performed and then for IVF patients. Data analysis was done using SPSS version ۲٦ statistical software and chi-square tests, Fisher's exact test, one-way analysis of variance and Pearson correlation. A p value of less than ۰,۰۵ was considered significant.

Results: According to the ultrasound performed, the average number of antral follicles (follicles less than ۱۰ mm) before treatment was ٤,٤۳±٤,۱۷. On average, the number of oocytes after treatment in patients was ۳,۰۹±۳,۱۷. The average βHCG hormone at the end of treatment and ۱٦ days after embryo transfer was ۹٤,۷۹±۲٦۵,۸٦ pmol/dL. FSH was ٦,۸۱±٤,۵٤ pmol/dL.

Conclusion: There was no difference in the amount of these hormones in women with positive and negative ovarian response, but there was a significant difference in pregnancy and pregnancy with positive outcome.

Keywords: Antral follicles, ectopic fertilization, infertility, follicle stimulating hormone

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Investigating the relationship between SNP rsV٤٥٦٦٦ and miRNA hsa-mir-٣٦١٥ in the pathogenesis of liver cancer (Research Paper)

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Introduction: Liver cancer, particularly hepatocellular carcinoma (HCC), is one of the most common and deadliest forms of cancer worldwide. Various factors including viral infections, environmental toxins, and genetic elements play a role in the development of this disease. In this study, we have explored the role of the OIT٣ gene and its association with miRNA hsa-mir-٣٦١٥, SNP rsV٤٥٦٦٦, and LNC FAMV٨B-AS١ in the progression of HCC.

Methods: Gene expression data were extracted from the GEO database with the identifier GSE: ١٣٦٢٤٧. Bioinformatic analyses were conducted to identify gene expression patterns and their correlation with disease progression. Additionally, the impact of SNP rsV٤٥٦٦٦ on the expression of the OIT٣ gene and its interaction with miRNA hsa-mir-٣٦١٥ and LNC FAMV٨B-AS١ was examined. miRNA and snp were obtained from miRNASNP v٣ database. And LncRRIsearch and genecards were used to obtain lnc.

Results: Findings indicated that the OIT٣ gene is significantly downregulated in HCC samples compared to normal levels. The SNP rsV٤٥٦٦٦ was associated with the reduced expression of OIT٣, and this downregulation may occur through interaction with miRNA hsa-mir-٣٦١٥ and LNC FAMV٨B-AS١. These findings highlight the important role of these molecules in gene regulation and the progression of HCC.

Conclusion: Our study suggests that OIT٣ could serve as a biomarker for the diagnosis and prognosis of HCC progression. Furthermore, interactions between SNP rsV٤٥٦٦٦, miRNA hsa-mir-٣٦١٥, and LNC FAMV٨B-AS١ could be considered as new targets for targeted therapies. These insights could contribute to the development of novel therapeutic approaches for HCC.

Keywords: liver cancer, SNP rsV٤٥٦٦٦ , LNC FAMV٨B-AS١ ,miRNA hsa-mir-٣٦١٥

Investigating the role of environmental microorganisms , biological and chemical agents in the control of fascioliasis: A review article (Review)

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Introduction: Fascioliasis, an important parasitic disease caused by liver fluke species of the genus Fasciola, significantly impacts both human and animal health. This disease causes considerable economic losses in the livestock industry and poses a threat to public health. The life cycle of Fasciola species is complex and involves both definitive and intermediate hosts. Adult flukes reside in the bile ducts of definitive hosts, primarily ruminants and occasionally humans. Eggs are shed in feces and develop in freshwater environments. Miracidia hatch from the eggs and infect suitable snail intermediate hosts, typically of the family Lymnaeidae. Within the snail, the parasite undergoes asexual reproduction, eventually producing cercariae that encyst on aquatic vegetation as metacercariae. Infection occurs when definitive hosts ingest these metacercariae. Over the past decade, extensive research has been conducted on controlling this parasite using environmental and chemical methods.

Methods: For this review article, a comprehensive literature search was performed across several electronic databases, including PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar. The search focused on identifying studies published between ٢٠١٠ and ٢٠٢٤, with an emphasis on research investigating the role of environmental microorganisms, biological agents, and chemical interventions in the control of fascioliasis. Key search terms such as "Fasciola," "biological control," "environmental microorganisms," "chemical agents," and "parasite management" were used to ensure broad coverage of relevant literature. Special attention was given to studies that explored the interactions between parasites and environmental factors, with a particular focus on biological control methods.

Results: Actinomycetes are recognized as significant natural bacteria due to their wide range of biological activities. These activities include parasitism and the production of bioactive compounds such as toxins, antibiotics, and enzymes. They can synergistically affect parasites by either directly inhibiting their growth or enhancing the activity of microbial antagonists, thereby contributing to the suppression of the parasite population. A study demonstrated that Streptomyces griseolus, isolated from Egyptian soil, exhibits strong biocontrol effects against Fasciola gigantica eggs. These findings suggest that S. griseolus has high potential for use as a biological control agent against this helminth. Research indicates that probiotics such as Lactobacillus casei, enhances the innate immune system in various animal species when administered orally or intraperitoneally. This enhancement leads to improved acquired immunity.These findings suggest that the use of beneficial microorganisms could be a promising strategy for the biological control of fascioliasis. Also, in a study, it was shown that Fasciola hepatica infection in school-aged children from Peru leads to significant changes in the

composition of the gut microbiota. Specifically, the study found that bacterial genera such as Lactobacillus, Bacteroides, Clostridium, and Bifidobacterium were significantly less prevalent in children infected with F. hepatica compared to those who were not infected.Researchers conducted a study to examine the activity of serine proteases in F.hepatica miracidia and the results revealed that serine protease activity in miracidia was effectively inhibited by both chemical inhibitors (such as phenylmethylsulfonyl fluoride and pepstatin) and herbal inhibitors (like soybean Bowman-Birk inhibitor). These findings suggest that the use of protease inhibitors, particularly herbal ones, may be a promising approach for controlling the life cycle of F.hepatica.

Conclusion: This review demonstrates that significant progress has been made over the past decade in using environmental microorganisms and chemical agents to control Fasciola species. The research highlights the potential of various biological control methods, including the use of Actinomycetes like Streptomyces griseolus, probiotics such as Lactobacillus casei, and the manipulation of gut microbiota. These approaches show promise in enhancing host immunity and directly inhibiting parasite growth. Additionally, the study of serine proteases in F. hepatica miracidia has opened new avenues for intervention, with both chemical and herbal inhibitors showing efficacy in disrupting the parasite's life cycle. These findings suggest that a multi-faceted approach, combining biological control methods with targeted chemical interventions, may offer the most effective strategy for managing fascioliasis. However, while these advancements are encouraging, further research is crucial to address existing challenges and develop sustainable, long-term solutions.

Keywords: fascioliasis, environmental microorganisms, biocontrol, Actinomycetes

Investigating the role of menstrual blood stem cells in differentiating the expression of inflammatory and stem genes: indicators for the diagnosis and treatment of endometriosis

(Review)

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Introduction: From a scientific point of view, a stem cell is a non-specialized cell that has unlimited self-replication and the ability to differentiate into different types of cells. It is present in the menstrual environment. These cells have the stem cells of cord blood and brain and can cause damage. They are easily available and can be collected every month without the use of drugs or invasive procedures. They have potential for treating diseases such as prostate cancer, skin ulcers, infertility in old age, uterine adhesions, endometriosis, etc. Endometriosis is a condition in which endometrial glands and uterine stroma grow outside the uterine lining (endometrium) and uterine muscle. This tissue can occur in all tissues of the body except the spleen, but the most common location, occurring in ٥٠٪ of cases, is the pelvis, particularly the ovaries. Menstruation in this environment can lead to the formation of chocolate cysts or endometriomas. The most common symptoms include regular monthly pain, infertility, and chronic pelvic pain. The cause of endometriosis is still unknown, but studies have shown that differences in the expression of certain genes in menstrual blood cells may contribute to the development of this disease. The purpose of this study is to investigate the differences in the expression of inflammatory genes (IL-١β, COX-٢,TNF-α), angiogenesis (VEGF), surface markers (CD١٠, CD٩, ER-α (Estrogen Receptor)), stemness genes (OCT٤, NANOG, and SOX٢), and genes related to apoptosis (BAX and BCL-٢) in the menstrual blood- derived mesenchymal stem cells of endometriosis patients (E-MenSCs) and healthy women, as well as to explore the use of NE-MenSCs (non-endometriosis derived mesenchymal stem cells) for early diagnosis and treatment of endometriosis.

Methods: Samples were taken from the menstrual blood of healthy and diseased women, and the menstrual blood of healthy women was also used to create a conditioned medium (CM) with stem cells (NE-MenSCs). Q-PCR and real-time flow cytometry experiments were used to investigate the differences in the expression levels of inflammatory genes, angiogenesis, surface markers, stemness genes and genes involved in apoptosis.

Results: The results obtained from real-time qPCR and flow cytometry tests showed that E-MenSCs have high cell proliferation, and the ratio of the BAX gene effective in apoptosis to the anti-apoptotic gene BCL-٢ is lower compared to NE-MenSCs. In relation to surface marker genes, the expression level of CD٩ was low compared to NE-MenSCS, while the expression level of ER-α and VEGF in E-MenSCs was higher than NE-MenSCs. Also, the expression level of CD١٠, which is an effective marker in the diagnosis of endometriosis, was higher in E-MenSCs, and significantly decreased after treatment with CM.. In addition, the inflammatory genes IL-١β and COX٢, which had a higher

expression in E-MenSCs, decreased in expression by ٣٤,٤٦٪ and ٥,٣٪, respectively, after CM treatment. However, TNF-α, which had a low expression in E-MenSCs, had a significant increase in expression after CM treatment. The stemness genes OCT٤ and NANOG, which had low expression in E-MenSCs, increased their expression by ٥٢,٨٪ and ١٨,٥٣٪ respectively after treatment with CM, while SOX٢ with high expression in E-MenSCs decreased by ٦٤٪ after treatment with CM.

Conclusion: The investigation in this study showed that the use of conditioned medium (CM) derived from NE-MenSCs can have a positive effect on the expression of inflammatory genes, angiogenesi, stemness, and surface markers, as well as genes involved in apoptosis. However, further research and extensive testing are needed to fully understand the therapeutic potential of menstrual blood stem cells for the treatment of endometriosis.

Keywords: Endometriosis, Mesenchymal stem cells, Conditioned medium, Stemness genes, Inflammatory genes

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Investigating the therapeutic effects of Sotorasib on brain metastases in patients with Non-small cell lung cancer (Review)

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Introduction: Brain metastases affect approximately ٢٥-٥٠٪ of non-small cell lung cancer (NSCLC) patients, significantly worsening prognosis and severely limiting treatment options. Sotorasib, a targeted therapy specifically developed for NSCLC with KRAS G١٢C mutations, has shown promising results in treating brain metastases, In this group of patients. KRAS mutations are among the most common oncogenic drivers in NSCLC, with the G١٢C variant being notably prevalent. Sotorasib works by irreversibly inhibiting the KRAS G١٢C protein, effectively blocking the signaling pathways that drive tumor growth and survival. This mechanism is particularly crucial for patients with brain metastases, where conventional therapies like chemotherapy often fail due to the blood-brain barrier.

Methods: Clinical trials, notably the CodeBreaK studies, have provided critical insights into the efficacy of sotorasib in patients with KRAS G١٢C-mutated NSCLC, including those with stable brain metastases. In this study, we evaluated the impact of sotorasib on the treatment of brain metastases in patients with KRAS G١٢C-mutated lung cancer, based on the latest research findings. Also, we explored the challenges and future prospects associated with this therapeutic approach.

Results: Studies have demonstrated that sotorasib can achieve intracranial activity, with some patients experiencing significant tumor reduction in the brain. While challenges remain, particularly in achieving complete responses in the brain, current evidence supports the continued investigation and use of sotorasib as part of a comprehensive treatment strategy for these patients.

Conclusion: Results showed the development of sotorasib can be a significant advancement, especially for treatment of brain metastases in NSCLC patients with KRAS G١٢C mutations, who have historically had limited therapeutic options.

Keywords: Non-small cell lung cancer, Brain metastases, Sotorasib, KRAS mutations, G١٢C variant.

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Investigation of BIRC٥ expression in colorectal cancer (Research Paper)

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٢.
٣.

Introduction: Colorectal cancer (CRC) is the third most common cancer worldwide, accounting for approximately ١٠٪ of all cancer cases and is the second leading cause of cancer-related deaths worldwide. Therefore, it is necessary to discover more effective therapeutic targets and diagnostic/prognostic biomarkers in this cancer. The oncogenic role of BIRC٥ in various cancers such as breast, lung, and gastric cancers has been identified. On the other hand, bioinformatics studies showed that BIRC٥ may be up-regulated in CRC. For this reason, the aim of this study was investigation of BIRC٥ expression in colorectal tissue samples and evaluation of its potential as therapeutic target and diagnostic biomarker in this cancer.

Methods: The colorectal tumor samples and adjacent normal tissue samples were collected from thirty patients. After total RNA extraction from samples and cDNA synthesis, Real-time PCR was used to measure the BIRC٥ expression. Paired t-test was used for comparison of BIRC٥ expression in tumor and normal samples and receiver operating curve (ROC) was used to assess the diagnostic value of BIRC٥.

Results: The qPCR results showed that the expression of BIRC٥ was up-regulated in thirty paired colorectal cancer specimens (logFC= ٣,٥٠٢, p-value= ٠,٠٠٠٢). The AUC of ROC curve was ٠,٨٤ (p-value=٠,٠٠٠٣) and revealed that the expression level of BIRC٥ can detect up to ٨٤٪ of cases of colorectal cancer and can be used as a diagnostic biomarker.

Conclusion: BIRC٥ may acts as an oncogene in the CRC and may be have important role in CRC progression and metastasis. This is suggested that the potential of this gene as a therapeutic target and biomarker in the different stages of CRC is evaluated in the large populations.

Keywords: BIRC٥ , colorectal cancer, cancer progression, cancer metastasis, qPCR

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Investigation of acute toxicity and abnormality of reproductive system by cisplatin in rat (Research Paper)

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Introduction: Infertility is defined as the inability to achieve pregnancy after one year of unprotected sex. Male infertility is the main cause of this issue and various factors such as hormonal imbalance, genetic factors and environmental factors play a role in it. Exposure to a variety of drugs, including chemotherapy drugs, has been linked to male fertility problems, including infertility and reproductive disorders. Cisplatin is a very effective chemotherapy drug used to treat most solid tumors. But one of its side effects is testicular poisoning, which can lead to fertility abnormalities. This study examines the effects of cisplatin toxicity in Wistar rat infertility and highlights the potential risks associated with exposure to chemotherapy drugs and the need for greater attention to drugs in reproductive health.

Methods: In this study, ٣٦ adult male Wistar rats weighing about ٢٠٠ to ٣٥٠ grams were obtained from the animal house of Mashhad University of Medical Sciences. The animals had free access to food and water during the study. Then the animals were randomly assigned to ٣ groups of ١٢ were divided and were dosed for ١٤ days. They were randomly divided into three groups of ١٢ each. The first group of the control group received normal saline intraperitoneally with a dose of ٤ mg/kg, the second group received cisplatin with a dose of ٤ mg/kg intraperitoneally. was injected and the third group of cisplatin group was injected intraperitoneally with a dose of ٧mg/kg.After ١٤ days, rats were anesthetized and sacrificed with carbon dioxide for weighing and tissue sampling, and after that, testis, seminal vesicle, epididymis, vas deferens and prostate tissues were separated.

Results: After ١٤ days of cisplatin injection with a dose of ٤mg/kg and a dose of ٧ mg/kg, which were under dose monitoring, the dose of ٤ mg/kg did not cause abnormalities, but we came to the conclusion that the injection of a dose of ٧ mg/kg caused necrosis and Damage to the seminiferous tubules also caused a decrease in the index of the testis, seminal vesicle, epididymis, vas deferens and prostate.

Conclusion: Studies have shown that chemotherapy drugs such as cisplatin can cause atrophy of the reproductive organs as well as abnormality of testicular germ cells including spermatogonial cells and spermatids, and by producing free radicals, oxidative stress and DNA damage, it causes abnormality of the reproductive system.

Keywords: reproductive system_rat _Cisplatin

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Investigation of adenosine deaminase deficiency and its relationship with Mycobacterium tuberculosis (TB) (Review)

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Introduction: An autosomal recessive disorder is adenosine deaminase ٢ (DADA٢) deficiency, a monogenic disease caused by mutations in the ADA gene, first described in ٢٠١٤. This gene is used to diagnose tuberculosis in humans and animals. Adenosine deaminase (ADA) is also a useful biomarker for the diagnosis of tuberculous pleuritis (TBP). Adenosine deaminase (ADA) deficiency is an inherited disorder that damages the immune system and causes severe combined immunodeficiency (SCID).People with SCID lack nearly all immune protection against bacteria, viruses, and fungi.

Methods: During a research in ٢٠٢٠; Patients with DADA٢ who presented with pure red blood cell aplasia or bone marrow failure had frequent infections, hepatosplenomegaly and gingivitis. Patients with DADA٢ vasculitis, patients with pure red cell aplasia, and BMF are largely resistant to TNF inhibitors. Pure erythrocyte aplasia and BMF were associated with missense mutations with minimal residual enzyme activity, leading to complete loss of function. During a ٢٠٢٢ study, pediatric pleural tuberculosis, a paucibacillary disease, was diagnosed by the ADA with relatively high sensitivity and low specificity.

Results: In recent years, it is said that these people suffer from frequent infections as well as stroke and sometimes anemia as well as tuberculosis (mycobacterium tuberculosis). In general, the body of affected people is not able to preserve and maintain lymphocytes, especially lymphocytes (T group of white blood cells that play a very important role in fighting microbes) and the goal of gene therapy in adenosine deaminase deficiency, Empowering the body to produce. And the effective preservation of lymphocytes has entered the field of root treatment of this disease. During this method, by using gene therapy methods, defective ADA genes can be replaced with healthy genes.

Conclusion: During a ٢٠٢٢ study, pediatric pleural tuberculosis, a paucibacillary disease, was diagnosed by the ADA with relatively high sensitivity and low specificity.During a ٢٠٢٢ study, pediatric pleural tuberculosis, a paucibacillary disease, was diagnosed by the ADA with relatively high sensitivity and low specificity.

Keywords: Adenosine deaminase, Mycobacterium tuberculosis, gene, gene defect

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Investigation of KIFC١ expression in gastric cancer (Research Paper)

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Introduction: Gastric cancer is the one most common cancer in the world. In most cases, the disease is diagnosed at a stage when common therapies do not have a significant impact on the patient's life. Therefore, the need to study effective molecular mechanisms to introduce molecular markers for rapid detection of prognosis is strongly felt. KIFC١ is overexpressed in various cancers including breast, liver, bladder and ovarian cancers. According to the bioinformatics studies, KIFC١ may be oncogenic gene in gastric cancer. For this reason, the aim of this study was investigation of KIFC١expression in stomach tissue samples and evaluation of its potential as therapeutic target and diagnostic biomarker in this cancer.

Methods: The gastric tumor samples and adjacent normal tissue samples were collected from thirty patients. After total RNA extraction from samples and cDNA synthesis, Real-time PCR was used to measure the KIFC١ expression. Paired t-test was used for comparison of KIFC١ expression in tumor and normal samples and receiver operating curve (ROC) was used to assess the diagnostic value of KIFC١.

Results: The qPCR results showed that the expression of KIFC١ was up-regulated in thirty paired gastric cancer specimens (LogFC=٤,٥, p-value = ٠,٠٠٠١). The AUC of ROC curve was ٠,٩ (p-value=٠,٠٠٠١) and revealed that the expression level of KIFC١ can detect up to ٩٠٪ of cases of gastric cancer and can be used as a diagnostic biomarker.

Conclusion: Finally, the authors suggest that the considerably up-regulation of KIFC١ in gastric tumor samples and its potential as biomarker highlight the need to further investigation of this lncRNA in larger population and cohort studies.

Keywords: KIFC١, Gastric cancer, cancer progression, cancer metastasis, qPCR

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Investigation of LINC۰۱۰۱۲ expression in colorectal cancer (Research Paper)

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Introduction: Colorectal cancer (CRC) is the third most common cancer worldwide, accounting for approximately ۱۰٪ of all cancer cases and is the second leading cause of cancer-related deaths worldwide. LncRNAs involved in the tumor formation, angiogenesis, proliferation, migration, and etc. The oncogenic role of LINC۰۱۰۱۲ in various cancers such as cervical cancer has been identified. On the other hand, bioinformatics studies showed that LINC۰۱۰۱۲ may be up-regulated in CRC. For this reason, the aim of this study was investigation of LINC۰۱۰۱۲ expression in colorectal tissue samples and evaluation of its potential as therapeutic target and diagnostic biomarker in this cancer for first time.

Methods: The colorectal tumor samples and adjacent normal tissue samples were collected from thirty patients. After total RNA extraction from samples and cDNA synthesis, Real-time PCR was used to measure the LINC۰۱۰۱۲ expression. Paired t-test was used for comparison of LINC۰۱۰۱۲ expression in tumor and normal samples and receiver operating curve (ROC) was used to assess the diagnostic value of LINC۰۱۰۱۲.

Results: The qPCR results showed that the expression of LINC۰۱۰۱۲ was up-regulated in thirty paired colorectal cancer specimens (logFC= ۲,٦۹٤, p-value= ۰,۰۰۵۹). The AUC of ROC curve was ۰,۷ (p-value=۰,۰۱۸) and revealed that the expression level of LINC۰۱۰۱۲ can detect up to ۷۰٪ of cases of colorectal cancer and can be used as a diagnostic biomarker.

Conclusion: LINC۰۱۰۱۲ may acts as an oncogene in the CRC and may be have important role in CRC progression and metastasis. This is suggested that the potential of this LncRNA as a therapeutic target and biomarker in the different stages of CRC is evaluated in the large populations.

Keywords: Linc۰۱۰۱۲, colorectal cancer, cancer progression, cancer metastasis, qPCR

Investigation of LINC٠١٤٨٤ expression in gastric cancer (Research Paper)

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Introduction: Gastric cancer is the one most common cancer in the world. In most cases, the disease is diagnosed at a stage when common therapies do not have a significant impact on the patient's life. Therefore, the need to study effective molecular mechanisms to introduce molecular markers for rapid detection of prognosis is strongly felt. Long intergenic noncoding RNAs (lincRNAs) are of paramount importance in the underlying molecular mechanisms of cancer initiation and progression. They can be used as molecular biomarkers to diagnose and track disease progression or as therapeutic targets. The oncogenic role of LINC٠١٤٨٤ in various cancers such as bladder urothelial carcinoma has been identified. According to the bioinformatics studies, LINC٠١٤٨٤ may be involved in the gastric progression and metastasis. For this reason, the aim of this study was investigation of LINC٠١٤٨٤ expression in stomach tissue samples and evaluation of its potential as diagnostic biomarker in this cancer for first time.

Methods: The gastric tumor samples and adjacent normal tissue samples were collected from thirty patients. After total RNA extraction from samples and cDNA synthesis, Real-time PCR was used to measure the LINC٠١٤٨٤ expression. Paired t-test was used for comparison of LINC٠١٤٨٤ expression in tumor and normal samples and receiver operating curve (ROC) was used to assess the diagnostic value of LINC٠١٤٨٤.

Results: The qPCR results showed that the expression of LINC٠١٤٨٤ was up-regulated in thirty paired gastric cancer specimens (LogFC=٢,٣٩٩, p-value = ٠,٠١٦٨). The AUC of ROC curve was ٠,٧ (p-value=٠,٠١٦) and revealed that the expression level of LINC٠١٤٨٤ can detect up to ٧٠٪ of cases of gastric cancer and can be used as a diagnostic biomarker.

Conclusion: Finally, the authors suggest that the considerably up-regulation of LINC٠١٤٨٤ in gastric tumor samples and its potential as biomarker highlight the need to further investigation of this lncRNA in larger population and cohort studies.

Keywords: LINC٠١٤٨٤, Gastric cancer, cancer progression, cancer metastasis, qPCR

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Investigation of phenotypic and genotypic resistance to aminoglycosides in clinical isolates of Staphylococcus aureus. (Research Paper)

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Introduction: Staphylococcus aureus is known as a nosocomial pathogen capable of causing a wide range of infections, from a simple skin infection to fatal necrotizing pneumonia, osteomyelitis, food poisoning, urinary tract infections, scaly skin syndrome, and toxic shock syndrome. This bacterium has a high ability to gain resistance to various antimicrobial agents. This has caused the spread of infections caused by this bacterium and also the occurrence of problems such as increased mortality, increased length of hospitalization of patients in hospitals, and increased treatment costs, which makes doctors treat infections caused by Staphylococcus aureus limited have faced many.

Methods: Bacterial sampling and isolation Clinical isolates of Staphylococcus aureus were collected from blood, urine, joint fluid, sputum, wound, and abscess samples of patients referred to Rasht medical diagnostic laboratories and confirmed by culture and biochemical tests to identify the bacteria. To determine the antibiotic sensitivity of clinical isolates of Staphylococcus aureus to aminoglycosides, an antibiogram test was performed by diffusion method . Molecular identification and frequency of resistance genes Genomic DNA extraction of Staphylococcus isolates was done using a Cinagen DNA extraction kit (Cat. No. PR٨٨١٦١٤). To confirm the diagnosis of Staphylococcus aureus isolates, a pair of specific ٢٣SrRNA primers and to identify resistance genes were used using the specific primers of the aac(٦')-Ie-aph(٢") and aph(٣')-IIIa genes.

Results: Determination of antibiotic resistance of isolates In this study, ٥٠ isolates of Staphylococcus aureus were identified. ٨٩,٣٨٪ of samples were resistant to kanamycin and ٧٠,٢٨٪ of samples were resistant to gentamicin. In examining the MIC of gentamicin in ٢٠ isolates, ٥٪ of the samples had an MIC of ٢٥٠ µg/ml, ٣٥٪ of the samples had an MIC of ١٠٠٠ µg/ml, and ٦٠٪ of the samples had an MIC of ٢٠٠٠ µg/ml. Frequency of aac(٦')-Ie-aph(٢") and aph(٣')-IIIa genes In the genotypic study, the frequency of aac(٦')-Ie-aph(٢") gene was ٧٠٪, and the frequency of aph(٣')-IIIa gene was ٩٣٪. Except for ١١ isolates, both genes were the same in the rest.

Conclusion: Aminoglycosides are powerful bactericidal agents that are often used in combination with beta-lactams or glycopeptides in the treatment of staphylococcal infections. In this study, out of ٥٠ drug-resistant isolates, ٨٧,٢٪ were resistant to kanamycin, ٧٤,٥٪ were resistant to gentamicin, and the MIC of gentamicin was high in resistant isolates. In the present study, the frequency of aminoglycoside modifying genes including aph(٣)-IIIa and aac(٦)-Ie-aph(٢)-I in ٣١ resistant strains was investigated by PCR. In this study, in ٣١ isolates with resistant phenotype, the frequency of aac(٦)-Ie-aph(٢)-I gene was ٧٠٪ and the frequency of aph(٣)-IIIa gene was ٩٣٪. In the study of Rayos et al., ٢٠١٦ in Madrid, Spain, in ٥٥ isolates of Staphylococcus aureus resistant to methicillin, the most common aminoglycoside modifying genes were aac(٦')Ie-aph(٢")Ia (٨٧,٣٪) and followed by It

was ant(٤')Ia (٥٢,٧٪) and aph(٣")IIIa (٥٢,٧٪) .(٣٦) During the study of Ghaznavi Rad et al. (٢٠١٢) in Arak, out of ٩٨ cases of Staphylococcus aureus isolated from clinical samples, ٧٧,٣٪ of the isolates had the acc(٦')/aph(٢") gene and ١٦,٩٪ The samples had aph(٣')-IIIa gene and ١,٨٪ of isolates had ant(٤')-Ia gene. Also, ١٦,٩٪ of isolates had both aac(٦')/aph(٢') genes. and aph(٣')-IIIa and ١,٨٪ of the isolates had all three genes . The results show high resistance to aminoglycosides in Staphylococcus aureus strains, and high presence of aminoglycoside modifying genes aac(٦')/aph(٢') and aph(٣')-IIIa.

Keywords: S. aureus, aminoglycosides, aac(٦’)-Ie-aph(٢”) and aph(٣’)-IIIa genes

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Investigation of PNLDC۱ gene polymorphism as a risk model of gene signature in predicting platinum response and survival in ovarian cancer (Research Paper)

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Introduction: Introduction: Ovarian cancer is one of the most deadly cancers of women, which is considered as one of the most important causes of global mortality worldwide. Currently, one of the most important treatment challenges in this category of patients is the identification of people at risk without clinical symptoms, which can play an important role in increasing the survival of these patients. Therefore, the use of biomarkers can be a potential indicator in identifying platinum treatment response and help in clinical decisions and improve prognosis

Methods: Materials and methods: In this study, ۵۰ tissue samples from patients with ovarian cancer after chemotherapy and platinum-based treatment were examined and confirmed by a pathologist. Also, ۵۰ healthy tissue samples were selected as the control group. Then, DNA of the samples was extracted using a special kit, and polymorphism of PNLDC۱ gene was analyzed using Tetra-ARMS PCR technique.

Results: Findings: Among the patients, ۱۹ cases (۳۸٪) had bilateral involvement and ۳۱ cases (۶۲٪) had unilateral involvement. Also, among ۳۱ patients with unilateral involvement, ۱۷ cases (۵۵٪) had right-sided involvement and ۱٤ cases (٤۵٪) had left-sided involvement. Among the ۱٤ patients with involvement on the left side of the body, ۳ (۲۱٪) patients had polymorphisms in the PNLDC۱ gene. Among ۱۷ patients with involvement on the right side of the body, ۵ (۲۹٪) patients had polymorphism in PNLDC۱ gene. Among the ۱۹ patients with involvement on the left side of the body, ۳ (۱۶٪) patients had polymorphisms in the PNLDC۱ gene. There was a no significant relationship between polymorphism in PNLDC۱ gene and ovarian cancer disease. According to the results and statistical analysis, there was no relationship between the PNLDC۱ gene polymorphism as a risk of the gene signature model in predicting survival and platinum response.

Conclusion: Conclusion: The present study showed that PNLDC۱ gene polymorphism is not associated with ovarian cancer and cannot be used as a biomarker. However, for a better understanding of the relationship between these polymorphisms and the risk of ovarian cancer, more studies with a larger sample size on other races, ethnicities and geographical regions are needed.

Keywords: Keywords: ovarian cancer, biomarkers, platinum, PNLDC۱, polymorphism

Investigation of puberty and intellectual maturity in Iranian with Down syndrome: specifying targets for intervention (Research Paper)

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Introduction: Research suggests that adolescents with Down syndrome experience the same physical and hormonal changes that occur in other people during puberty, the only minor differences observed are the puberty age of boys and the reproductive period of girls, that is, these people also reach puberty like other . Only the social maturity, social communication and self-control in these are delayed and need support from the families. It is important that the expression of sexual feelings by these people is accepted by the family and society, and let's accept that according to their age, have sexual feelings and needs. They are like normal people and they need sex education at puberty and they want to live independently and start a family like other people. Children with DS are just as motivated as all other children to explore, learn, and gain independence for life, despite their limitations in cognitive and adaptive functioning and failure to meet developmental and sociocultural standards for personal independence and social responsibility. The primary aim of this study was to investigate physical and sexual, intellectual maturity in a sample of iranian adolescents with Down syndrome using two widely-used Tanner's physical maturity test and Neo's intellectual maturity test.

Methods: The study was conducted on Iranian with Down syndrome with medical records at Aria Beheshtian Association and People with Down syndrome referred to Valiasr Bomehen Health Center, a total of ٣٠ females and ٣٠ males in two age groups of ١٤ to ١٨ years (١٠ girls and ١٠ boys) to investigate the physical and sexual maturation process according to Tanner criteria. The group of ١٩ to ٤٠ years (٢٠ girls and ٢٠ boys) to investigate intellectual maturity with the principle that intellectual and psychological maturity occurs throughout life and specifically, adaptive growth from late adolescence to the years before death. Sampling was purposefully selected from people with Down syndrome who were educable and had the ability to read and write, memorize poetry, and sports and art skills (in order to be able to read and understand Neo questionnaires). Then the test results of the two groups of case and control were compared in different aspects of personality, including the degree of extroversion or introversion, compatibility and emotional stability, interactions and social communication and feeling of sympathy with others, aesthetics, duties and managing one's. The structural equation modeling method was used to analyze the data and data were processed using SPSS ٢٣ software and Cronbach's alpha and correlation index. In order to comply with the ethical charter of the research, only people who themselves and their parents were volunteers and willing to participate in the research were used.

Results: In clinical examinations, according to Tanner's criteria, physical and sexual maturity in people with Down syndrome was similar to the control group, and physical manifestations and expression of sexual needs were observed in both groups. Therefore, the sexual needs and necessary education during puberty for people with Down syndrome should be considered and accepted by the family and society. On the other hand, the results of the NEO test showed that people with Down syndrome were able to answer all the questions in the field of neuroticism, extroversion and conscientiousness, although they needed more time to answer and sometimes the guidance of a consultant, but in the field Being open to experience and adaptability, despite the consultant's guidance and enough time, they could not answer all the questions. These results show that the support of parents and society for people with Down syndrome is a constant need.

Conclusion: Today, with the increase in life expectancy and longevity of people with Down syndrome as a result of advanced health care and treatment, improving the knowledge and attitude of society about the physical, sexual and intellectual maturity of people with Down syndrome will help to improve their quality of life in the future.

Keywords: Down syndrome, puberty, intellectual maturity, sexual feelings, knowledge and attitude of society

Investigation of surface modification on the size and zeta potential of PLGA nanoparticles

(Research Paper)

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Introduction: There is a huge emergence using nanoparticles in novel drug delivery platforms and polymeric nanoparticles are the second most popular type of nanostructures. PLGA (poly(lactic-co-glycolic acid)) is a kind of highly studied synthetic polymer because of its biodegradability, biocompatibility, and extended drug release. Besides the nature of polymeric structures, their surface, size, and zeta potential play important roles in the efficient delivery of nano-carriers and their bio-fate . In this study, we aimed to tune the surface of PLGA nanoparticles with substances such as PVA, poloxamer١٨٨, poloxamer٤٠٧, tween٢٠, and tween٨٠ at different ratios and investigate the nanoparticle's mean diameter and zeta potential.

Methods: Nanoparticles were prepared using precipitation and single-emulsion techniques. ٣٠ mg of PLGA was dissolved in ٣ ml of acetone or dichloromethane and added to the ٣٠ ml water-based phase. The size and zeta potential of nanoparticles were analyzed by DLS, SEM, and zeta analyzer, respectively.

Results: The mean diameter and zeta potential of Tween٨٠ and tween٢٠ coated nanoparticles were varied from ٢٢٥-٣٠٠ nm, ١٧٠-٦١٠ nm, and -١٠ to -٢١ mV, and -١٣ to -١٨ mV, respectively. Poloxamer١٨٨ and poloxamer٤٠٧ coated nanoparticles had mean sizes of ٢٣٠-٤٠١ nm and ١٤٨-٣٥٨ nm, respectively. Moreover, their zeta potential varied from -١٢ to -١٩ mV and -١٢ to -١٦ mV, respectively.

Conclusion: According to the results of our study, it was observed that there is an optimum concentration of surfactants for achieving superior size and zeta potential of nanoparticles.

Keywords: Nanoparticle; PLGA; PVA; Tween; Poloxamer.

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Investigation of THAP۷ and GTF۳A genes in glioblastoma cancer in U۸۷ cell line (Review)

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Introduction: Glioblastoma multiforme is the most common and aggressive primary tumor in the adult brain. This tumor is formed inside the brain tissue and gradually gets bigger and penetrates the surrounding tissues. Despite years of research and numerous clinical trials, survival is still poor. In this study, using integrated bioinformatics analysis, the most important transcription factors were selected in the first step, and then the expression of the genes obtained from the previous step was studied at the cellular level and in the laboratory on glioblastoma cell lines.

Methods: Analysis of the GSE۷۵۱۴۷ dataset was conducted in the bioinformatics department to identify genes showing differential expression in glioblastoma. The Enrichr database was utilized to examine signaling pathways. The panther database was used to ascertain the characteristics of the genes. The STRING database was used to analyze protein-protein interactions, while the X۲K web database was used to analyze transcription factors and kinases. In conclusion, THAP۷ and GTF۳A genes were chosen for experimental confirmation in the laboratory. Cell lines U۸۷ and HUVEC were grown in the lab. RNA was isolated and converted into cDNA. Following the design and purchase of primers, the Real-Time PCR method was used to analyze the relative gene expression.

Results: The data of laboratory studies revealed that the THAP۷ and GTF۳A genes were selected according to the results of bioinformatics analysis Relative expression of THAP۷ and GTF۳A genes in U-۸۷ cell line were significantly decreased compared to HUVEC cell line.

Conclusion: The results of this study determined THAP۷ and GTF۳A genes in glioblastoma cell lines can be considered as potential tumor suppressors in glioblastoma cancer.

Keywords: Glioblastoma, Tumor Suppressor, Transcription Factor

Investigation of the Association Between Chlamydia trachomatis Infections and the Risk of Cervical Cancer (Research Paper)

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Introduction: Cervical cancer is one of the most common malignancies affecting women worldwide. Numerous studies have suggested a potential link between infections with Chlamydia trachomatis, a common sexually transmitted bacterium, and the development of cervical cancer. This study aims to investigate the correlation between Chlamydia trachomatis infections and the risk of cervical cancer in a specific population sample.

Methods: A cross-sectional study was conducted involving a sample size of ٥٠٠ participants, including ٤٠٠ women and ١٠٠ men, recruited from several healthcare centers. The mean age of the participants was ٣٤,٥ years. Participants underwent screening for Chlamydia trachomatis infection using polymerase chain reaction (PCR) tests, and cervical cancer risk was assessed through Pap smears and histological examinations.

Results: Out of ٤٠٠ women, ١٥٠ tested positive for Chlamydia trachomatis. Among these, ٣٠ women were diagnosed with cervical intraepithelial neoplasia (CIN), a precursor to cervical cancer, and ١٠ women were diagnosed with cervical cancer. In the group of ٢٥٠ women who tested negative for Chlamydia trachomatis, ١٥ were diagnosed with CIN and ٣ with cervical cancer. No cases of cervical cancer were detected among the men, and ٢٠ men tested positive for Chlamydia trachomatis.

Conclusion: The study found a statistically significant association between Chlamydia trachomatis infection and an increased risk of developing cervical cancer. Women infected with Chlamydia trachomatis were more likely to develop cervical intraepithelial neoplasia and cervical cancer compared to those who were not infected. These findings underscore the importance of regular screening and early detection of Chlamydia trachomatis to potentially reduce the risk of cervical cancer.

Keywords: Chlamydia trachomatis, cervical cancer, cervical intraepithelial neoplasia, cancer risk

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Investigation of the colonization rate of Staphylococcus aureus on the skin of psoriasis patients

(Research Paper)

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Introduction: Psoriasis is a lifelong inflammatory disease that involves the skin, joints, cardiovascular system, and CNS. Its outward symptoms include redness, peeling, and itching. One of the important aspects in understanding this disease is to examine the changes in the skin microbiome of psoriasis patients. Staphylococcus aureus usually exists on the skin and mucous membranes of humans, and approximately ۱۰-۲۰٪ of people carry it without symptoms. S.aureus acts as an opportunistic pathogen and contributes to the inflammatory processes associated with psoriasis by affecting the Th۱/Th۱۷ axis. The aim of this study is to investigate the colonization rate of S.aureus on the skin of patients with psoriasis compared to healthy control subjects.

Methods: This cross-sectional study was designed with the aim of investigating the colonization rate of S.aureus bacteria on the skin of patients compared to control subjects. The participants in this study included ۲۱ patients with psoriasis who visited the skin clinic of Tajrish Hospital located in Tehran. ۲۱ healthy individuals who did not have psoriasis and matched the patient group in terms of age and sex. A skin sample was taken from the forearm of a person using a sterile swab from ۵ square centimeter and inoculated into liquid BHI culture medium and incubated for ٤٨ hours at ۳۷°C. After DNA extraction by boiling method and with the help of specific primers, PCR reaction was performed to detect the presence or absence of S.aureus. The samples that were positive for the presence of S.aureus were cultured in the special mannitol salt agar culture medium after preparation of serial dilutions. The obtained data were analyzed using SPSS version ۲٦ software.

Results: In microbial cultures, ۳۸٪ (۸ out of ۲۱ patients) of the samples of psoriasis patients led to the growth of S.aureus, while this figure was only ۵,۹٪ (۲ out of ۲۱ healthy people) in the control group. The Mann-Whitney test showed that the number of S.aureus clones in the skin of patients with psoriasis was significantly higher than that of the control group ($p<۰,۰۵$). This increase in the number of clones was observed especially in the inflamed areas of the patients' skin.

Conclusion: The results showed that patients with psoriasis have significant changes in the frequency of S.aureus compared to the control group. A better understanding of the interactions of S.aureus on the skin microbiome and the immune system may lead to the development of new therapeutic strategies. This study emphasizes the importance of investigating the increase in S.aureus colonization on the skin in order to better understand the pathogenesis of psoriasis and improve the quality of life of patients.

Keywords: Psoriasis , skin microbiome ,Staphylococcus aureus, molecular detection

Investigation of the effect of Ouabain on IBD by molecular docking method (Research Paper)

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Introduction: Inflammatory bowel disease (IBD) is one of the inflammatory conditions. There are two forms of IBD: ulcerative colitis and Crohn's disease. UC is a mucosal inflammatory disease involving the rectum and colon. Crohn's disease may occur along any portion of the GI tract. IBD is associated with the activation of nuclear factors such as NF-κB, which may enhance the transcription of pro-inflammatory mediators resulting in diarrhea, abdominal pain, bleeding, and many extraintestinal symptoms. IκBα is named for the nuclear factor of kappa light polypeptide gene enhancer in B-cell inhibitor alpha; one member of a family of cellular proteins that inhibit the NF-κB transcription factor. One compound that can effect IκBα is Ouabain. Ouabain is an aglycone plant-based compound, Strophanthus gratus, utilized as a medication in traditional medicine and as poison. It finds application in treating hypotension and problems in the cardiovascular system. This study will give an overview of the binding affinity between Ouabain and IκBα.

Methods: In this research, the IκBα structure was obtained from the UniProt website, and then Obligatory changes, such as deleting ions, and water molecules, and also working on subunit A of IκBα, were performed using Chimera software. The three-dimensional structure of Ouabain was downloaded from the PubChem website. Center; X:-٣,٩٤٣٨, Y:٤٧,٦٠٢٥, Z:١٣,١٠٨٦, and Dimensions (Angstrom); X, Y, Z: ٢٥,٠٠٠٠. Finally, the molecular docking process was conducted using AutoDock Vina in PyRx ٠,٨ to assess the binding status of Ouabain to IκBα.

Results: By using PyRx software. The results are followed. For each model, the data belongs to their binding affinity, RMSD lower bound and RMSD upper bound, respectively: Model #١ : [-٧,٥, ٠,٠, ٠,٠] Model #٢ : [-٧,٤, ١٥,٠٢٧, ١٧,٢٧٢] Model #٣ : [-٧,٣, ١٤,٢٠٩, ١٨,٣١٣] Model #٤ : [-٧,٢, ١٥,٣٧٥, ١٧,٥٣٩] Model #٥ : [-٧,١, ١٤,٨٣, ١٨,٩٣٢]

Conclusion: According to the results obtained from the molecular docking of the Ouabain drug and IκBα, it was determined that according to the negative binding energy, the drug could bind well to its receptor and exert its effects, so the Ouabain drug can be a suitable drug to prevent the progress of IBD.

Keywords: Ouabain, IκBα, molecular docking, IBD, NF-κB

Investigation of the Functional Impact of Narcolepsy Type ١ including Persistent Orexin Deficiency on REM Sleep Behavior Disorder (RBD) (Review)

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Introduction: Rapid eye movement (REM) sleep behavior disorder is a REM sleep parasomnia first described in the mid-١٩٨٠s in the United States and in ١٩٩٥ in the United Kingdom. This disease is a movement control disorder due to the loss of REM-related muscle atony and is characterized by complex, intense and often violent sleep behaviors during REM sleep. This behavior can lead to damage to the patient and cause fracture, dislocation and even subdural hematoma. Clinical features during sleep include abnormal sounds, abnormal motor behavior, and changes in dream mentality. Narcolepsy is a debilitating neurological disorder characterized by instability of sleep or wakefulness states and pathological intrusion of REM sleep-related events into wakefulness. It affects approximately ١ in ٢,٠٠٠ people in the United States. Narcolepsy type ١ (NT١) is a group of sleep disorders that have benefited from great scientific advances in the last two decades. Deficiency of orexin, a neurotransmitter involved in the regulation of rapid eye movement sleep, is responsible for the main symptoms of NT١, which include: drowsiness, including cataplexy, nocturnal sleep disturbances, sleep-related hallucinations, and sleep paralysis. The onset of this disease usually occurs during adolescence. According to studies, the association of non-sleep-related symptoms, such as obesity, precocious puberty, psychiatric and cardiovascular complications, has subsequently been recognized. Diagnostic tools have improved, but sleep-onset rapid eye movement episodes in polysomnography and multiple sleep latency testing are key measures. The pathogenic mechanisms of narcolepsy type ١ have been partially elucidated after the discovery of a strong association of HLA class II and orexin or hypocretin deficiency. In addition, new technologies, such as the use of deep learning analysis of electroencephalographic signals, reveal a complex pattern of sleep abnormalities in human narcolepsy. The aim of this study is the functional impact of narcolepsy type ١ on persistent orexin deficiency in REM sleep behavior disorder (RBD).

Methods: This review study was conducted in ٢٠٢٤ by searching keywords such as: Narcolepsy type ١, Orexin Deficiency, REM, RBD in reliable databases such as: PubMed, Scopus and Web of Science.

Results: Much progress has been made since the first description of narcolepsy at the end of the ١٩th century. Today, this disease is distinguished as type ١ and type ٢ narcolepsy. The discovery that NT١ is caused by hypocretin or orexin deficiency, along with neurochemical studies of this system, has helped determine how this neuropeptide regulates sleep-wake organization in humans. Current analyzes suggest that the main functions of the hypocretin/orexin system are (١) maintaining wakefulness in the face of moderate sleep deprivation; (٢) promotion of passive wakefulness, especially in the evening, driven by the circadian clock; (٣) inhibition of REM sleep, with possible

differential modulatory effects on different components of the sleep stage, explaining REM sleep dissociation events in NT١; Narcolepsy is also associated with an inability to stabilize sleep, a more complex phenotype that may result from secondary alterations or the central role of hypocretin in coordinating the activity of other sleep-wake promoting systems. In addition, in the ١٩٦٠s, the discovery of rapid eye movement sleep at the onset of sleep led to a better understanding of the main sleep-related symptoms of this disease. This condition may be violent and lead to harm to oneself or others without any conscious awareness. After waking up, the patient can remember the contents and information of his dream. Most patients with REM behavior disorder eventually develop neurodegenerative diseases such as Parkinsonism, dementia with Lewy bodies, or multiple system atrophy. There are also secondary causes of RBD associated with Parkinsonism, narcolepsy, or the use of antidepressants. The patient may be warned about the future development of these neurological disorders. Its medicinal and therapeutic measures are also such that in severe cases, melatonin or clonazepam may be prescribed for the patient. RBD is usually idiopathic or secondary to neurological problems such as Parkinson's disease. Also, in the absence of lumbar puncture, the diagnosis based on neurophysiological tests (day and night) and the presence of cataplexy is a pathognomonic symptom.

Conclusion: Also, since orexin is a potent arousal-enhancing agent, it is reasonable to assume that orexin receptor antagonists will be effective as drugs for the treatment of insomnia. To date, several orexin receptor antagonists with different pharmacological properties have been developed.

Keywords: Narcolepsy Type ١, Orexin Deficiency, REM, RBD

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Investigation of the impact of coagulation markers in predicting mortality for severe COVID-۱۹ in hospitalized patients (Research Paper)

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Introduction: The COVID-۱۹ pandemic has created significant challenges for global healthcare systems and there is a need to fully investigate the factors that affect patient outcomes, especially in severe cases requiring special care. Therefore, studying predictive factors of mortality in patients with severe cases of this disease is of particular importance and identifying these factors can be effective in the success rate of treatment for these patients.

Methods: A descriptive-analytical, cross-sectional, and retrospective study was conducted in the intensive care unit of a hospital in Tehran city from March ۲۰۲۲ to April ۲۰۲۳. laboratory data related to coagulation factors of ۳۹۵ patients with severe COVID-۱۹ were collected. Data analysis was performed using statistical tests.

Results: The evaluated coagulation factors included platelet level, PT, INR, ferritin, D-dimer, and fibrinogen. In deceased patients, platelet levels were lower, but there was no significant difference compared to recovered patients (p=۰,۵۸۷). Although this study showed higher levels of PT and INR in deceased patients, they did not have a significant difference compared to the living group (p=۰,۱۳۲, p=۰,۲٤۸) and ferritin and D-dimer levels were significantly higher in deceased patients (p=۰,۰٤۷, p=۰,۰۵۷, p=۰,۰٤۷).

Conclusion: The systemic status of patients, including the level of some inflammatory factors, affects the mortality rate of COVID-۱۹. Appropriate interventions and preventive management strategies aimed at addressing these risk factors are essential for improving patient outcomes and can impact the quality of patient care in hospital settings.

Keywords: Covid-۱۹, mortality, risk factors

INVESTIGATION THE EFFECT OF COMMON MUTATIONS OF TRPM٨,SUGCT,UFL١-AS١ GENES IN MIGRAINE PATIENTS IN TEHRAN (Review)

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Introduction: Migraine continues second among the world's causes of disabilitymost people who have -there are ٤ types of migraine headaches: frontal, temporal, occipital and rhinogenic.Preventive therapy may also improve quality of life and prevent the progression to chronic migraines. Some indications for preventive therapy include four or more headaches a month, eight or more headache days month, debilitating headaches, and medication-overuse headaches. Migraine is a complex brain disorder that is explained by the interaction of genetic and environment factors.Genetic studies have also shown the importance of common genetic factors between migraine and diseases such as depression and high blood pressure.

Methods: Using the PCR technique and gel electrophoresis,we check the SNP sequences of TRPM٨,SUGCT and UFL١-AS١ genes.

Results: Results from twin studies show that genes play an important role for susceptibility to migraine. The propensity for migraine to run in some families but not in others arises predominantly from alleles shared by family members and not the shared family environment, and that environmental influences on migraine are unique to the affected family memberSNPs

Conclusion: This project helps us to inform the patient about the occurrence of mutations in the desired genes and the risk of developing migraines.domain ١٦(PRDM١٦) gene, the rs١٠١٦٦٩٤٢ near the transient receptor potential cation channel subfamily M member ٨ (TRPM٨) gene, However, data from subsequent studies examining the role of these variants and their relationship with migraine remain. as well as CYP٢C٩*٢ and the rs٤٣٧٩٣٦٨ mutations, have all been identified as genetic predictive risk factors of VTE in women. is within the four and a half LIM domains protein ٥ (FHL٥) gene. allele AA or AG genotype of rs١٣٢٠٨٣٢١ were associated with a reduced risk of migraine.

Keywords: Migraine,SNP,PCR,Genes

Invetigation of antimicrobial peptides drived from amphibians (Review)

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Introduction: Frog skin serves as a potent source of peptides with diverse biological properties, particularly host defense peptides that exhibit cytotoxic effects against bacteria, fungi, protozoa, viruses, and mammalian cells. Since the discovery of magainins from the skin secretions of the African frog *Xenopus laevis* by Michael Zasloff in ۱۹۸۷, numerous antimicrobial peptides (AMPs) have been identified across different frog species. These AMPs not only provide protection against harmful microorganisms but also play roles in endotoxin neutralization, chemotaxis, and wound healing. Unlike immunoglobulins, these peptides are readily accessible from frog skin glands and act quickly against various pathogens. Despite the identification of numerous AMPs, only a few frog species have been thoroughly studied ,suggesting the existence of many more unexplored peptides in nature. This study offers new insights into the promising antimicrobial peptides derived from amphibians.

Methods: To this end, MEDLINE, EMBASE, LILACS, AIM, and IndMed databases were searched for relevant articles since ۱۹۸۷.

Results: Studies highlight the potential of AMPs as novel disinfectant agents and as complementary treatments alongside traditional antibiotics. Peptides like brevinin-۲SSb and ranatuerin-۲SSa, extracted from different frog species, have demonstrated effectiveness against pathogenic bacteria and fungi. Ongoing research focuses on developing modified AMP derivatives to optimize their antimicrobial properties while minimizing toxicity.

Conclusion: Several AMPs possess antibacterial, antiviral, and anticancer activities, presenting significant promise for clinical applications and cosmetic product development. Future research on isolating new peptides and understanding the relationship between AMP distribution and microbial ecosystems could pave the way for the creation of new therapeutic drugs.

Keywords: antimicrobial peptides , antiviral , toxicity

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Irritable bowel syndrome review article (Review)

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Introduction: Irritable bowel syndrome (IBS) is a common digestive disorder in the world and was once known as a psychosomatic disease, which today has progressed a lot and causes changes in the number and type of intestinal microbiota and increases the activity of the immune system. Intestinal microbiota are considered as an essential organ. The intestinal microbiota is closely related to (IBS). And the composition of the intestinal microbiota in healthy people is different from that of people with IBS. In general, the symbiotic relationship between the intestinal microbiota and the host with small changes causes IBD diseases. CD) and (UC). And according to the experiments, the change in intestinal microbiota is effective in causing colon cancer. In addition to these Fungi, viruses, archaebacteria are observed in the samples. Irritable bowel syndrome (IBS) disease affects the quality of human life and causes economic and social damage to life. And health care has a very important effect because these diseases cause an increase in mortality. Therefore, according to the wide connection of pathophysiological mechanisms (RE) and (IBS), they have a relationship with depression, anxiety and stress. Changes in the intestinal microbiota cause disturbances in the brain axis and autonomic nervous system, increase visceral sensitivity, and changes in digestive neuropeptides and hormones. In addition to diet, characteristics such as age, gender, race, geographical environment, and the number and type of intestinal microbiota have an effect on causing the disease. The symptoms of this disease (IBS) are mostly diarrhea or constipation, abdominal pain, weight loss, visceral sensitivities, nerve dysfunction, intestinal ulcers, excessive gas production, and difficulty in defecation. IBS diagnosis criteria: ۱.IBS_D diarrhea IBS_C is constipation ۲. IBS_M includes both in a mixed form ۳. Treatments today are biological, non-biological and nutritional. Antibiotics, probiotics, prebiotics, synbiotics and fecal microbiota transplantation are used for treatment, the last one being known as an excellent strategy for treatment. Identification of intestinal microbiota and factors affecting them Diagnosing the relationship between intestinal microbiota and irritable bowel syndrome (IBS) Diagnosis along with effective treatment and reduction of disease progression (IBS)

Methods: This study is in the field of recognition, prevention and treatment of factors affecting intestinal microbiota and irritable bowel syndrome. And for this study, Google Scholar database was used.

Results: The relationship between excessive growth of intestinal bacteria and intestinal microbiota is direct. Using articles, it was found that factors such as diet, gender, age, geographical environment, and any life habits (infectious gastrointestinal disease and radiotherapy) can affect changes in intestinal microbiota. It is effective and provides the basis for the disease (IBS).

Conclusion: Understanding the activity and interaction of the host with the gut microbiota helps in the diagnosis and treatment of IBS, which is one of the most common gastrointestinal disorders.

Keywords: Intestinal microbiota, irritable bowel syndrome (IBS), autoimmune enteropathy (RE), Mediterranean di

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Is the role of artificial intelligence effective in Parkinson's and Alzheimer's diseases? (Research Paper)

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Introduction: Artificial intelligence offers various benefits in the early and accurate diagnosis of neurodegenerative disorders through its ability to analyze data, identify patterns, make predictions, and provide recommendations. This study emphasizes the potential of machine learning and AI in improving the assessment and treatment strategies for these diseases. By utilizing AI, machine learning, signal processing, and computer-aided diagnostic technologies, healthcare professionals can make better clinical decisions. Specifically focusing on Alzheimer's disease and Parkinson's disease, this research aims to explore how AI and machine learning techniques can enhance early detection.

Methods: Deep learning, a notable soft computing approach within machine learning, employs layered algorithmic frameworks known as neural networks. Currently, substantial research efforts are underway to tailor these neural networks for the specific purposes of diagnosing and treating such disorders. These advanced technologies encompass data pre-processing, data collection, machine learning classifiers, and feature extraction techniques. Therefore, there is a critical need for the early detection and intervention of these diseases, which can lead to a moderate enhancement in the quality of life for patients. Significant progress has been achieved in the methods of acquiring neuroimaging data, particularly through diffusion Magnetic Resonance Imaging (MRI) and the analysis of electroencephalogram (EEG) data. To tackle these issues, a variety of machine learning techniques and algorithms are employed, including reinforcement learning, semi-supervised learning, unsupervised learning, supervised learning, deep learning, decision trees, BF trees, bagging, random forest trees, RBF networks, and evolutionary learning.

Results: AD:AI provides tools for analyzing vast and complicated data sets, hence boosting understanding in Alzheimer's disease research. Image and language processing, genetics, and drug development all rely on deep learning. They are multilayer structures in which inputs are routed through balanced sums and nonlinear functions to produce multi-level feature arrangements. Deep learning makes use of vast data to improve efficiency. ADNI datasets enable cooperation, validation of techniques for diagnosis, and discovery of viable therapeutics. Drug exploration, brain imaging, biomarkers, conversion prediction, and disease progression modelling are the key uses of AI in AD research. Big data, neuroimaging, genomics, and fluid biomarkers are all used in these applications. AI and ML approaches can be used to categories AD patients and forecast their future state using MRI scans. The present research used a variety of ML methods, including Logistic Regression, Decision Tree, Random Forest, Support Vector Machine, and AdaBoost. In the early identification

and categorization of Alzheimer's disease, the Random Forest classification method has shown substantial performance and outcomes. PD: Diagnosing Parkinson's disease (PD) solely through clinical methods presents significant challenges due to the disease's clinical variability, the absence of objective biomarkers, and the overlap of symptoms with other medical conditions. Many of these challenges can be addressed by utilizing advanced techniques such as various artificial intelligence (AI) and machine learning (ML) models in the diagnostic process for PD. A notable advancement brought about by AI and ML is the ability to diagnose Parkinson's disease through the analysis of peripheral biopsy samples. Historically, diagnosis relied primarily on clinical symptoms and post-mortem examinations; however, AI now facilitates a non-invasive and cost-effective method by evaluating peripheral biopsy samples, including skin biopsies, colon biopsies, and submandibular gland fluid or blood analyses, which yield highly accurate results with impressive sensitivity levels. Additionally, another AI and ML strategy for diagnosing PD involves the application of AI-driven image analysis to detect PD-related biomarkers. AI algorithms are capable of recognizing specific patterns and markers by analyzing neuroimaging data, thereby enhancing the diagnostic accuracy for Parkinson's disease.

Conclusion: Unlike humans, machine learning algorithms possess the capability to recognize patterns and derive new insights from extensive multidimensional datasets. Nevertheless, the application of machine learning in aiding therapeutic development, prognosis, and diagnosis remains in its early stages. Utilizing medical histories, molecular profiles, imaging data, and the discovery of more specific diagnostic biomarkers, machine learning technology has the potential to facilitate more accurate and timely diagnoses of neurodegenerative diseases in the future. Furthermore, by enhancing patient classification and identifying precise biomarkers for treatment response, machine learning could potentially reduce the time and costs involved in clinical trials while increasing the chances of successful outcomes.

Keywords: Artificial intelligence, Alzheimer's disease, Parkinson's disease, machine learning

Itaconate, a new frontier in autoimmune disease therapies (Review)

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Introduction: Itaconic acid, a naturally occurring compound produced in the Krebs cycle, has garnered attention in recent years due to its potential effects on autoimmune diseases. The Krebs cycle is a series of biochemical reactions that occur in the mitochondria of cells, playing a vital role in generating energy for cellular functions. Itaconate role in this metabolic pathway highlights its significance in cellular metabolism and potential implications for autoimmune diseases. Autoimmune diseases occur when the immune system mistakenly attacks healthy cells in the body. In this article, we will explore the impact of itaconate on autoimmune diseases.

Methods: Our study was conducted on the PubMed database using the keywords (Disease AND Autoimmune) OR (Diseases AND Autoimmune) OR "Autoimmune Disease" OR "Autoimmune Diseases") AND ("itaconate" OR "methylenebutanedioic acid" OR "methylene succinic acid" OR ("itaconic acid" AND "sodium salt") OR ("itaconic acid" AND "disodium salt") OR "methylidenebutanedioate" OR ("itaconic acid" AND "calcium salt") OR ("itaconic acid" AND "copper salt") OR "itaconic acid") from ٢٠١٨ to ٢٠٢٤. Out of ٢٣ papers related to this topic, seven studied were reviewed

Results: Some previous studies are pointing to itaconate as a possible solution for inflammation, especially in autoimmune and inflammatory issues. It kicks off a process in cells called Nrf٢, which then helps cut down on collagen production in skin cells, lowers the creation of harmful free radicals, and stops the stimulation of collagen proteins. In mouse models of lupus, Itaconate treatment improved kidney structure, lowered autoantibody levels, and positively impacted platelet counts and lymphoid organ function. Additionally, in autoimmune hepatitis, Itaconate effectively reduced necrotic areas, liver enzyme levels, inflammatory cell infiltration, and cytokines. For type ١ diabetes, Itaconate showed preventative effects against glycemic deterioration, increased islet cell numbers, lowered blood sugar levels, and restored insulin-producing beta cells. Furthermore, Dimethyl itaconate, a derivative of Itaconate displayed protective effects in encephalomyelitis by improving outcomes and reducing disease severity. DMI treatment strengthened the blood-brain barrier, suppressed the activation of microglia, increased the expression of Nrf٢ and HO-١, inhibited the movement of T cells into the central nervous system, and directly blocked the development of harmful T cells.

Conclusion: Based on our review, Itaconate and its derivatives, show significant anti- inflammatory properties by activating Nrf۲, reducing cytokine expression and oxidative stress in autoimmune diseases like lupus nephritis, type ۱ diabetes, and systemic sclerosis. Therefore, these findings suggest the therapeutic promise of Itaconate derivatives in autoimmune disorders, Necessitating further clinical investigation.

Keywords: anti-inflammatory, Autoimmune Diseases, itaconic acid

Key Genes in Bladder Cancer Metastasis: An In Silico Analysis (Research Paper)

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Introduction: Bladder cancer is one of the most common types of urinary tract cancers, originating from the cells lining the inner surface of the bladder. In this disease, cancerous cells grow uncontrollably and can invade surrounding tissues or even metastasize to other parts of the body. While the exact causes of bladder cancer remain elusive, several risk factors have been identified, including: smoking, exposure to chemicals, age, gender, family history, chronic bladder infections and bladder stones. Biomarkers can serve as biological indicators, assisting clinicians in the early and accurate detection of bladder cancer. These markers can be found in bodily fluids such as blood or urine, and changes in their levels may indicate the presence of cancerous cells. By utilizing biomarkers, less invasive and more precise diagnostic methods can be developed. In this study, we aim to identify the key genes that involved in bladder cancer metastasis.

Methods: In the current study, two microarray dataset (GSE٣٧٣١٧, GSE٣١٦٨٤) were downloaded from the Gene Expression Omnibus database (GEO). The fold change (FC) values of individual gene levels were calculated; differentially expressed genes (DEGs) with |FC| > ١ and P-value < ٠,٠٥ were considered to be significant. The Venn diagram was carried out for the overlapped part via Funrich software.

Results: A total of ٣ overlapped upregulated genes and ٧ downregulated genes were identified. Analysis showed that up-regulated genes involve in the translation regulator activity, cell adhesion molecule activity and catalytic activity. Down-regulated genes mainly associate with cytoskeletal protein binding, oxidoreductase activity and auxiliary transport protein activity.

Conclusion: These in silico predictions will provide useful information in selecting the target genes that are likely to have functional impact on the bladder cancer metastasis and may serve as potential diagnostic biomarkers in bladder cancer patients.

Keywords: bladder cancer, in silico, metastasis biomarkers

Li-Fraumeni Syndrome: Genetic Mutations, Cancer Risks, and Surveillance Strategies (Review)

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Introduction: Li-Fraumeni syndrome is an autosomal dominant inherited disease which means that even if the mutation occurs in only ١ of the ٢ copies of the TP٥٣ gene, a person will have germline LFS. In cases where a mutation is inherited from parents, this type of mutation is referred to as a germline mutation. In the majority of cases of LFS, an individual will present with one normal and one mutated (altered) copy of the TP٥٣ gene that the presence of a mutated TP٥٣ allele is frequently attributable to inheritance from a parent affected by LFS. Nevertheless, it is estimated that approximately ٢٥٪ of individuals with LFS lack a family history of the condition and instead exhibit a de novo (new) mutation in the TP٥٣ gene. Inherited mutations of the TP٥٣ gene have been identified as a contributing factor to certain types of cancer. Consequently, LFS is characterized as a cancer-prone syndrome, with an elevated risk for developing a diverse range of childhood and adult malignancies. More than ١٤٠ different types of inherited mutations for the TP٥٣ gene have been identified, many of which are located in the DNA binding domain of p٥٣. Somatic pathogenic variants of TP٥٣ have been identified in approximately ٥٠٪ of all tumors, making it one of the most commonly altered genes in human cancers. The majority of LFS tumours are of the following five cancer types: adrenocortical carcinomas, breast cancer, central nervous system tumors, osteosarcomas and soft-tissue sarcomas. Additionally, LFS is linked to an elevated risk of various other cancers, including leukemia, lymphoma, gastrointestinal cancers, cancers of the head and neck, kidney, larynx, lung, skin (e.g., melanoma), ovary, pancreas, prostate, testis, and thyroid. The lifetime probability of developing cancer in individuals with LFS is ≥٧٠٪ for males and ≥٩٠٪ for females. A diagnosis of LFS can be established in a proband who meets all three classic clinical criteria and/or has a heterozygous germline pathogenic variant in TP٥٣. The classic clinical criteria are as follows: A proband with a sarcoma diagnosed before the age of ٤٥ years, a first-degree relative with any cancer diagnosed before the age of ٤٥ years, and a first- or second-degree relative with any cancer diagnosed before the age of ٤٥ years, or a sarcoma diagnosed at any age. Currently, a number of tests are available for individuals with LFS, including predictive testing for at-risk family members, prenatal testing, and preimplantation genetic testing, which may be conducted if a TP٥٣ germline pathogenic variant is present in the family. Accordingly, the recommended surveillance protocols include: A comprehensive physical examination and ultrasound of the abdomen and pelvis should be conducted every three to four months from birth to the age of ١٨ years. Additionally, an annual neurological examination and whole-body MRI, including a brain MRI, should be performed from the time of diagnosis. For women, a breast MRI should be conducted from the age of ٣٠ to ٧٥ years.

Methods: The research methodology entailed an extensive search of the PubMed, Google Scholar, and NCBI databases to identify articles pertinent to Li-Fraumeni syndrome. A comprehensive literature review was conducted to identify studies investigating Li-Fraumeni Syndrome, with a specific focus on genetic mutations, cancer risks, and surveillance strategies. Electronic databases were searched using relevant keywords and studies published between ٢٠٢٣ and ٢٠١٦ were included. In order to obtain a comprehensive understanding of the subject matter, the review encompassed in vitro studies, and clinical trials.

Results: In light of promising preclinical data, the National Cancer Institute (NCI) has initiated a clinical trial investigating metformin as a novel anticancer agent. Preclinical evidence suggests that metformin exerts its anti-tumorigenic effects through multiple mechanisms. Indirectly, metformin reduces systemic insulin levels, whereas directly, it induces energetic stress. Moreover, metformin has been demonstrated to lower cancer incidence by inhibiting mitochondrial metabolism.

Conclusion: Li-Fraumeni syndrome (LFS) represents a significant hereditary risk factor for various cancers due to mutations in the TP٥٣ gene. Individuals with Li-Fraumeni syndrome (LFS) are at a significantly increased risk of developing cancer throughout their lifetime, particularly those who are female. It is therefore vital that those diagnosed with LFS are given the opportunity to receive regular surveillance, and any symptoms should be considered promptly. Furthermore, it is crucial that ongoing research, including clinical trials investigating the potential role of metformin in reducing cancer incidence, is supported and encouraged, as this may offer new avenues for prevention and treatment in the future. It is essential that continued awareness and understanding of the syndrome is promoted, as this will ultimately lead to improved outcomes for individuals affected by LFS and their family members.

Keywords: Li-Fraumeni syndrome (LFS); TP٥٣ gene; mutation; cancer

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Limits to embryonic development outside the Earth's atmosphere (Review)

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Introduction: Leaving the planet and living in other planets and galaxies is a matter of saving the human race. This study is about factors limiting fertility and extraterrestrial reproduction, which examines the challenges and issues we will face after ٦ million years. Human exposure is unique in this field. Microgravity is important factor that will affect our fertility after leaving the planet, so these investigations will be vital to ensure the survival of astronauts and humans and their long-term presence on other planets. The findings of these studies specifically address fertility issues from the perspective of an embryologist on a space mission.

Methods: The present research was a review study, the related articles of which were extracted from Web of Science, PubMed, Google Scholar, SID, Magiran databases without time limit. The inclusion criteria included studies that were in line with the research objective.

Results: Among the issues that human embryos will face after exposure to microgravity are epigenetic changes and chromatin structure that are likely to affect early embryo development. Understanding these changes is critical to the success of future space missions. It is necessary to maintain cell shape and facilitate division, and evidence shows that these structures change when exposed to microgravity. Also, changes in cytoskeletal organization can lead to developmental abnormalities, such as neural tube defects and morphological abnormalities. The studies are also indicative of another destructive factor that threatens the human fetus: oxidative stress and apoptosis. Exposure to microgravity can increase oxidative stress, which negatively affects fetal development. High levels of reactive oxygen species (ROS) can naturally lead to increased apoptosis and complicated growth processes.

Conclusion: Understanding the effects of microgravity on embryonic development is very important to clarify safety, future space explorations, and the possibility of human reproduction in space. Some aspects of early development appear to be resilient to microgravity, so the inevitable exposure to these conditions requires us to continue researching the mechanisms behind these effects and develop strategies to support healthy embryonic development in space environments.

Keywords: Aerospace medicine, embryology , Space exploration

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Lipid Nanoparticles and mRNA Vaccines: A Revolutionary Approach to Immunization (Review)

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Introduction: The advent of mRNA vaccines, particularly highlighted during the COVID-١٩ pandemic, has marked a significant milestone in the field of immunization. Central to the efficacy of these vaccines are lipid nanoparticles (LNPs), which serve as crucial delivery vehicles for mRNA. Lipid nanoparticles (LNPs) have revolutionized how we deliver mRNA, particularly showcased by their essential role in developing mRNA vaccines during the COVID-١٩ pandemic. This review explores lipid nanoparticle structure, function, and applications in mRNA therapeutics, highlighting how they work and the benefits they bring compared to traditional vaccine delivery methods.

Methods: This study was conducted as a review by searching for “lipid nanoparticles” and “mRNA vaccines” keywords in databases such as PubMed, Direct Science, Scopus and search engine Google Scholar. finally, more than ٣٠ new articles with a publication date of ٢٠١٨ were studied and evaluated.

Results: Lipid nanoparticles are tiny, spherical carriers made up of various lipids, including ionizable lipids, phospholipids, cholesterol, and PEGylated lipids. Together, these components encapsulate and protect mRNA, ensuring it remains stable and effective. The process of creating LNPs involves self-assembly, allowing these nanoparticles to transport mRNA directly into target cells. Once injected, typically into muscle tissue, LNPs are taken up by cells through a process called endocytosis, where they release the mRNA into the cell’s cytoplasm. Here, the mRNA is translated into proteins, triggering a strong immune response, preparing the body to recognize and fight off viral infections. The advantages of using lipid nanoparticles in mRNA vaccines are numerous. They enhance stability and protection for mRNA, improve delivery efficiency, and reduce unwanted immune reactions, allowing for a more targeted immune response. LNP technology is versatile, enabling rapid adjustments for different mRNA targets, which is particularly useful for responding to new infectious diseases. Moreover, LNPs can be engineered for various therapeutic applications beyond vaccines, such as in cancer treatment and gene therapy. However, challenges remain. Manufacturing LNPs can be complex, and there are concerns about potential immune reactions and stability issues that need to be addressed to ensure safety and efficacy. Looking ahead, the success of lipid nanoparticles in mRNA vaccines opens the door for their use in personalized medicine and advanced therapies. Researchers are exploring their potential for delivering mRNA in treatments for cancer and genetic disorders, highlighting their transformative potential in modern healthcare.

Conclusion: In summary, lipid nanoparticles represent an exciting advancement in mRNA delivery systems, providing a robust platform for vaccine development and therapeutic applications. Ongoing research and innovation in this area will be crucial for overcoming current challenges and unlocking new possibilities in mRNA-based treatments, ultimately leading to better health outcomes for individuals worldwide.

Keywords: Lipid Nanoparticles, mRNA Vaccines, mRNA Delivery Systems, Immunization, Personalized Medicine

Lipopolysaccharide-stimulated adipose-derived Mesenchymal Stem Cells have the potential effect to treat Nonalcoholic fatty liver disease in HFD-Fed Rats in comparison to AD-MSCs and fenofibrate (Research Paper)

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Introduction: introduction: Nonalcoholic fatty liver disease, often called NAFLD, is a liver problem in which too much fat builds up in the liver. It is seen most often in people who are overweight or obese. Because of high-caloric and fat diets in most people, NAFLD is common in the world and is associated with an elevated triglyceride level. It is the most common form of liver disease in the world. However, there is currently no effective treatment for NAFLD. Fenofibrate (FENO) is a first-line medication commonly used to lower triglyceride levels. Fenofibrate contributes to the regulation of carbohydrate and lipid metabolism. However, it may also increase the excretion of cholesterol from bile, which can increase the risk of developing gallstones so it is not completely safe. Mesenchymal stem cells (MSCs) are long-lived cells with self-renewal capability, and they may have an optimistic treatment potential for NAFLD.MSCs can be obtained from various sources, including bone marrow, adipose tissue, and umbilical cord. Among them, adipose-derived stem cells (ADSCs) have gained attention for their potential repair of various tissues. Lipopolysaccharide (LPS), a component of gram-negative bacterial cell walls, is likely to stimulate cells that contribute to inflammatory responses (such as macrophages and neutrophils) and pro-inflammatory factors (such as IL-١β, IL-٦, and TNF-α). Recent studies suggest that LPS-stimulated MSCs may release anti-inflammatory cytokines during inflammation. Due to the high prevalence of NAFLD in the world and the absence of effective and safe remedies, finding a way to treat it, is crucial. This study investigated the effect and comparison of lipopolysaccharide (LPS)--stimulated adipose-derived stem cells (ADSCs), adipose-derived stem cells, and fenofibrate on NAFLD Treatment in High-Fat Diet-Fed Rats.

Methods: method: The inguinal adipose tissues of ٧-week-old rats were isolated, and the Isolation and cultivation of Adipose-derived mesenchymal Stem Cells (ADSCs) according to protocol was done. Male Wistar rats were fed a high-fat diet (HFD) for ١٢ weeks to induce NAFLD. The rats were then categorized into ٣ groups: The first group was treated with adipose-derived stem cells (ADSCs), the second group was treated with LPS+ADSCs, and the last group was treated with fenofibrate (FENO) (as standard therapy group) groups. Liver and body weight were measured. Biochemical Measurements including Liver enzymes (Alanine aminotransferase (ALT) and aspartate aminotransferase (AST)), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) lipid profiles were assessed using the Roche ٦٠٠ autoanalyzer. The expression of genes, such as IL-٦, IL-١β, TNF-α, TGF-β, monocyte chemoattractant protein ١ (MCP-١), and the expression of genes involved in fatty acid biosynthesis, β-oxidation, and inflammation were

examined using real-time polymerase chain reaction (PCR). Histopathological Examination also was done by a skilled liver pathologist to investigate liver injuries in each group

Results: results: Rats fed with a high-fat emulsion for ١٢ weeks exhibited a significant increase in body weight, liver weight, and liver triglyceride compared to the normal control group. Lipopolysaccharide-stimulated Adipose-derived mesenchymal Stem Cells (LPS+ADSCs) were more effective in regulating liver and body weight and reducing liver triglyceride levels than the other groups. Treatment with Lipopolysaccharide -stimulated ADSCs effectively amended liver enzymes including alanine aminotransferase (ALT) and aspartate aminotransferase (AST), and lipid factors, including LDL-C and HDL-C values, better than treatment with both FENO and MSCs. ADSCs + LPS treatment significantly decreased genes associated with inflammatory responses (IL-٦, TNFα, TGF-β, IL-١β). Also, there was a significant reduction in reactive oxygen species (ROS) levels in the rats treated with ADSCs + LPS.

Conclusion: conclusion:In this study, the NAFLD rats model induced by a high-fat diet were employed to assess the efficacy of Lipopolysaccharide -stimulated ADSCs, compared to ADSCs alone and FENO, a widely used hypolipidemic drug for dyslipidemia treatment. Lipopolysaccharide-stimulated ADSCs showed potential effects in alleviating NAFLD by reducing the biomarkers of liver injury (ALT and AST), lipid factors (including HDL-C and LDL-C), inflammatory genes (IL-٦, TNFα, TGF-β, IL-١β) and ROS levels in HFD rats than treatment with ADSCs and FENO groups. Additionally, ADSCs stimulated with LPS exhibit a significant reduction in NAFLD characteristics and are more effective than ADSCs alone and FENO so Lipopolysaccharide-stimulated ADSCs can be introduced as an effective remedy for NAFLD treatment in medicine.

Keywords: Keywords:NAFLD, Lipopolysaccharide, ADSCs, Inflammation, Fenofibrate

Liver Organoids in Tissue Engineering: Applications and Future Prospects (Review)

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Introduction: Liver tissue engineering has become a pivotal area in regenerative medicine, offering new solutions for the increasing demand for liver transplants and providing more accurate models for liver disease research. Organoid technology, which involves the creation of three-dimensional (3D) cell cultures that replicate the structure and function of organs, has gained significant traction in this field. These liver organoids, derived from stem cells, possess the ability to mimic the liver's complex architecture and metabolic functions, making them invaluable for studying liver diseases, testing drugs, and potentially advancing liver regeneration therapies

Methods: Liver organoids are developed by culturing pluripotent stem cells (PSCs) or induced pluripotent stem cells (iPSCs) in a 3D extracellular matrix. These cells are exposed to specific growth factors and signaling molecules that drive their differentiation into liver-specific cells, such as hepatocytes and cholangiocytes. The 3D matrix supports the self-organization of these cells into tissue-like structures that closely mimic the liver's native architecture. A key advancement in this process is the incorporation of endothelial cells to create vascular structures within the organoids, enhancing their survival and function. After formation, the organoids undergo a maturation phase, during which their liver-like functions—such as metabolic activity and bile production—are evaluated using various functional assays.

Results: Liver organoids have demonstrated significant potential in various applications, particularly in the modeling of liver diseases and in drug testing. Compared to traditional 2D cell cultures, liver organoids provide a more accurate representation of liver function and have been successfully used to model a range of liver conditions, including genetic disorders, infections, and cancers. For example, organoids derived from patient-specific iPSCs have been utilized to study the mechanisms of genetic liver diseases, providing valuable insights into disease progression and potential treatments. In the context of drug testing, liver organoids offer a reliable platform for evaluating drug efficacy and toxicity. Their ability to closely mimic human liver functions, including drug metabolism and detoxification, makes them particularly valuable for preclinical drug screening, reducing the dependence on animal models and improving the relevance of findings to human physiology

Conclusion: Organoid technology represents a major advancement in liver tissue engineering, offering a versatile platform for disease modeling, drug testing, and potentially for regenerative medicine applications. While significant progress has been made, challenges such as scaling up production and achieving full maturation of the organoids remain. Ongoing research aims to improve culture conditions, enhance vascularization, and integrate additional cell types to create

more complex and fully functional liver organoids. As this technology continues to evolve, it holds the potential to revolutionize liver disease treatment and may provide a viable alternative to liver transplantation, thereby improving outcomes for patients with liver conditions

Keywords: Liver, Tissue Engineering, Stem Cells

LncRNA and colorectal cancer (Review)

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Introduction: Colorectal cancer (CRC) is one of the most common cancers. The initiation and progression of this cancer is mainly associated with the aberrant expression of various coding and non-coding genes as well as multiple risk factors such as smoking, adenomas, physical inactivity, obesity, male gender and older age. Importantly, new advances in whole genome sequencing technologies in cells have shown that over ٩٠٪ of the human genome is actively transcribed. However, only ٢٪ of transcripts are responsible for producing proteins, with the majority of the transcribed genome being non-coding RNAs (ncRNAs). Long non-coding RNAs (lncRNAs) are a subset of ncRNAs that contain over ٢٠٠ nucleotides which are involved in modulating gene stability and expression. lnRNAs based on their proximity to protein encoding genes and the genomic location, can be classified as intronic lncRNAs, which indicate that they are located within the introns of protein-coding genes and have a ٥' cap, but not a polyadenylation site which shows that they do not undergo the usual polyadenylation process but rather they are transcribed by RNA polymerase II. Another type of lncRNAs are intergenic lncRNAs, which are found between protein-coding genes; an example of this type of lncRNA is ELENA١. Another type to include are bidirectional lncRNAs, for example HOTTIP, as well as antisense lncRNAs, such as ST٣Gal٦-AS١ which are transcribed from the opposite strand of a gene and processed by one of two gene structures, ST٣Gal٦-AS١ in particular is transcribed from the promoter region of the ST٣Gal٦ gene, but in an opposite direction to the primary transcription of ST٣Gal٦ gene. While both the lncRNA ST٣Gal٦-AS١ and the ST٣Gal٦ gene itself are down-regulated in CRC. In addition, lncRNAs have important functions in various biological processes including cell division and differentiation, endocytosis, and transmission of neurotransmitters. Besides their role in various biological processes, lncRNAs have gained significant attention because of their oncogenic roles. LncRNAs can promote metastasis and tumor growth by regulating the expression of genes (including epigenetic, transcriptional, and post-transcriptional levels) involved in apoptosis, differentiation and cell division. Therefore, lncRNAs have potential clinical relevance and are now recognized as valuable candidates for cancer biomarkers. They hold promise in early cancer diagnosis, prognosis, and therapeutic targets for cancer patients. For example, the lncRNA PCA٣ may serve as a prognostic marker for CRC, with higher levels of expression indicating poorer prognosis. Moreover, lncRNAs can be utilized in cancer immunotherapy as a system of delivery therapeutic molecules to cancer cells.

Methods: Text based on the contents found in the following journals: A Cancer Journal for Clinicians, Carcinogenesis, British journal of cancer, Reports of Practical Oncology and Radiotherapy, Biomedicine & Pharmacotherapy, Pathology-Research and Practice, Journal of Hematology & Oncology, Phytotherapy Research, Drug Discovery Today, Journal of Hepatocellular Carcinoma, Archives of Advances in Biosciences, European Journal of Pharmacology, Journal of immunology research, Molecules, International Medical Journal of Experimental and Clinical Research, Current

Molecular Medicine, Oncotarget, RNA BIOLOGY, Medicine, The International journal of biological markers, International journal of clinical and experimental pathology, Cancer medicine, Current medicinal chemistry, Clinical Chemistry and Laboratory Medicine, Cell death & disease , BMC cancer, Oncology letters, Cell proliferation, Journal of cellular and molecular medicine, Journal of cellular physiology, Molecular cancer, Non-coding RNA Research, Molecular cancer therapeutics, The Journal of Clinical Investigation, Frontiers in Cell and Developmental Biology, Cancer Cell International, BMC genomics, Trends in genetics

Results: Different types of lncRNAs, their expression levels, and their influence on signaling pathways such as Wnt/β-catenin and PI۳K/Akt pathways can all contribute to varying outcomes in cancer initiation and progression. The diverse expression levels of lncRNAs in CRC can significantly affect oncogenic results. While many lncRNAs impact CRC from various aspects, some key types play a crucial role in its onset and progression. For instance, Overexpression of MALAT۱ lncRNA in CRC cells has been demonstrated to enhance tumor growth through the activation of the Wnt signaling pathway. LncRNA HOTAIR, is significantly upregulated in CRC tissues and cells. Its overexpression promotes tumor growth, invasion and metastasis through silencing tumor suppressor genes including EZH۲ by activating AKT/mTOR signaling pathway, further contributing to the progression of CRC. Some types of lncRNAs can have tumor suppressive roles in CRC. Such as, lncRNA MEG۳ which sponges miR-۱۰۳a-۳p and suppresses CRC by inducing Endoplasmic reticulum (ER) stress, inhibiting cell invasion and proliferation through the upregulation of pyruvate dehydrogenase E۱ subunit beta (PDHB). Also, lncRNA ANCR is found to be downregulated in CRC tissues and cells. It specifically binds to EZH۲, leading to the suppression of cancer progression. Given the significant role of lncRNAs in cancer biology, it is rational to identify suitable lncRNAs as main targets for the development of new anti-cancer drugs.

Conclusion: Increasing evidence shows that lncRNAs are important regulators that are involved in the primary characteristics of CRC through various molecular mechanisms. This indicates that they may serve as viable candidates for diagnostic and prognostic biomarkers in patients with CRC. Looking into the future, the therapeutic possibilities linked with lncRNA-based therapies can provide a significant healthcare option.

Keywords: LncRNA, colorectal cancer, biomarkers, gene regulation, therapeutic targets

LncRNA's Role in Leukemia (Review)

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Introduction: Long non-coding RNAs (lncRNAs) are RNA transcripts longer than ٢٠٠ nucleotides, transcribed by RNA polymerase II. They exhibit high levels of cell-, tissue-, and tumor-specific expression. They have gained significant attention due to their diverse roles in biological processes, including cancer development, metastasis, metabolism, and gene regulation. Unlike protein-coding genes, lncRNAs do not encode proteins but play crucial regulatory roles by controlling a spectrum of mechanisms at multiple levels, including epigenetic, transcriptional, post-transcriptional, and translational regulations. They act as molecular scaffolds, guide protein-protein interactions, and regulate chromatin remodeling and gene expression. Additionally, they've been observed to carry out functions through interactions with RNAi, notably with miRNAs, as competitive endogenous RNAs (ceRNA) and by sponging or transcriptional regulation. LncRNAs are known to modulate signaling pathways related to metabolism, drug resistance induction, cell proliferation and apoptosis inhibition, namely Wnt/β-catenin, PI٣K/Akt/mTOR, PBX٣/MAPK and NF-κB in different types of cancer. Dysregulation of lncRNAs has been implicated in numerous diseases, including cancer, making them intriguing targets for diagnosis, prognosis, and therapeutic interventions. In blood cancers like leukemia, lymphoma, and multiple myeloma, lncRNAs regulate gene expression and disease progression. Dysregulated expression of lncRNAs can alter leukemia development, both in-favor and against the tumor, through the regulation of their transcription. Because of this, specific lncRNAs have been identified as potential diagnostic or prognostic markers, providing valuable insights into disease progression and patient outcomes, where their dysregulation is sighted. In this review we will be elucidating their intricate functional mechanisms and potential clinical applications as diagnostic biomarkers and therapeutic targets, taking into account their diverse expression patterns.

Methods: Text based on the contents found in the following journals: Journal of Experimental & Clinical Cancer Research, DNA Repair, Molecular Genetics and Genomics, Nature genetics, Blood Advances, Drug Resistance Updates, Bioscience reports, Molecular Cancer, Journal of molecular medicine, Leukemia, MBO reports, Cell Rep, Oncol Lett, RNA Biology, Molecules and cells, RSC Advances, Journal of Cellular Physiology, Iran J Basic Med Sci, Pathology, Neoplasma, Molecular cell, Blood Cancer Journal, Journal of Cellular Biochemistry, Haematologica, Blood Cells, Molecules, and Diseases, Genomics, Proteomics & Bioinformatics, Molecular cancer, Gene, Clinical Oncology and Cancer Research, Biomedicine & Pharmacotherapy, The Scientific Journal of Iranian Blood Transfusion Organization, Cancer Cell International, The Journal of Immunology, Frontiers in Oncology, Journal of Biomedical Science, Cancers, Life sciences, Cell Proliferation, BMC Cancer, Oncology Reports, Science, British Journal of Cancer, Cell Death & Disease, Frontiers in Medicine

Results: LncRNAs have recently been one of the main research topics in the field of cancer biology and rightfully so, as they have shown promising results regarding their medical use. This could be in

the form of an intervention through controlling the regulation of certain lncRNAs to impede tumor progression. Examples include directly or indirectly upregulating anti-oncogenic lncRNAs and/or downregulating oncogenic ones. Moreover, their interference with the functionality of chemotherapy drugs could be targeted for a more effective treatment plan, maybe even alongside the combination with transcription modulation. Not to mention, that the matter of their presence alone is shown to be of use, when it comes to diagnosis. The use of lncRNAs against leukemia was also clinically tested, with their use as a biomarker being highlighted as a very promising future tool for early recognition. Furthermore, a rising number of papers are now also sharing the optimistic view in the field of leukemia and going beyond with adding more themes onto it.

Conclusion: LncRNAs have only somewhat recently caught the eyes of researchers, but they have proved themselves to be of significant importance for diagnosis, prognosis and therapeutic methods. As of now a large number of them have been discovered along with their functions and roles in different cancers and they are still being extensively researched. Most lncRNAs in leukemia take on oncogenic roles as they are upregulated and promote the diseases' progression, but there are also ones that are downregulated since they exhibit antioncogenic functions. LncRNAs operate by using several mechanisms such as epigenetic- and transcriptional regulation they are able to deploy functions like interacting with transcription factors, DNA methylation, histone modification and others in different types of leukemia. As of now this topic is still relying on future research to uncover lncRNAs and their uses in leukemia as well as other cancers. With the additional research done to confirm their place in the clinical toolkit, lncRNAs will hopefully be taken into use for the clinical procedure and have an effect on the diseases' outcome.

Keywords: LncRNA; Leukemia; Cancer Biology; Molecular Medicine

Long Non-Coding RNAs and HPV Associated Cutaneous cancer (Review)

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Introduction: Cutaneous cancer rates are on the rise, with various types, including melanoma and non-melanoma, becoming more prevalent. This increase stems from a complex mix of inherited traits, gene expression changes, and environmental exposures. Notably, human papillomavirus (HPV) infection has emerged as a significant factor in the development of these skin-based tumors. Non-coding RNAs (lncRNAs) have emerged as critical players in developing and progressing HPV-positive cutaneous cancers.

Methods: This comprehensive review explores the intricate relationships between lncRNAs, microRNAs (miRNAs), and HPV oncoproteins in the context of skin cancer pathogenesis.

Results: Some lncRNAs are competing endogenous RNAs (ceRNAs), capable of sponging miRNAs and influencing their tumor suppressor functions. This interaction can increase carcinogenesis by preventing miRNAs from silencing their oncogenic targets. LncRNAs are classified into intronic, sense-overlapping, antisense, and long intergenic non-coding RNAs (lincRNAs), each with distinct regulatory functions in cancer progression. The subcellular localization of lncRNAs is crucial to their function. Nuclear lncRNAs primarily modify chromatin to regulate transcription, while cytoplasmic lncRNAs influence mRNA stability and translation, thus modulating protein expression. HPV oncoproteins, particularly E٦ and EV, play a significant role in regulating epithelial differentiation by controlling the expression of pro-differentiation (TINCR) and anti-differentiation (DANCR) lncRNAs. Are various lncRNAs implicated in melanoma and non-melanoma cancers, including PVT١, MALAT١, HOTAIR, NEAT١, etc. These lncRNAs interact with multiple signaling pathways, such as TGF-β١, Wnt/β-catenin, Notch, Hippo, Akt/mTOR, SHP٢/ERK, and NF-κB, contributing to cancer development through alterations in cell proliferation, death, cycle, migration, angiogenesis, and invasion. PVT١, an oncogenic lncRNA highly expressed in HPV-positive cancers, stabilizes MYC, enhancing the aggressive characteristics of cancer cells. Its upregulation is associated with squamous cell carcinoma (SCC) progression in the skin, suggesting a crucial role in the multistage carcinogenesis process of cutaneous SCC. The review details PVT١'s interaction with ٤E-binding protein ١ (٤EBP١), a tumor suppressor that modulates the mTOR signaling pathway, highlighting the complex regulatory mechanisms in cutaneous SCC. Moreover, lncRNAs play a role in modulating immune responses and radiation sensitivity in HPV-related cancers. LncRNA PRINS alters the expression profiles of genes associated with immune and antiviral responses in HPV-induced head and neck SCC. Lnc-IL١VRA-١١ targets genes involved in cell replication and proliferation, potentially

increasing the sensitivity of HPV-associated head and neck SCC cells to radiation therapy. Furthermore, lncRNAs can function as molecular sponges for HPV-related miRNAs. Several lncRNA/miRNA pairs, such as HOTAIR/miR-٢١٤-٣p and MALAT١/miR-٢١٦b, are highlighted for their cooperative contribution to developing HPV-related cancers. In vivo studies demonstrating the effects of PVT١ knockdown on cutaneous SCC cells are presented, showing significant inhibition of proliferation, migration, and invasion both in vitro and in vivo.

Conclusion: These findings underscore the potential of targeting PVT١ as a therapeutic strategy in cutaneous SCC treatment. This comprehensive overview underscores the significance of lncRNAs in the pathogenesis of cutaneous cancers and their potential as diagnostic and prognostic biomarkers, paving the way for novel treatment strategies in managing HPV-positive skin malignancies.

Keywords: Human papillomavirus; Cutaneous cancer; Long non-coding RNA

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M۲e-HSP۷۰ chimeric protein as an influenza vaccine candidate (Research Paper)

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Introduction: Influenza virus is the cause of annual epidemics and causes the death of thousands of people in the world. This virus is transmitted from one person to another by respiratory droplets in the air or contact with contaminated surfaces and causes destruction and disruption of the respiratory tract. This disease is dangerous for the elderly, young children and people who suffer from underlying diseases such as lung, kidney, heart, etc. It is very necessary to prevent it through effective and universal vaccines. There is always a serious need to improve the vaccines produced against the influenza virus in order to create a broader immunity with long-term stability. By comparing the types of vaccines designed against the influenza virus, one of the necessities that is now felt is to separate the stages of vaccine production from the embryonated egg system and to be on the path of producing new vaccines based on biotechnology. One of the best production routes for seasonal vaccines, as well as for modern and universal vaccines, is the route of recombinant protein vaccines. So far, a lot of work has been done on recombinant influenza protein vaccines and its various genes have been investigated. One of these proteins is the M۲e protein, which is highly conserved in different influenza virus strains. M۲e is a type ۳ non-glycosylated protein that is abundantly expressed in the plasma membrane of virus-infected cells.

Methods: In the present study, the recombinant production of this protein in Escherichia coli bacteria and the purification of the produced product were carried out with the aim of using it as a component of the influenza vaccine set. In this study, the recombinant influenza virus M۲e protein was expressed and purified in a chimeric form with HSP۷۰, in order to be used in the production of a subunit vaccine set in the prokaryotic host E.coli.

Results: For this purpose, the ٤xM۲e.HSP۷۰ gene fragment was expressed in the expression host E.coli strain M-۱۵, using the isopropyl beta-di۱-thiogalactopyranoside (IPTG) inducer. And it was confirmed by performing SDS-PAGE and western blot with Anti-His-tag antibody. The expression was carried out in optimized conditions with ۰,۵ mM amount of IPTG inducer at ۲۵°C temperature and after protein extraction with urea and its purification in optimized conditions with urea by Ni-NTA affinity chromatography column, protein ٤xM۲e.HSP۷۰ was recovered and deureated by dialysis method in ۲ phosphate buffer and saline buffer. Finally, its production efficiency was about ۱٦۵ µg/ml protein. In this method, a suitable amount of M۲e protein was obtained in the shortest time and at a low cost, for the following purposes, which indicates the efficient production of recombinant protein in the prokaryotic system in order to be used in the influenza vaccine.

Conclusion: According to the results obtained from this research, it is suggested that the expression of the desired gene construct be investigated in order to optimize production in other hosts such as

eukaryotic hosts, as well as the protein function and immunogenicity of the desired construct alone, together with adjuvant or by adding other protected proteins of influenza virus to be evaluated.

Keywords: Influenza A virus, M۲e, HSPV۰, Protein expression, E.coli

machine learning and thyroid cancer metastasis (Review)

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Introduction: Thyroid cancer is a malignancy that can spread to other parts of the body, most commonly via lymphatic spread in papillary carcinoma and blood spread in follicular and anaplastic carcinoma. Machine learning techniques show promise in predicting thyroid cancer metastasis by analyzing patient data. This comprehensive study aims to investigate the prediction of distant metastasis in thyroid cancer through the application of various machine learning (ML) models. Distant metastasis significantly impacts patient prognosis, necessitating early identification of high-risk individuals to optimize treatment strategies and improve survival rates. The ability to predict metastasis accurately can lead to more personalized care, allowing clinicians to tailor interventions based on individual patient risk profiles.

Methods: This research was conducted by searching keywords, including machine learning and metastasis prediction, and thyroid cancer, through databases, including Scopus and PubMed. Upon examining the articles, a comprehensive conclusion was derived from the collective findings.

Results: The study showed that the dataset was usually from the National Institutes of Health (NIH) Surveillance, local, and End Results (SEER) database, encompassing demographic and clinicopathological characteristics of thyroid cancer patients from ۲۰۱۰ to ۲۰۱۵. Multiple machine learning algorithms, including Random Forest (RF), Support Vector Machine (SVM), Decision Trees (DT), and Extreme Gradient Boosting (XGBoost), were utilized to construct predictive models for distant metastasis, cervical lymph node metastasis (CLNM), lung metastasis (LM), and bone metastasis (BM) in patients with papillary thyroid carcinoma (PTC) and thyroid cancer (TC). Through univariate and multivariate analyses, the study identified independent risk factors such as age, gender, histological type, and lymph node involvement. Among the evaluated models, RF consistently demonstrated superior predictive performance, achieving an area under the receiver operating characteristic curve (AUC) of ۰,۹٤۸ for distant metastasis, ۰,۸۸۹ for CLNM, ۰,۹۹ for LM, and ۰,۹۱۷ for BM. The models' effectiveness was further validated using metrics like sensitivity, accuracy, and F۱ score. The BM prediction performance showed a sensitivity of ۰,۹۲۹, an accuracy of ۰,۹۰٦, and an F۱ score of ۰,۹۰۸.

Conclusion: The findings indicate that ML-based prediction models can significantly aid in clinical decision-making by accurately identifying patients at risk for various types of metastases. The RF model, in particular, provides a robust framework for predicting outcomes, thereby facilitating personalized treatment strategies and improving patient management in thyroid cancer cases. The

integration of these predictive models into clinical practice has the potential to enhance early diagnosis and intervention, ultimately leading to better patient outcomes.

Keywords: Machine learning prediction thyroid cancer metastasis

Magnetic and electric field study on bio-infections behavior (Research Paper)

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Introduction: Nucleation causes as a result of concentration gradient toward a core.cancering could cause as result of changes in combination.and diffusion causes polluting the whole body. Sptum appears by nucleation;which is a mixture of infections and some body products else.Kidney stone disease cause as a result of crystallization. Chemical infection ,dffuses via lungs and nasal system. Nucleation is the process of concentrating and aggregation of a species which leads to crystallization or precipitation. The ability of banning harmful processes will be discussed in this paper. Molecule polarity applies force to it in a electric or magnetic force. Dipole moments do so. This phenomenon is applied in electrophoresis which is important in Biotechnology. Freezing colud be effected by electricity[١].vapor pressure which is important in Crystallization is effected by electricity.some matter's Crystallization will be done by electricity.Polymorphism and solubility are effected by electricity as well.Electricity in case of internal and external electrical fields seems to be useful to controll the pollution.

Methods: The simulation of biological membrane is applied to test the possibility of it controlling. The simulated membrane is formed by bird egg as a result of constructional reassemblances[٢]. a.)Phospholypids:Animal cell cytoplasm is surrounded by two layers of phospholipids. The polar end of phospholipid molecules is towards the outside of the cell and the non-polar end (fat) is towards the inside of the cell (nucleus and cytoplasm) [٣].Licetine makes the micelle formation and double layers specially in aqua area. b.)Microfilaments: Microfilaments form the cellular skeleton. These fibers are influential in the formation and strength of the cell [٣].Chalaza consists of fibers , carbohydrates ,glycoproteins which are simillsar to celluar structures. c.).Proteins: Proteins are involved in the vague parts of the cell structure [٣]. various kinds of proteins(lyzozymes, Ovalbumin , ...) are involved in egg structure which are similar to celluar proteins.Food gelatins are also added to simulate collagen and glycoproteins as well.The role of proteins in the cell membrane for the exchange of materials is very prominent.[٣]

Results: A radio frequency carries energy ,in counterpoint electricity carries energy via particles(electron).while radio frequency passes any obstacle,electricity needs conductor to move. Radio frequency(electro magnetic wave) is consisted of magnetic and electric fields which is called polarity.By considering the the results of Single magnetic or electric fields Poynting vector[٦] is useful to rectify the effects .So as to electro magnetic fields. This ability called polarization and the mean is called polarizan.

Conclusion: Using Polarizans to effect the pollution for removing and enclosuring them is discussed in the article. By this ability pollution's nucleation and concentrating is used to enclose and remove them by the mean of electromagnetic wave and external electric field.

Keywords: infection,bio hazard,electric field,electromagnetic wave,Biotechnology

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Magnetic nanovesicles for the diagnosis and treatment of neurological diseases (Review)

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Introduction: Neurological diseases are increasingly being recognized as a global health challenge worldwide. There are significant issues for effective diagnosis and treatment of neurological diseases due to the presence of central nervous system (CNS) barriers. Magnetic nanovesicles are now well suggested as a potential theranostic option for improving the management of neurological disorders.

Methods: This work provides a summary of major CNS disorders and the physical barriers limiting the access of imaging/therapeutic agents to the CNS environment. The unique features of magnetic nanovesicles are discussed. Furthermore, a deeper understanding of magnetic nanovesicles as a promising combined strategy for diagnostic and/or therapeutic purposes in neurological disorders is provided.

Results: The diagnostic or therapeutic efficacy of nanovesicles can be significantly expanded by the addition of magnetic targeting, provided by the incorporation of magnetic nanoparticles. Magnetic nanovesicles are able to enrich at the target position, enhance cellular uptake, improve therapeutic efficacy, and thus minimize adverse effects of drugs under a magnetic field.

Conclusion: The multifunctionality of magnetic nanovesicles offers the ability to overcome the CNS barriers and can be used to monitor the effectiveness of treatment. Various in vivo experiments have demonstrated that magnetic nanovesicles possess remarkable potential for the management of neurological disorders. Although some issues need to be addressed, magnetic nanovesicles-based therapies will afford an effective theranostic strategy for neurological disorders in the future.

Keywords: Central nervous system (CNS), blood-brain-barrier (BBB), nanovesicle, magnetic nanoparticles

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Making a Natural Paint Solvent Based on Green Chemistry to Replace the Chemical Paint Solvent (Review)

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Introduction: In this project, it has been tried to find a suitable alternative to industrial solvents; Therefore, by selecting natural materials suitable for the properties of abrasiveness, degreasing, softening and antibacterial, a solvent compatible with the skin and the environment was made. In this project, sawdust is used as an abrasive, salt is used as an antibacterial agent, cleaner, surfactant and abrasive, from shebater butter and watermelon kernel oil as a softener, moisturizer and hydrator, from loofah plant as abrasive and exfoliant, from kaolin clay as an abrasive, antibacterial and analgesic for skin inflammation, and from beeswax as a preservative, disinfectant and analgesic for inflammation Dermal has been used. By mixing these materials under suitable environmental conditions with measured percentages, the expected solubility for oil paints was obtained.

Methods: Laboratory Method

Results: After determining the percentages of the substances, all the materials were melted by the Bon-Marie method, beeswax, argan oil, and shebater butter, and after they became worm-like, they were mixed with a mixture of sawdust, lake salt, and loofah plant, which had already been finely milled and sifted with a sieve. This product was stabilized at ambient temperature, and settling and biphasing did not occur for the product.

Conclusion: This product, along with its excellent solvency, without wear and burning sensation, not only gave the hand softness, freshness, and moisture, but also had a very pleasant smell

Keywords: Solvent Paint, Natural, Bio-Component, Paint

Making infection-resistant implants with nanotechnology (Review)

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Introduction: Implants are medical devices that save the lives of thousands of people every year in different ways. The existence of these implants has a major problem, and that is the high risk of infection by them. The surface of implants can be a suitable home for bacteria and provide a platform for their growth. This infection alone can increase the death rate. What is an implant? An implant is a set of parts that are surgically fixed inside the jaw, on which an artificial tooth is placed, and finally it looks similar to a natural tooth. In general, to place a dental implant, several steps must be done so that the constituent parts are placed next to each other and the patient can use it instead of a natural tooth. What is nanotechnology? Nanotechnology is the science of making materials smaller. Nanotechnology or nanotechnology is a field of applied knowledge and technology that covers a wide range of subjects. Its main topic is the containment of matter or devices with dimensions less than one micrometer, usually around ١ to ١٠٠ nanometers. In fact, nanotechnology is the understanding and application of new properties of materials and systems in these dimensions that exhibit new physical effects - mainly affected by the dominance of quantum properties over classical properties. Nanotechnology is a highly interdisciplinary knowledge and is related to fields such as materials engineering, medicine, pharmacy and drug design, veterinary medicine, biology, applied physics, semiconductor devices, supramolecular chemistry, and even mechanical engineering, electrical engineering, and chemical engineering.

Methods: Use of nanoparticles Smart implant

Results: The use of nanoparticles is a new emerging feature against ilm-mediated, drug-resistant, and device-driven antagonists. He used zinc gas nanoparticles (Zno), nanoparticles, gold carbon nanoparticles and iron oxide nanoparticles respectively. Smart implant: The researchers made a smart implant that is resistant to the growth and accumulation of bacteria and has a longer lifespan than other implants. This smart implant is made using a material that contains nanoparticles of barium titanate, which is resistant to the growth and accumulation of bacteria. . Also, this smart implant is equipped with an internal light source that obtains its required power from natural tooth movements such as chewing and provides the possibility of radiation therapy in the tooth tissue. According to researchers, the life of artificial teeth can be significantly increased by using smart implants. In this new implant, a combination of two technologies is used: ١) A substance containing nano particles that is resistant to the accumulation of bacteria. ٢) Installing a light source to perform phototherapy, which supplies the energy it needs through natural movements of the mouth, including chewing or brushing teeth. Phototherapy can solve many health problems, but unfortunately, it is not possible to replace or recharge the battery of the light source after implant placement. For this reason, a piezoelectric material has been used in this project. In addition to the inhibitory effect against the accumulation of bacteria and the occurrence of inflammation, this substance can produce the electrical power required for phototherapy through natural movements

of the mouth. In this research, the barium titanate (BTO) material, which has piezoelectric properties and is used in capacitors and transistors, was investigated, and in order to measure the antibacterial property potential of this material, BTO nanoparticle composite discs were exposed to Streptococcus mutans. took After that, the inhibitory effect of discs on biofilm formation was observed and it was seen that its inhibitory effect increases with increasing BTO concentration. According to recent findings, BTO repels bacteria for a long time by creating a negative surface charge because the cell wall of bacteria also has a negative charge. It is worth mentioning that this long-term effect of BTO is very important because the occurrence of contamination and bacterial infection is a time-consuming process. Another advantage of this material is its stable power generation properties and high mechanical strength compared to other materials used in dentistry.In addition, this substance is biocompatible and does not harm the gum tissue and can be used without causing side effects.

Conclusion: In this article, we tried to talk about the developments of the latest smart implant. According to the information of this article, it was found that new technologies have been added to smart implants, which definitely have a great impact on improving the performance of implants. But still newer technologies can be used to make and design smart implants In any case, the reason for using the latest smart implant is to reduce the complications and risks caused by placing the implant in the teeth. With the help of these implants, the need to take oral medications will decrease and the possibility of the implant being reversed by the tooth will also decrease. However, the practicality of each of these technologies is a question and ambiguity that exists for many people.

Keywords: Dental-implant-resistant-bacteria-nanotechnology

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Management of Shoulder Myofascial Trigger Points Can Decrease Neck and Shoulder Pain in Persons with Myofascial Pain Syndrome (Review)

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Introduction: Myofascial pain syndrome is a chronic condition that causes pain in the musculoskeletal system. The pain is typically related to trigger points in muscles. When pressure applied to trigger points, they can radiate pain to the affected area. Sometimes without pressure they also induce radicular pain. Myofascial trigger points in shoulder muscles can cause muscle stiffness, fatigue, headaches and postural abnormalities such as rounded shoulders and forward head posture. Therefore, management of myofascial trigger points are critical to restore the normal function of shoulder joint. The aim of the current study is to investigate the effect of treatment of shoulder muscles trigger points on shoulder pain in persons with myofascial pain syndrome

Methods: ١٥ persons (٩ women and ٦ men, and age range of ٤٦ ± ١٢,٣) with shoulder muscles trigger points participated in this study. All participants had no previous neck problems. Shoulder and neck pain intensity was measured by Visual Analogue Scale (VAS). The VAS consists of a ١٠cm line, with two end points representing ٠ (no pain) and ١٠ (pain as bad as it could possibly be). Participants were asked to rate their current level of pain by placing the mark on the line. VAS was determined before and after treatment period. Treatment procedures for shoulder muscles with trigger points included direct pressure on trigger points, stretching, using ultrasound and electrical stimulations. VAS results before and after treatment were analyzed using t pair test.

Results: Mean ± standard deviation of VAS before and after treatment was ٨ ± ٣,٢٤ and ٣ ± ٤,١, respectively. Significant decrease in VAS was identified after treatment in persons participated in the current study (P<٠,٠٥).

Conclusion: Results of the current study indicated that physical treatment of shoulder muscle trigger points can reduce pain and discomfort in persons with myofascial trigger points syndrome. Pain reduction in these persons might be helpful to have a better quality of night sleep and also improve their activities of daily living

Keywords: Myofascial syndrome, Trigger points, Physical treatment

Mechanism of effect of diferuloylmethane or curcumin in cancer treatment (Review)

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١.
٢.
٣.

Introduction: Cancer is one of the main causes of death in the world. Curcumin, the main ingredient of turmeric, which is widely used in the food industry, has shown anti-cancer properties on various types of cancer, and its main mechanisms of action include inhibition of cell proliferation and suppression. Invasion and migration, promoting cell apoptosis, inducing autophagy, reducing cancer stemness, increasing the production of reactive oxygen species, reducing inflammation, stimulating ferroptosis, intestinal microbiota, and adjunctive therapy. In addition, the anticancer effect of curcumin has been shown in clinical trials, while its poor solubility in water And the low bioavailability of curcumin can be improved with various nanotechnologies that increase the clinical effects, although curcumin shows side effects such as diarrhea and nausea, but it is generally safe and tolerable. This is an updated review article on prevention and The management of cancer by curcumin is due to the specificity of its mechanisms of action.

Methods: In this review study, the effects and mechanisms of curcumin on various cancers are summarized based on the results obtained from cell and animal models as well as clinical results published in the last five years, and special attention has been paid to the mechanisms of its effect. In addition, several technologies have been discussed to improve the bioavailability of curcumin. Finally, the adverse effects of curcumin have also been highlighted. This article will be useful for the application of curcumin in cancer prevention and management. In order to review the studies conducted in line with the topic of searching for Latin articles in the scientific databases of ISI Science Direct Scopus PubMed has been used because there are many articles related to curcumin in this study, it has been tried to use more articles which had a deeper and more important topic called research, in the selected articles, at least one of the following topics had been worked on Investigating the chemical structure, physical and chemical characteristics and reactions of curcumin in different chemical environments Curcumin bioavailability Antioxidant and anti-inflammatory properties of curcumin in the human body Curcumin bioavailability The effects of curcumin on various diseases ٦- Drug delivery using modern technology From the studied articles, ٢١ articles were selected, all of which were Latin, two review articles and the rest are scientific research.

Results: In a clinical trial to evaluate the effects of curcumin on various types of cancers, for example, a quasi-experimental design has been conducted in which ٤٠ stage two and three cervical cancer patients were given ٤ grams of curcumin per day for one week, which was simultaneously exposed to radiation. He also receives treatment They investigated. The results showed that the use of curcumin decreased the level of anti-apoptotic survivin protein in ١٥ patients, i.e. ٧٥٪, and increased the level of survivin in ٥ patients (i.e. ٢٥٪). Out of these ٤٠ patients, ٢٠ of them were monitored with placebos, and in ١٢ of them, ٦٠٪ survivin levels increased, and in ٨ of these

patients, survivin levels decreased in the placebo group. The results showed that curcumin is an effective radiation sensitizer. In the treatment of patients with cervical cancer. In addition, ١٥٠ female participants with advanced and metastatic breast cancer received curcumin ٣٠٠ mg per week + paclitaxel (٨٠ mg per square meter of body surface) or placebo + paclitaxel (٨٠ mg per square meter of body surface) for ١٢ received intravenously for a week. The results showed that curcumin improves the patient's self-assessed performance status and at the same time reduces fatigue and increases quality of life . Also, in ٩٧ patients with prostate cancer, who took ١٤٤ grams of curcumin daily for ٦ to ٣٦ months, the increase of specific antigen Prostate was suppressed during curcumin administration. However, curcumin did not show significant effects in some cases, for example, a randomized controlled trial showed that the effect A significant part was not observed with the supplementation of nano curcumin (١٢٠ mg) per day in prostate cancer patients undergoing radiation therapy. In addition, treatment with cocumin (٦ grams per day for ٦ weeks) had no significant benefit in metastatic castration-resistant prostate cancer. Contradictory results may be due to complex factors involved in clinical trials and require further research. Another study showed that curcumin significantly reduced tumor weight and tumor size in nude BALB/C mice with subcutaneous grafts. ٧٠٩١/SGC gastric cancer cells promoted miR٣٤a expression.

Conclusion: Cancer is a serious public health problem. Many studies have shown the effectiveness of curcumin in the prevention and management of various cancers such as Thyroid, breast, gastric, colorectal, liver, pancreatic, prostate, and lung cancers have reported potential mechanisms involving inhibition of cell proliferation. Cancer, suppression of invasion and migration, promotion of cell apoptosis, induction of autophagy, reduction of cancer stem, increase in production of reactive oxygen species, reduction of inflammation Stimulation, fructose regulation of intestinal microbiota and adjuvant treatment. Meanwhile, such nanomaterials can be used to prolong the release by targeted delivery of curcumin to cancer tissues and further increase its bioavailability. and the anticancer activities of curcumin have been developed These studies have shown that curcumin is safe and well tolerated, although some side effects such as diarrhea and nausea have been reported. will be In the future, the anticancer activity of curcumin on more cancers should be evaluated and its relative mechanisms should be investigated. and methods Another should be studied to improve the bioavailability of curcumin in order to increase its anticancer activity. Also clinical trials More needs to be done to evaluate the anticancer effects of curcumin on humans.

Keywords: anticancer,curcumin, safety, bioavailability, mechanism

Mechanism of Fertilization (Review)

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Introduction: Sexual reproduction occurs through fertilization during which two haploid gametes fuse to produce a genetically unique individual. Fertilization, the process by which the spermatozoon and the egg unite, occurs in the ampulary region of the oviduct.In nature, fertilization occurs only after both the oocyte and the spermatozoon have completed their final stages of cytoplasmic maturation. Sperm–oocyte interaction is a complex process of cell–cell interaction that requires species- specific recognition and binding of the two cells. Successful fertilization still requires controlled and correct activation of both sperm and oocyte.

Methods: Before spermatozoa can fertilize oocytes, they must first undergo biochemical and physiological modifications within the female reproductive tract. This process, referred to as capacitation, involves the removal of cholesterol and many glycoproteins from the surface of the spermatozoon, resulting in increased fluidity of the cell membrane. Capacitation, which commences in the uterus, is completed in the isthmus. The zona pellucida (ZP) is an extracellular matrix surrounding the oocyte and the early embryo that exerts several important functions during fertilization and early embryonic development A number of different molecules regulate these pathways, including calcium, bicarbonate, GABA, progesterone, angiotensin and cytokines. Phosphorylation of sperm proteins is an important part of capacitation, and this has been shown to be associated with the change in the pattern of sperm motility known as hyperactive motility, recognizable by an increase in lateral head displacement. There is also some evidence that spermatozoa can translate some mRNA species during capacitation

Results: In the human, capacitation in vivo probably starts while the spermatozoa are passing through the cervix. A low molecular weight motility factor found in follicular fluid, ovary, uterus and oviduct may increase sperm metabolism (and hence motility) by lowering ATP and increasing cyclic AMP levels within the sperm. Chemically defined media with appropriate concentrations of electrolytes, metabolic energy sources and a protein source (serum albumin) will also induce the acrosome reaction in a population of washed sperm. The removal or redistribution of glycoproteins on the sperm cell surface during capacitation exposes receptor sites that can respond to oocyte signals, leading to the acrosome reaction Capacitation is temperature dependent and only occurs at ۳۷–۳۹°C. Sperm surface components are removed or altered during capacitation. In vitro, the acrosome reaction cannot occur until capacitation is complete.

Conclusion: Several important molecules that regulate avian fertilization have been discovered but this is mainly derived from experiments that referred to mammalian studies. Because there are no efficient methods yet that would allow us to produce gene-manipulated birds, knowledge of the avian fertilization mechanism is limited. Placentation across mammalian species is vastly different

despite the similar goal of supporting the development of the offspring during gestation. Advances in technology such as single-nuclei RNA sequencing allow for further investigation of gene expression in distinct cell populations and how these change across developmental time.

Keywords: Fertilization, sperm capacitation, gamet activation, Acrosomal reaction

Mechanisms related to atorvastatin and insulin administration on nitric oxide production and vasodilation in vascular endothelial cells (Review)

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Introduction: Vascular endothelial cells play an important role in cardiovascular disorders. Atorvastatin is a oral medicine that reduces blood cholesterol levels by inhibiting ٣-hydroxy-٣-methylglutaryl coenzyme A reductase (HMG-CoA-R), thereby reducing endothelial cell damage. Subcutaneous insulin administration reduces blood glucose levels and vascular complications in hyperglycemic patients. NO is a factor produced in endothelial cells by endothelial nitric oxide synthase (eNOS). NO is critical to vasodilation. The aim of this study was to evaluate the mechanisms related to atorvastatin and insulin administration on nitric oxide production and vasodilation in vascular endothelial cells.

Methods: For this review, ٤٠ articles were found in the first stage. Strategy search in this case was as follows: the first five words (atorvastatin, insulin, nitric oxide, vasodilation, and endothelial cells) in the mesh PubMed dataset were initially identified. Then, we combined five words in the pattern of using AND and OR. In this study, human, animal, and in vitro studies were conducted were used.

Results: According to the conducted studies, atorvastatin is a lipophilic statin that easily passes through vascular endothelial cells. It increases eNOS mRNA stability and eNOS protein activity by inhibiting the RhoA/ROCK signaling pathway. Insulin increases eNOS activity by activating the PI٣K/PDK١/AKT pathway. NO leads to vasodilation by activating cGMP-dependent protein kinase (PKG). In addition, PKG inhibits the RhoA/ROCK pathway.

Conclusion: Atorvastatin and insulin activate mechanisms in vascular endothelial cells, leading to increased NO production, decreased vasoconstriction, and increased vasodilation.

Keywords: Atorvastatin, insulin, nitric oxide, vasodilation

Mechanistic Insights into the Role of Superoxide Dismutase in Skin Aging: A Novel Approach for Cosmeceutical Applications (Review)

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Introduction: Skin aging is a complicated biological process that is primarily impacted by variables associated with oxidative stress, which include an imbalance between an organism's antioxidant defense systems and the production of reactive oxygen species. One of the most important enzymatic antioxidants is superoxide dismutase, which catalyzes the neutralization of superoxide radicals-the most common ROS-into oxygen and hydrogen peroxide. SOD is considered the key protecting factor against cellular damage, characteristic of skin aging, by lessening oxidative stress. Its application in cosmeceutical formulations increases with the aim of stimulating collagen synthesis and inhibiting inflammation and degradation of the extracellular matrix that results in youthful skin. This review focuses on senescence action by SOD and its benefit and activity percutaneously.

Methods: This review compiles and analyzes data from scientific literature available in PubMed, and Google Scholar. AI-assisted research tools, such as Typeset.io, were employed to streamline the identification of relevant studies. The analysis focused on in vitro and in vivo studies that investigated the role of SOD in preventing skin aging. The impact of different SOD isoforms on oxidative stress reduction, collagen synthesis, and inflammation control was a key area of focus. Additionally, studies on SOD's clinical applications in dermatology, particularly its use in cosmeceuticals, were reviewed to provide a comprehensive understanding of its efficacy.

Results: The protective effects of SOD against aging are mediated through various signaling pathways, such as the AMPK and Nrf٢/HO-١ pathways, which regulate antioxidant response and promote collagen synthesis. Notably, studies have demonstrated that stable forms of SOD, such as highly stable SOD (hsSOD), can exert potent anti-aging effects. For example, in both in vitro and in vivo models, hsSOD reduced oxidative stress, enhanced skin thickness, and improved elasticity by promoting the formation of type I collagen. Furthermore, overexpression of SOD in transgenic models has been linked to increased collagen production and skin firmness, reinforcing its role in anti-aging skincare. SOD's anti-inflammatory properties also contribute to its anti-aging potential. The enzyme downregulates pro-inflammatory cytokines like TNF-α, IL-١β, and IL-٦, which are known to accelerate aging by inducing chronic inflammation. Through modulation of NF-κB and MAPK pathways, SOD reduces inflammation, thus preventing damage to skin cells and maintaining their function. In clinical settings, topical applications of SOD have shown promising results in improving skin texture, reducing wrinkles, and enhancing overall skin hydration. Additionally, oral supplementation with SOD has been found to increase total antioxidant status (TAS) in individuals with photoaged skin, reducing transepidermal water loss (TEWL) and improving skin moisture levels.

These findings underscore the broad applicability of SOD in addressing various aspects of skin aging, from structural degradation to inflammation and hydration.

Conclusion: The multifaceted role of superoxide dismutase in skin aging highlights its therapeutic potential in cosmeceutical and dermatological formulations. By neutralizing ROS, promoting collagen synthesis, and modulating inflammatory responses, SOD offers a comprehensive approach to delaying the aging process and maintaining skin health. The enzyme's ability to preserve skin structure, reduce oxidative stress, and enhance cellular resilience makes it a valuable ingredient in anti-aging products. Further advancements in the stability and bioavailability of SOD, particularly through innovative delivery systems, could enhance its efficacy and broaden its application in personalized skincare solutions. Moreover, understanding the genetic variability in SOD production and activity could offer insights into tailoring treatments for individuals with varying antioxidant needs. With further research, SOD has the potential to become a key ingredient in future anti-aging skincare therapies. However, more clinical studies are needed to optimize its use and confirm its long-term safety in cosmeceutical products.

Keywords: Superoxide Dismutase – Antioxidant – Aging – Cosmeceuticals – Dermatology

Medical informatics (Review)

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Introduction: Overview of Medical Informatics in Microbiology The integration of medical informatics in microbiology plays a crucial role in understanding the complexities of the human microbiome. As research in this field expands, the availability of data regarding microbiome composition and its functions grows significantly. This wealth of information allows researchers to explore the associations between the microbiome and various diseases more comprehensively. However, the unique characteristics of microbiome data, such as its compositional and heterogeneous nature, necessitate advanced analytical methods. Machine learning (ML) emerges as a powerful tool for analyzing these datasets, enabling the prediction of disease states through taxonomy-informed feature selection and the identification of state-specific microbial signatures. Such approaches not only aid in diagnostics but also hold promise for personalized medicine, enhancing therapeutic strategies tailored to individual microbiome profiles (L. Marcos-Zambrano et al.).

Methods: Role of Data Management Systems in Microbial Research The importance of data management systems in microbial research cannot be overstated, as these systems are essential for handling the vast amounts of data generated in microbiome studies. With the rise of advanced technologies such as high-throughput sequencing, researchers are inundated with complex data that require sophisticated tools for storage, analysis, and interpretation. Effective data management systems streamline the process of organizing this information, ensuring that researchers can efficiently access and utilize the datasets necessary for their investigations. Furthermore, integrating machine learning techniques within these systems enhances the ability to draw meaningful insights from the data, facilitating the identification of biomarkers and predictive models that inform clinical practices. Ultimately, robust data management is a critical foundation for advancing our understanding of the human microbiome and its implications for health and disease (L. Marcos-Zambrano et al.). Integration of Genomic Data in Microbial Informatics The complexity of microbiome data demands an innovative approach to analysis, particularly through the integration of machine learning techniques within data management systems. High-throughput sequencing generates large volumes of diverse data that are challenging to interpret without sophisticated analytical tools. These tools can help identify patterns and correlations between microbial communities and host health outcomes, which is essential for developing personalized medical interventions. Moreover, effective data management ensures that researchers can efficiently store, retrieve, and analyze these datasets, thereby enhancing their ability to discover novel biomarkers and predictive models. As highlighted in recent studies, the combination of robust data handling and advanced analytical methods like machine learning represents a significant advancement in our understanding of the human microbiome's role in health and disease (L. Marcos-Zambrano et al.).

Applications of Machine Learning in Microbial Diagnostics The integration of machine learning (ML) not only aids in the analysis of intricate microbiome data but also enhances the predictive capabilities of microbial diagnostics. By employing ML techniques, researchers can uncover hidden relationships within complex datasets, allowing for better identification of disease markers and health outcomes. This capability is particularly significant given the diverse nature of microbiome data, which often includes sparse and compositional aspects that traditional analytical methods struggle to address (L. Marcos-Zambrano et al.). As a result, ML applications facilitate a more nuanced understanding of how specific microbial communities influence health conditions, paving the way for personalized treatment strategies tailored to individual microbiomes. Such advancements are crucial for developing effective diagnostics, prognostics, and therapeutic approaches in microbial medicine. Challenges in Data Sharing and Interoperability Uncovering these intricate relationships through machine learning is vital for advancing diagnostics in the medical field. Moreover, the integration of blockchain technology can significantly improve data sharing in microbial diagnostics by ensuring data integrity and patient privacy. As highlighted in research, traditional data management systems face challenges related to security and interoperability (Pratik Thantharate and Anurag Thantharate). By utilizing a blockchain framework, like ZeroTrustBlock, researchers can secure sensitive health information while enhancing collaborative opportunities across diverse healthcare IT systems. This combination not only facilitates robust data sharing but also adheres to ethical and legal standards essential in healthcare settings (Yaara Sadeh et al.). Consequently, leveraging machine learning alongside blockchain could lead to more effective and equitable health outcomes by harnessing shared knowledge while protecting individual privacy.

Results: Future Trends in Medical Informatics for Microbiology Uncovering these intricate relationships through machine learning is vital for advancing diagnostics in the medical field. Moreover, the integration of blockchain technology can significantly improve data sharing in microbial diagnostics by ensuring data integrity and patient privacy. As highlighted in research, traditional data management systems face challenges related to security and interoperability (Pratik Thantharate and Anurag Thantharate). By utilizing a blockchain framework, like ZeroTrustBlock, researchers can secure sensitive health information while enhancing collaborative opportunities across diverse healthcare IT systems. This combination not only facilitates robust data sharing but also adheres to ethical and legal standards essential in healthcare settings (Yaara Sadeh et al.). Consequently, leveraging machine learning alongside blockchain could lead to more effective and equitable health outcomes by harnessing shared knowledge while protecting individual privacy. Furthermore, the growing body of microbiome-related studies necessitates advanced analytical tools to interpret complex datasets, as machine learning can uncover significant associations that aid in disease prediction and personalized medicine (L. Marcos-Zambrano et al.).

Conclusion: Future Trends in Medical Informatics for Microbiology Uncovering these intricate relationships through machine learning is vital for advancing diagnostics in the medical field. Moreover, the integration of blockchain technology can significantly improve data sharing in microbial diagnostics by ensuring data integrity and patient privacy. As highlighted in research,

traditional data management systems face challenges related to security and interoperability (Pratik Thantharate and Anurag Thantharate). By utilizing a blockchain framework, like ZeroTrustBlock, researchers can secure sensitive health information while enhancing collaborative opportunities across diverse healthcare IT systems. This combination not only facilitates robust data sharing but also adheres to ethical and legal standards essential in healthcare settings (Yaara Sadeh et al.). Consequently, leveraging machine learning alongside blockchain could lead to more effective and equitable health outcomes by harnessing shared knowledge while protecting individual privacy. Furthermore, the growing body of microbiome-related studies necessitates advanced analytical tools to interpret complex datasets, as machine learning can uncover significant associations that aid in disease prediction and personalized medicine (L. Marcos-Zambrano et al.).

Keywords: medical informatics

Medical Nanorobots: A New Era in Targeted Cancer Therapy (Review)

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Introduction: Despite significant breakthroughs in the diagnosis and treatment of malignant diseases, cancer remains a major global health challenge with high morbidity and mortality. As current therapeutic measures are often limited by tumor relapse and metastasis, innovative and effective treatment strategies are urgently needed. Recent and evolving advances in nanotechnology and nanomaterials have introduced novel approaches to cancer diagnosis and therapy. The development of nanorobots, a product of advanced nanotechnology and microfabrication techniques, has revolutionized cancer treatment by enabling precise interventions at the cellular level (١). Nanorobots can convert various energy sources into propulsive forces, enabling autonomous mobility. This holds great promise for precision in tumor diagnosis and therapy by overcoming the challenges posed by Brownian motion and facilitating targeted navigation to specific locations, in contrast to nanoparticle-based drug delivery systems, which depend solely on the enhanced permeability and retention (EPR) effect or active targeting through blood circulation. Because of their strong propulsion capabilities, nanorobots can readily traverse tissues and enhance drug uptake into cells, leading to the enhanced accumulation of therapeutic agents (٢-٤).Nanorobots designed for medical applications need to adhere to specific size criteria, ranging between ٠,٥ and ٣ µm, with individual components measuring ١ to ١٠٠ nm—a range crucial for navigating through capillaries in the human body (٥, ٦). These nanosized machines can deliver payloads (e.g., drugs, genes, sensing molecules) and perform specific biomedical functions such as diagnosis and therapy, enabling them to target tumor or disease sites. Nanorobots are powered by either active or passive systems, depending on their design and function. Such systems may receive external power sources (e.g., near-infrared (NIR) light, ultrasound, magnetic forces) or utilize biological mediums such as blood flow. A key difference between nanorobots and nanocarriers is the active power system of nanorobots (٧).

Methods: To prepare this abstract for a poster review, we searched various databases, including Google Scholar and PubMed, using keywords related to micro/nanobots and cancer detection. We selected the most relevant papers for inclusion.

Results: In recent years, the practical application of micro- and nanorobots in cancer treatment has advanced from theoretical concepts to real-world implementation, moving from in vitro experiments to in vivo applications. For instance, Andhari et al. engineered a multi-component magnetic nanorobot using multi-walled carbon nanotubes (CNTs) loaded with doxorubicin (DOX) and an anticancer antibody. This self-propelling nanorobot can be driven by an external magnetic field in complex biological fluids, releasing anticancer drug payloads within three-dimensional (٣D) spheroidal tumors. This release is triggered by changes in intracellular H_2O_2 levels or local pH in the

tumor microenvironment. The nanorobot, chemically conjugated with magnetic Fe_3O_4 nanoparticles, is designed to preferentially release DOX in the intracellular lysosomal compartments of human colorectal carcinoma (HCT١١٦) cells by opening a gate on the Fe_3O_4 surface (٨). Similarly, Wang et al. developed a nickel-silver nanoswimmer that can be powered by an external magnetic field, capable of delivering micron-sized particles at speeds exceeding ١٠ μm/s. Upon reaching the vicinity of human cervical cancer (HeLa) cells, the nanoswimmer released drug-carrying microspheres to kill the cancer cells (٩). Felfoul et al. discovered that biohybrid microrobots derived from Magnetococcus marinus strain MC-١ can be effectively maneuvered using an external magnetic field to transport drug-loaded nanoliposomes to hypoxic areas within tumors (١٠). Garcia et al. demonstrated the use of ultrasound-driven nanowire motors to deliver drugs rapidly to HeLa cancer cells, with ٣٨٪ of the DOX payload released within ١٥ minutes of near-infrared (NIR) light irradiation (١١). In addition, Deng et al. created NK cell-mimic nanorobots with aggregation-induced emission (AIE) properties by wrapping an NK cell membrane around an AIE-active polymeric nanoendoskeleton, enhancing their ability to target cancer cells (١٢). Dolev et al. designed a nanorobot capable of detecting circulating cancer cells in the bloodstream and delivering drugs to tumor sites. This nanorobot stored energy in a built-in capacitor, harvesting power from the bloodstream (١٣). Shi et al. introduced a nanorobot-assisted multifocal cancer detection procedure (MCDP) that employed a niche genetic algorithm (NGA) for accurate cancer detection (١٤). Song et al. created robust, magnetic tri-bead microrobots that respond to NIR light, releasing drugs when local temperatures reach ٥٠°C. These microrobots showed strong biocompatibility and effectively targeted tumor cells in vitro, demonstrating the potential of nanorobotic chemotherapy-photothermal therapy (١٥). While these advancements demonstrate the exciting potential of nanorobots in cancer treatment, their clinical implementation faces significant challenges. These include the development of nanoscale components, precise movement control, and ensuring stability in the biological environment. Additionally, the body fluid environment, particularly at low Reynolds numbers, presents further difficulties for nanorobot accuracy and speed. Biological interference from circulating proteins, blood cells, and immune cells can obstruct nanorobot functionality, slowing or even stopping their movements, and potentially leading to their removal from the bloodstream. Addressing these challenges will be critical for the successful use of nanorobots in clinical cancer treatments (١٦-١٨).

Conclusion: The integration of nanorobots into cancer therapy marks a significant advancement in the field of targeted treatments, offering a promising solution to overcome the limitations of current modalities, such as tumor relapse and metastasis. As evidenced by recent studies, nanorobots have transitioned from theoretical concepts to practical applications, with successful in vitro and in vivo experiments. However, despite their great potential, the clinical application of nanorobots faces several technical challenges. These challenges include the need for precise control over nanorobot movement, the stability of nanoscale components, and the management of biological interferences such as blood proteins and immune responses, which may impede their efficiency. Overall, nanorobots represent a promising frontier in cancer therapy, but further research and development are essential to overcome the technical and biological obstacles that currently limit their widespread use.

Keywords: Autonomous mobility, Cancer, Drug delivery, Nanorobots, Targeted cancer therapy

Medical Students as Partners: A trend of student engagement in the current era (Review)

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Introduction: Over the years, medical education has emerged as a crucial area of study, preparing individuals who can significantly impact human health and well-being, both directly and indirectly. A comprehensive understanding of medical students' activities reveals that they engage in a variety of curricular and extracurricular pursuits. These extracurricular activities extend beyond purely educational endeavors, encompassing a diverse array of interests such as research, innovation, and social engagement. However, the novel hypothesis is going to introduce medical students as partners in their learning systems and approaches who pass the way along to their teachers. The present study is going to review the potential role and acts of medical students as partners in their educational process.

Methods: To determine the aims of the present study, a comprehensive systematic search was conducted through electronic databases including PubMed, Scopus, Embase, and Web of Science with the keywords “Medical Education”, “Medical Students”, “Students as Partners”, and other related MeSH terms up to August ٢٠٢٤. Original studies, review studies, and references of the review studies were included. Finally, the studies that indicate the aspects of the medical students' partnership in their educational process were reviewed.

Results: According to the reviewed studies, the following aspects can be stated for the make the medical students as partners in educational process; collaborative learning (as interdisciplinary teams: Medical students often collaborate with nursing, pharmacy, and other healthcare students to gain a holistic view of patient care; and peer teaching: They can teach each other about different specialties or skills, fostering a collaborative learning environment.), Research Contributions (as clinical research: Students can assist in conducting clinical trials, collecting data, and analyzing results, contributing to advancements in medical knowledge; and quality improvement projects: They can participate in initiatives aimed at improving patient care processes within healthcare settings.), patient advocacy (as community engagement: Medical students often engage in community health initiatives, advocating for patient needs and health education; and patient-centered care: Involving students in patient care discussions can enhance communication and ensure that patients' voices are heard.), innovation and technology (as health tech development: Students can partner with tech developers to create innovative solutions for healthcare challenges; and telemedicine initiatives: They may help implement telehealth services, improving access to care for underserved populations.), feedback mechanisms (as curriculum development: Student input can be invaluable in shaping medical education curricula to better prepare future healthcare providers; and quality assurance: Their perspectives on patient care can help identify areas for improvement in

healthcare delivery.), and leadership development (as leadership roles: Medical students can take on leadership positions in student organizations, helping to shape policies and initiatives that impact their peers and the community; and mentorship opportunities: Engaging with mentors in clinical settings allows students to develop leadership skills while contributing to the education of others.)

Conclusion: In conclusion, by actively participating as partners in various aspects of healthcare, medical students not only enhance their own learning experiences but also contribute significantly to the improvement of patient care and the healthcare system as a whole. This partnership fosters a culture of collaboration, innovation, and continuous improvement in medical practice.

Keywords: Medical Education, Medical Student, Students as Partners, Partnership

Meta-analysis of sarcoma cancer data and analysis and evaluation of indigenous phenotypes of Iran POPULATIONsdfdgf (Research Paper)

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١.

Introduction: Sarcomas known as a fatal tumor broadcasting in tissues such as bone or muscles. soft tissue sarcomas (STSs) and malignant bone tumors (MBTs) are responsible for almost ١٢٪ and ٦٪ of all types, respectively. Given the insidious onset, younger age at presentation and atypical presenting symptoms, these patients may be initially clinically misdiagnosed with benign processes including myositis, synovitis, bursitis or tendonitis. Sarcomas are infrequent and diverse malignant tumors, accounting for less than ١٪ of all adult malignancies and ١٢٪ of pediatric cancers. Among different types of sarcomas, primary sarcoma of the thorax, is one of the least-known sarcomas, likely due to difficulties in diagnosis of this malignancy.

Methods: In this study, we used the National Center for Biotechnology Information (NCBI) database to identify prevalent single-nucleotide polymorphisms (SNPs) associated with sarcoma, focusing on two factors, citation frequency and population prevalence. we collected information on pharmacological treatment related to sarcoma including comprehensive assessment of their associated side effects. Subsequently, we used Mega Gene software, a tool widely used in pharmacogenomics to analyze and evaluated the compiled data.

Results: In this study, we found that EWSR١ and SDHD genes cause the genetic occurrence of sarcoma disease with the percentage of genetic impact based on the probability of occurrence in the studied statistical communities of ٤٧,٨٢٪ and ٥٢,١٧٪, respectively. In these genes, ١١ SNPs in the EWSR١ gene and ١٢ SNPs in the SDHD gene were identified as common SNPs involved in the occurrence of sarcoma disease, which were selected based on the two factors CITATION and POULATION. Also, in this study, the relationship between the side effects of the drugs used and the phenotypes of single nucleotide polymorphisms in the human genome was investigated, and it was found that CISPLATIN, manufactured by MYLAN, had an effect on the SNP, Rs ١٤٢١٠٨٥, on the FTO gene and caused genetic events. HAIR LOSS phenotype in patients who used it.

Conclusion: we found that phenotypes such as breast cancer or colorectal cancer may appear with sarcoma cancer in patients with found SNPs pointed in this article and also found side effects of drugs used to treat sarcoma such as hair loss, insomnia, hearing loss may have genetics background. Before prescribing any drug for chemotherapy to people with sarcoma, oncologists should conduct tests for them so that they can prescribe and use the most appropriate and effective drug with the least side effects based on the genetic profile of each person.

Keywords: Sarcoma, cancer, SNP, side effects

Metagenomic Analysis in the Context of leukemia: Exploring Novel Phenotypic Sequences

(Research Paper)

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Introduction: In recent years, advancements in statistical methodologies for estimating single nucleotide polymorphism (SNP) heritability have revolutionized our understanding of the genetic factors that contribute to complex diseases. SNP heritability refers to the proportion of phenotypic variance in a population that can be explained by genetic variation, specifically the SNPs present within the studied cohort. This concept is pivotal in understanding how genetic variants influence drug responses, disease susceptibility, and other complex traits. In the context of leukemia treatment, understanding genetic variation is particularly crucial. Individual differences in drug response and adverse effects can significantly impact the effectiveness of chemotherapy or targeted therapies, highlighting the need for personalized approaches in oncology. This study investigates the role of SNPs in three key genes—DKC١, CTC١, and TERT—which are involved in telomere maintenance and have been linked to cancer progression and treatment outcomes. By exploring the SNP profiles in these genes, we aim to uncover their potential effects on drug response and adverse drug reactions, contributing to the development of more personalized, genetically informed treatment strategies for leukemia patients.

Methods: To assess the genetic factors influencing drug responses in leukemia, we utilized polymorphism data from the National Center for Biotechnology Information (NCBI) database, which provides a comprehensive resource of genetic variants linked to various diseases and traits. This database was specifically used to extract SNP data for the genes DKC١, CTC١, and TERT—all of which play pivotal roles in maintaining telomere integrity, a process essential for cellular aging, proliferation, and cancerogenesis. These genes were selected for their relevance to leukemia, as disruptions in telomere maintenance are known to contribute to tumorigenesis and therapeutic resistance. The MEGAGENE software was employed to analyze these SNPs, allowing us to estimate their heritability and evaluate how variations in these genes might influence both the efficacy of leukemia therapies and the occurrence of side effects. Through this approach, we sought to explore the genetic basis for variability in drug responses, with the ultimate goal of providing insights into how genetic testing can guide more effective and personalized leukemia treatment.

Results: Our analysis identified several SNPs within the DKC١, CTC١, and TERT genes that were significantly associated with variations in drug efficacy and adverse drug reactions in leukemia patients. Notably, certain polymorphisms in the DKC١ gene were linked to an increased susceptibility

to severe side effects during chemotherapy, suggesting that these genetic variants might predispose patients to higher risks of toxicity. Conversely, specific SNPs in the TERT gene were associated with improved therapeutic responses, indicating that these variants may enhance the effectiveness of certain chemotherapy drugs and reduce treatment resistance. The CTC\ gene, involved in telomere maintenance, showed both positive and negative associations with drug efficacy, suggesting that it may play a dual role in modulating treatment outcomes. Overall, SNP heritability estimates for these three genes indicated that genetic variations in DKC\, CTC\, and TERT contribute significantly to the observed variability in drug response and side effect profiles. These findings underscore the importance of genetic testing in predicting patient-specific treatment outcomes and highlight the potential for tailoring drug therapies to minimize side effects and maximize therapeutic efficacy.

Conclusion: This study demonstrates the critical role of genetic variation in influencing drug responses and adverse effects, particularly in the context of leukemia treatment. Our findings suggest that genetic testing for SNPs in key genes such as DKC\, CTC\, and TERT can provide valuable information for guiding treatment decisions. By identifying genetic polymorphisms that are linked to either improved therapeutic outcomes or increased risks of side effects, clinicians can more accurately select the most appropriate drugs for individual patients. This personalized approach could reduce the likelihood of adverse reactions and enhance the overall effectiveness of leukemia therapies. The results from this study support the integration of pharmacogenomic testing into clinical practice, where genetic information can be used to tailor treatments to the unique genetic profile of each patient. In addition, our findings reinforce the growing emphasis on personalized medicine in oncology, where genetic testing is becoming an essential tool for optimizing patient care and improving therapeutic outcomes. Future studies should aim to validate these findings in larger patient cohorts and further refine the genetic markers that can be used to predict drug responses, ultimately leading to more effective and individualized treatment strategies for leukemia and other cancers.

Keywords: SNP heritability, Personalized Medicine, DKC\, CTC\, TERT

Metformin protects spermatological damages induced by cisplatin in rats (Research Paper)

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Introduction: Cisplatin (CP), a commonly prescribed anticancer drug, causes serious organ toxicity, including damage to male reproductive systems. Because of its extensive use in cancer treatment, there is an immediate clinical need to find ways to reduce its harm to healthy tissue. The reproductive toxicity of CP is mediated by inflammation and oxidative cascades. Metformin (MET), a common antidiabetic medicine, improves reproduction and lifespan by targeting organs and tissues with antioxidant and anti-inflammatory properties. Recently, MET has been shown to be effective in several testicular dysfunction models. The aim of the current study was to determine if MET treatment protects rats against spermatological damage induced by CP.

Methods: ٣٢ adult male Wistar rats, weighing between ٢٨٠ and ٣٢٠ grams, were subdivided into four groups, each with ٨ animals. The control group received MET solvent IP for ٢٠ days and three IP injections of physiological saline (PS) on days ٨–١٠. Animals in the CP group were injected IP with MET solvent for ٢٠ days and given three IP injections of ٢ mg/kg CP on days ٨–١٠. For ٢٠ days, the MET ٢٥+ CP group received IP MET (٢٥ mg/kg) and three IP CP (٢mg/kg) injections on days ٨–١٠. The MET ٤٠+ CP group received three IP injections of CP (٢ mg/kg) on days ٨ to ١٠, in addition to ٢٠ days of IP treatment with MET (٤٠ mg/kg). After ٢٤ h from the last Met injection, animals were sacrificed and spermatological parameters as progressive motility, viability, and morphological abnormalities were assessed.

Results: CP group exhibited significantly decreased sperm motility and viability along with increased head, neck, and tail defects than control. The results showed that rats treated with MET dose ٢٥ mg/kg only showed improvements in sperm viability; other sperm parameters did not change significantly when compared to the CP group. However, treatment with a ٤٠ mg/kg dose of MET could prevent all spermatological damage caused by CP.

Conclusion: According to our study, CP causes spermatological impairment in adult rats, which can be dose-dependently alleviated with MET treatment. This implies that MET should be evaluated further as a targeted protective drug against testicular damage caused by chemotherapy agents.

Keywords: Cisplatin; Sperm; Metformin

Microbiology and infectious diseases (Review)

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Introduction: Overview of Microbiology: Definition and Scope Microbiology is a vast field that encompasses the study of microorganisms, which are defined as microscopic entities existing in various forms, including unicellular and multicellular organisms. These microbes play crucial roles in different ecosystems and human health, influencing both positively and negatively. For instance, while many microorganisms contribute to essential processes such as oxygen production and nutrient cycling, some can cause diseases in both humans and plants (K. Maraz and R. A. Khan). The classification of microorganisms into five primary groups—Bacteria, Archaea, Fungi, Protozoa, and Viruses—illustrates the diversity within this field and the myriad interactions they have with their environments. This diversity necessitates a comprehensive understanding of microbial functions, particularly how they maintain ecological balance and support life on Earth.

Methods: Types of Microorganisms: Bacteria, Viruses, Fungi, and Protozoa Microorganisms are fundamental to the functioning of ecosystems, acting not only as decomposers but also as essential contributors to nutrient cycling and soil health. For example, bacteria play a pivotal role in breaking down organic matter, which enriches the soil and supports plant growth (K. Maraz and R. A. Khan). Additionally, certain fungi form symbiotic relationships with plants, enhancing their ability to absorb nutrients, while protozoa contribute to controlling bacterial populations in various environments. Viruses, though often considered harmful, can influence microbial diversity and community dynamics. This intricate web of interactions highlights the importance of understanding microbial functions, as they are vital for maintaining ecological balance and supporting life on Earth. The complexity and diversity within these groups underscore the need for continued research in microbiology to unravel their myriad roles. Pathogenesis: Mechanisms of Infectious Disease Development Understanding the mechanisms of infectious disease development requires a comprehensive grasp of host-pathogen interactions. Infectious diseases often occur through complex processes where pathogens exploit vulnerabilities in host defenses. Advances in molecular medicine have enhanced our ability to diagnose and control these diseases, leading to innovative therapeutic strategies (R. F. Franca et al.). For instance, methodologies such as single-cell RNA sequencing allow scientists to explore the heterogeneity of immune responses at an unprecedented level, revealing how different immune cells react to infections (Wanqiu Huang et al.). This detailed insight not only aids in understanding how pathogens evade immune detection but also informs the design of targeted interventions and vaccines, ultimately improving public health outcomes and controlling the spread of infectious diseases. Transmission of Infectious Diseases: Routes and Factors The intricate dynamics of infectious disease transmission are shaped by various environmental and biological factors. For example, pathogens may utilize multiple routes for transmission, which can be influenced by their genetic makeup and the ecological context (N. Rudenko and M. Golovchenko).

Climate change has altered the distribution of vectors like ticks, increasing human exposure to diseases such as Lyme borreliosis. This rise in cases is also attributed to urbanization and changes in wildlife habitats leading to closer interactions between humans and potential reservoirs of infection. Furthermore, advancements in molecular medicine not only improve diagnostic capabilities but also facilitate targeted prevention strategies, emphasizing the importance of research into these transmission mechanisms to better control the spread of infectious diseases (R. F. Franca et al.). Diagnosis of Infectious Diseases: Techniques and Tools Advancements in molecular medicine have significantly transformed the landscape of infectious disease diagnosis and management. The development of techniques such as the polymerase chain reaction (PCR) has allowed for rapid and precise identification of pathogens, which is critical for effective treatment (R. F. Franca et al.). These methods enable healthcare professionals to detect even low levels of infectious agents, facilitating timely interventions that can prevent outbreaks. Moreover, innovations in vaccine technology are directly linked to these diagnostic improvements, as they allow for the creation of targeted vaccines that bolster immunity against specific pathogens. Consequently, the interplay between enhanced diagnostic tools and vaccine development is essential for controlling the spread of infectious diseases, ultimately contributing to improved public health outcomes.

Results: Prevention and Control of Infectious Diseases: Vaccination and Public Health Strategies Furthermore, the strategic implementation of vaccination programs is vital in controlling infectious diseases. Vaccination not only reduces the incidence of disease but also contributes to herd immunity, protecting those who are unable to be vaccinated due to medical reasons. This is crucial for maintaining public health, particularly in vulnerable populations (M. Ishikawa). Additionally, as new pathogens emerge, the ability to rapidly adapt vaccines through advancements in molecular techniques becomes increasingly important. The continuous evolution of vaccines, driven by improved diagnostic methods and a deeper understanding of pathogen behavior, ensures that public health responses remain effective against evolving threats. Thus, integrating innovative vaccination strategies with robust diagnostic capabilities forms a comprehensive approach to mitigating the impact of infectious diseases on society.

Conclusion: Prevention and Control of Infectious Diseases: Vaccination and Public Health Strategies Furthermore, the strategic implementation of vaccination programs is vital in controlling infectious diseases. Vaccination not only reduces the incidence of disease but also contributes to herd immunity, protecting those who are unable to be vaccinated due to medical reasons. This is crucial for maintaining public health, particularly in vulnerable populations (M. Ishikawa). Additionally, as new pathogens emerge, the ability to rapidly adapt vaccines through advancements in molecular techniques becomes increasingly important. The continuous evolution of vaccines, driven by improved diagnostic methods and a deeper understanding of pathogen behavior, ensures that public health responses remain effective against evolving threats. Thus, integrating innovative vaccination strategies with robust diagnostic capabilities forms a comprehensive approach to mitigating the impact of infectious diseases on society.

Keywords: microbiology

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Microbiome and Immune System: A Symbiotic Nexus for Health and Disease Prevention (Review)

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Introduction: The proper interaction between the microbiota and the immune system is a prerequisite for health preservation. The human microbiome is a huge reservoir of microorganisms that consist of bacteria, fungi, viruses, and parasites, and is an active participant in immune regulation. This interplay is not simple coexistence, instead, the relationship affects core physiological processes as diverse as metabolism and immunologic defense. Subsequently, immune control will also manipulate the resident microbiota, establishing a balance that is fundamentally important for well-being. Imbalances in this interplay lead to immune-related maladies like autoimmune diseases and inflammation. For example, the Human Microbiome Project is an exemplary project to investigate the close relationship between the microbiome and immunity, and it emphasizes the necessity for ongoing studies. The deeper science penetrates, the more crucial comprehending this interconnectedness appears to developing treatments that normalize equilibrium and protect against diseases. This paper is a theoretical analysis of the role of the microbiome in modulating immune responses and the possibility of changed medical treatments.

Methods: For this study on the microbiome and immune system as a symbiotic link for health and disease prevention, we conducted a comprehensive review of ٦٢ articles. These sources were selected based on their relevance to the interaction between the microbiome and immune system, focusing on their roles in maintaining health, preventing immune-related diseases, and their mutual influence on each other. This method allowed us to gather diverse perspectives and insights to support our exploration of this critical connection.

Results: The information has been unequivocal for years that a balanced microbiome is exceedingly important in immune response regulation, which is manifested as both the immune tolerance and the defense from the pathogen. The studies have informed us that the disbalance of the microbiome is due to both the use of antibiotics and the dietary changes or environmental factors being the “disruptors” causing dysbiosis, which again is the leading cause of autoimmune diseases, inflammatory conditions, and infections. Moreover, the findings reveal that the early-life exposure to a broad variety of microorganisms uncontrollably developed immune systems, such as the hygiene hypothesis. What concerns objective support is that the use of Probiotics, Prebiotics, and Postbiotics as manipulative measures in balancing the microbes and consequently in ameliorating the immune function. In addition, the research represents the immune system if its various

components are involved in promoting such relevant processes as antimicrobial peptides and cytokine regulation and that the immune system, through the cooperation of the microbiota, actively directs its composition. This mutual communication indicates the promising perspective of individualized theories for preventing or rectifying the microbiota, as well as the novel paths of treating diseases or immunity issues. As a whole, the studies accumulate the beneficial reasons for the survival of the mucosal immunity and the prevention of the disease.

Conclusion: The healthy connection between the microbiome and the immune system in humans is essential, which, in turn, brings about a number of the most significant possibilities in disease prevention and management. Summary of our study shows that the immune system is only one of the reasons why the microbiome may prosper, and the immune system's proper functioning may be disturbed without it (the microbiome), which confirms the microbiome is amongst the key factors that reverses overactive immune reactions that could be happening when the host’s immune system is not recognizing an organism properly. Environmental factors, antibiotics, or dietary changes can all disrupt this equilibrium and lead to immune dysregulation, thus, to the rise of autoimmune diseases, inflammation, and infections. The research also shows the key role of microbiota on immunity. It thus becomes apparent, during the development of microbiota, that keeping the microbial diversity and balancing is the crucial moment resulting in the tolerance of the immune system. High quality understanding of the interplay between the microbial imbalance and the immune system will be the clue for the development of more sophisticated biomedical treatments focusing on the restoration of and immunity and well-being. The possible avenues for intervention in the future are mainly driven by the studies that are conducted in the field of microbe-immune system axis.

Keywords: Microbiome, Immune System, Symbiosis, Disease Prevention

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Microbiome and Skin Health: Challenges and Future Prospects in Cosmetic Biotechnology (Review)

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Introduction: The skin microbiome, a complex ecosystem of microorganisms, plays a critical role in maintaining skin health by supporting barrier function, modulating immune responses, and preventing pathogen overgrowth. As interest in microbiome research grows, the cosmetic biotechnology industry has recognized its potential for developing novel skin care products aimed at enhancing or restoring microbial balance. This review discusses the role of the skin microbiome in skin health and cosmetic outcomes, the challenges faced in understanding and manipulating the microbiome for cosmetic use, and the future of microbiome-targeted products.

Methods: We conducted a comprehensive review of current literature using PubMed and Google Scholar databases to gather studies on skin microbiome composition, functions, and its implications for cosmetics. Peer-reviewed articles, clinical studies, and reviews focusing on probiotic, prebiotic, and postbiotic skin care, alongside advancements in biotechnology for microbiome analysis, were included. Additionally, regulatory perspectives on microbiome-based cosmetic products were examined through industry reports and guidelines.

Results: The skin microbiome is composed of bacteria, fungi, viruses, and other microorganisms that coexist in symbiosis with the human host. It plays a pivotal role in maintaining skin health, but individual microbiomes can differ significantly based on factors such as genetics, environment, and lifestyle. This variability presents a significant challenge for developing universally effective microbiome-targeted cosmetic products. Despite these challenges, several advancements have been made, including the introduction of probiotic and prebiotic-based skincare products. These products aim to support a healthy skin microbiome, leading to improved skin barrier function and reduced inflammation. However, regulatory barriers and a lack of standardization remain key obstacles for widespread market adoption.

Conclusion: The intersection of microbiome research and cosmetic biotechnology offers exciting possibilities for personalized skincare. Probiotic, prebiotic, and postbiotic formulations have shown promise in enhancing skin health by targeting microbial imbalances. Despite the challenges posed by individual variability and regulatory hurdles, continued advancements in biotechnological tools for microbiome analysis and manipulation will drive the future of the cosmetics industry. Personalized skin care based on individual microbiome profiles may soon become a reality, allowing for more tailored and effective cosmetic solutions.

Keywords: Skin microbiome, cosmetic biotechnology, probiotics, personalized skincare, prebiotics

MicroRNAs functional roles in Meningitis (Review)

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Introduction: Inflammation of the meninges with an abnormal cell count in the cerebrospinal fluid (CSF) characterizes meningitis, and viral meningitis is prevalent in many countries. Diagnosis relies on examining cerebrospinal fluid obtained from lumbar puncture as clinical findings are also unreliable. Delayed initiation of antibiotics can increase mortality rates. Noncoding RNAs (ncRNAs) perform diverse biological functions. MicroRNAs (miRNAs) have emerged as primary regulators in various inflammatory conditions, and their gene regulation appears to be crucial in controlling abnormal inflammatory responses. Research has demonstrated that miRNAs play a significant role in CNS inflammation disorders, including meningitis, and exert their effects through multiple pathways.

Methods: This study was directed in the database of PubMed, and Google Scholar from June ٢٠٠٢ to Aug ٢٠٢٤, by searching for keywords comprising MicroRNA, MiRNA, Mir-, and Meningitis, in both title and abstract. Inclusion criteria encompassed most of the studies published in English that investigated different pathways and functions of microRNAs, and their impacts on Meningitis.

Results: Several miRNAs, such as miR-١٥٥-٥p, miR-٩٣-٥p, miR-٣٠c-٥p, miR-١٣٥a, miR-١٢٤, and miR-١٧-٥p, were found to interact with different biomolecules like MMP٣, lncRSPH٩-٤, Cx٤٣, SOCS١, STAT٣, and eIF٢α, impacting infection and inflammation through various pathways. Notably, miR-١٤٦a and miR-١٥٥ were discovered to modulate neuroinflammatory responses triggered by bacteria by negatively regulating the EGFR/NF-κB and TLR-mediated NF-κB signaling pathways. Additionally, genes and proteins, including circ_٢٨٥٨, also play a role in regulating certain miRNAs that can affect meningitis.

Conclusion: In various studies, it has been found that certain miRNAs are elevated in different types of meningitis and may function as potential biomarkers. Their elevated levels or suppression can signify varied effects on the condition. MiRNAs have the ability to stimulate the growth of astrocytes and inhibit cell apoptosis. Additionally, in viral meningitis, it has been suggested that miRNAs can increase the production of structural proteins essential for packaging the viral genome. While miRNA-mediated regulation typically yields negative outcomes, instances of positive regulation following miRNA binding have also been documented. Specific blocking of some of these miRNAs could be a potential strategy for preventing and treating meningitis in the future. For instance, the inhibition of miR-١٥٥-٥p can potentially decrease Angiostrongylus cantonensis-induced meningitis. These discoveries could indicate possible targets for therapeutic interventions against meningitis in the future, paving the way for innovative treatment approaches.

Keywords: Meningitis, MicroRNAs, Non-coding RNAs

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MicroRNAs in Alzheimer's disease (AD). (Review)

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Introduction: Alzheimer's disease (AD) is the most prevalent form of dementia, accounting for about ٧٠٪ of dementia cases. The risk of AD significantly increases after the age of ٦٥, rising to ٣٠٪ for individuals over ٨٥ years old. The typical symptoms of Alzheimer's disease begin with episodic memory loss and then progress to cognitive and behavioral impairments. Although the underlying cause of AD remains unclear, neurological inflammation, extracellular plaques, and intracellular fibrillary neurological complexities are significant pathological markers of the disease. Accumulating evidence in AD research suggests that changes in the microRNA (miRNA) network could contribute to the disease's risk. MiRNAs are conserved small non-coding RNAs that regulate gene expression at the posttranscriptional level and are crucial for neuronal function and survival. Recent profiling experiments in humans indicate that several specific miRNAs are dysregulated in disease conditions, some of which have been implicated in the regulation of key genes involved in AD. This review aims to summarize current findings on miRNA research, providing a robust foundation for future studies seeking to understand the potential role of miRNAs in AD pathophysiology.

Methods: In our research, we examined articles from several reputable sources including Scopus, PubMed, Google Scholar, Civilica, and ScienceDirect. Our search terms focused on miRNA, Alzheimer's disease, and biomarkers. We specifically targeted recent articles and their respective references, ultimately selecting ٩٦ out of ١١٠ articles as key sources. Our search was confined to articles published in English and Persian.

Results: Regulating gene expression through translation control is a pivotal factor that influences the disparity between mRNA and protein levels. Clinical research data highlights the significance of amyloid-B (AB٤٢), total tau (T-tau), and phosphorylated tau (P-tau) biomarkers in reflecting key aspects of AD pathophysiology. Variances in miRNA expression in patient tissues and their distinct enrichment in plasma, serum, and other bodily fluids have been observed, potentially indicating their utility in routine clinical diagnosis. Furthermore, studies have linked AD to platelet and vascular irregularities.

Conclusion: The personal and societal impact of AD poses challenges in quantification. The breadth of its effects spans multiple dimensions. Individuals diagnosed with AD encounter difficulties in recollecting daily activities and may manifest sleep and behavioral disturbances. Economically, the impact of AD is substantial and escalating. Concurrent with global population aging, the worldwide AD patient count is projected to reach ١١٥ million by ٢٠٥٠. As of now, there is no definitive AD treatment, but various symptomatic therapies, including anti-cholinesterase drugs and NMDA antagonists, are available. These treatments yield temporary enhancements in cognitive functions. The aforementioned intervention goals and strategies may foster the development of novel

pharmacological compounds. These compounds can be explored through various drug discovery techniques and potentially provide avenues for addressing AD, leading to the formulation of new treatment regimens for the disease.

Keywords: miRNA, Micro RNA, Alzheimer's disease, Biomarkers.

miR-١٥٥ and miR-٩٢ levels in ALL, post-transplant aGVHD, and CMV: possible new treatment options (Review)

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Introduction: Acute lymphoblastic leukemia (ALL) is a malignancy of lymphoid progenitor cells. Occurring ٨٠٪ of the time in children, it still constitutes a catastrophic disease when it comes to adults [١]. ALL is classified as B and T lymphoblastic leukemia (T-ALL, B-ALL) [٢]. In adults, ٧٥٪ of cases develop from precursors of the B cell lineage, with the remainder of cases consisting of malignant T cell precursors [١]. ALL can be cured in ٩٠٪ of children, whereas only ٤٠٪ of adult patients respond to treatment, possibly due to chromosomal abnormality and insensitivity to treatment. The hallmarks of ALL are chromosomal abnormalities and genetic alterations impacting the differentiation and proliferation of lymphoid precursor cells [١, ٣]. Many ALL subtypes are characterized by constellations of structural rearrangements, submicroscopic DNA copy number alterations, and sequence mutations, several of which have clear implications for risk stratification and targeted therapeutic intervention [٤]. Recently, an increasing number of studies showed that the microRNA (miRNA) expression profiles in acute leukemia have cooperative interactions in the development of leukemia. Therefore, the miRNA expression profile can be used as biomarkers in diagnosis, differential diagnosis, prognosis, and therapy of hematologic cancers [٥]. In developed countries, the overall survival of patients with ALL has increased to more than ٨٠٪; however, those children cured of ALL still show a significant risk of short and long-term complications as a consequence of their treatment. Accordingly, there is a need not only to develop new methods of diagnosis and prognosis but also to provide patients with less toxic therapies [٦].

Methods: In this cross-sectional study, ٧٠ newly diagnosed adults with ALL were recruited. The expression level of microRNA-١٥٥(miR-١٥٥) and microRNA-٩٢(miR-٩٢) was evaluated by real-time SYBR Green PCR. The correlations between the miRNAs mentioned above and the severity of disease, CMV infection, and acute graft vs. host disease after hematopoietic stem cell transplantation (HSCT) were assessed. B cell and T cell ALL distinction in the level of miRNAs was provided.

Results: After the statistical analysis, our results indicated a marked increase in the expression of miR-١٥٥ and miR-٩٢ in ALL patients vs. healthy controls (*P = ٠,٠٠٢–*P = ٠,٠٣, respectively). Also, it was shown that the expression of miR-١٥٥ and miR-٩٢ was higher in T cell ALL compared to B cell ALL (P = ٠,٠١–P = ٠,٠٠٤, respectively), CMV seropositivity, and aGVHD.

Conclusion: Our study suggests that the plasma signature of microRNA expression may act as a powerful marker for diagnosis and prognosis, providing knowledge outside cytogenetics. Elevation of miR-١٥٥ in plasma can be a beneficial therapeutic target for ALL patients, with consideration of higher plasma levels of miR-٩٢ and miR-١٥٥ in CMV + and post-HSCT aGVHD patients.

Keywords: miRNA, CMV, aGvHD , PBMCs , HSCT

MiR-٣٤a-loaded extra cellular vesicles derived from ٤T١ cells, effectively reduced ٤T١ cell migration capacity time-dependently (Research Paper)

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Introduction: Changes in tumor suppressor miRNAs is one of the leading cause of cancer progression. Mir-٣٤a is a well-known anti-tumor miRNA. An obstacle for therapeutic application of this miRNA is proper delivery vehicle. Characteristics of small extracellular vesicles (sEVs) make them a favored vehicle for delivering of therapeutic agents. As in triple negative breast cancer, finding an ideal therapeutic method is a real challenge, we aimed to apply tumor derived sEVs (tsEVs) for miR-٣٤a delivery in ٤T١ cells and evaluated its anti-migratory effects.

Methods: ٤T١ cells were cultured under proper cell culture condition and after reaching to a an approximate of ٨٠٪ confluency, FBS-free medium was added to the cells and after ٤٨ hours, the conditioned media was gathered for tsEV purification by commercial kit. The purified tsEVs were characterized by scanning electron microscopy (SEM), dynamic light scattering (DLS) and bicinchoninic assay (BCA). To load miR-٣٤a, modified CaCl٢ method was conducted. Confirmation of loading was done by Real-time PCR method.٤T١ cells were cultured in ٦ well plate and after ٢٤ hr a scratch was created by a ٢٠٠µl pipette tip, afterwards each well was treated by ٢٥µg/ml of tsEVs and miR-٣٤a-tsEVs, respectively. Untreated cells were considered as control group. An image was taken from each treated group after ٠, ٦, ١٢ and ٢٤ hr. The images were analyzed by image J software according to percentage of re-filled scratch area. Statistical analysis was performed by ANOVA test and Graph pad Prism ٨ software.

Results: Our data showed that treatment with miR-٣٤a-tsEV significantly reduced migration capacity of ٤T١ cells in a time-dependent manner, which the highest scratch test was detected in this group after ٢٤ hr. In contrast tsEV group showed the highest invasion capacity after ٢٤ hr.

Conclusion: Taken together, our results revealed that, tsEV modification for loading miR-٣٤a might be considered as a new way of miR-٣٤a delivery into triple negative breast cancer cells which may provide new insights toward using this method for miRNA-replacement therapy.

Keywords: Breast cancer, exosome, invasion, scratch test

MIR۷-۳HG Long non-coding RNAs and testicular germ cell tumors (TGCT): an update of potential biomarkers (Research Paper)

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Introduction: Malignant testicular tumors are rare, but testicular germ cell Tumors (TGCT) is the most common cancer among men between ۱۵ and ٤۰ years of age and is the leading cause of cancer-related mortality and morbidity in this age group. Although it has been shown that the expression of many genes play a role in the pathogenesis of this disease, there is little information about the changes in the expression of MIR۷-۳HG long non-coding RNA in this cancer. The aim of this study was to investigate the expression changes of MIR۷-۳HG gene in TGCT and introduce it as a diagnostic and prognostic biomarker.

Methods: In order to investigate the expression changes of MIR۷-۳HG in TGCT, TCGA data provided by oncodb database was used. Also, the Roc-curve chart was used to evaluate the diagnostic biomarker potential.

Results: Our results showed that the expression level of MIR۷-۳HG non-coding RNA in cancer samples of TGCT patients is significantly increased compared to normal samples (log FC=-٤,۸, p-value ۱,۱e-۲۹, FDR < ۰,۰۰۱). Also, the ROC-curve chart indicated that the expression changes of this gene can be used as a diagnostic biomarker to diagnose people with this type of cancer (AUC = ۰,۹۹۸۷, p-value < ۰,۰۰۰۱).

Conclusion: The results of our study showed that the expression level of MIR۷-۳HG is decreased in TGCT patients. We also showed that the expression level of MIR۷-۳HG can be considered as a diagnostic and even prognostic biomarker.

Keywords: MIR۷-۳HG, long non-coding RNAs, TGCT, biomarker

Mitochondria at the Crossroads: Unveiling the Link Between Sjögren's Syndrome and Mitochondrial Dysfunction (Review)

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Introduction: Sjögren's Syndrome (SS) is a chronic autoimmune disorder primarily characterized by the destruction of exocrine glands, leading to symptoms such as dry mouth and eyes. Despite significant research, the precise mechanisms driving this glandular dysfunction remain unclear. Emerging evidence suggests a potential link between mitochondrial dysfunction and the pathogenesis of autoimmune diseases, including SS.

Methods: A comprehensive review of the literature was conducted, focusing on clinical observations, molecular studies, and experimental data that investigate mitochondrial involvement in SS. The review also examines how mitochondrial dysfunction can influence key pathological processes, such as oxidative stress, apoptosis, and immune responses

Results: The review reveals that mitochondrial dysfunction plays a critical role in the pathophysiology of SS. Mitochondrial abnormalities, such as impaired oxidative phosphorylation and increased production of reactive oxygen species, lead to significant cellular damage and energy deficits in exocrine glands. That is why the administration of antioxidants may be effective in the prevention and treatment of this syndrome. This dysfunction exacerbates oxidative stress, promoting chronic inflammation and contributing to the glandular destruction characteristic of SS. Additionally, mitochondrial-mediated apoptosis and the release of mitochondrial DNA act as triggers for sustained immune responses, furthering tissue damage and autoimmune activity. Moreover, mitochondrial dysfunction impacts immune cell behavior, particularly in T cells and macrophages, driving a pro-inflammatory phenotype that worsens the autoimmune response in SS. This dysfunction is also implicated in the formation of ectopic lymphoid structures within the salivary glands, which are associated with severe disease and increased autoantibody production. These findings suggest that mitochondrial dysfunction is a driving factor in SS pathogenesis, highlighting the potential for novel therapeutic strategies targeting mitochondrial health to slow disease progression and improve patient outcomes.

Conclusion: Understanding the role of mitochondrial dysfunction in SS opens new avenues for therapeutic intervention. Targeting mitochondrial health through antioxidants, mitochondrial biogenesis enhancers, and personalized medicine approaches based on mitochondrial biomarkers could offer promising strategies for managing this debilitating disease. Further research is needed to

fully elucidate the complex interplay between mitochondria and autoimmune processes in SS, which could lead to more effective treatments and improved patient outcomes.

Keywords: Sjögren's Syndrome, mitochondrial dysfunction , autoimmune diseases, reactive oxygen species

Mitochondrial cristae in health and disease (Review)

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Introduction: Mitochondria are oval-shaped intracellular organelles ۰,۵–۱۰ µm in diameter that exist in a majority of cells and are enclosed by two membranes. Owing to their function of efficient adenosine triphosphate (ATP) generation via aerobic respiration to sustain normal cellular activities, mitochondria are often called the “powerhouse of the cell.” Mitochondrial oxidative phosphorylation (OXPHOS) is the central mechanism of energy generation and is carried out by the electron transport chain (ETC) located in the inner membrane of the mitochondria. By coupling the oxidation of reducing equivalents produced by the tricarboxylic acid (TCA) cycle and the transportation of electrons, ATP production is driven by the ETC. Mitochondria contain their own DNA (mtDNA), which encodes proteins required for OXPHOS and is replicated independent of nuclear DNA. In addition to energy production, mitochondria also engage in other processes, including reactive oxygen species (ROS) generation, calcium flux, and apoptosis, to maintain cellular homeostasis.intramitochondrial phospholipid transport by conserved Ups-Mdm۳۵ complexes and MICOS (mitochondrial contact site and cristae organizing system) cooperatively contribute to tubular crista formation, whereas mitochondrial inner membrane fusion by Mgm۱ plays a critical role in lamellar crista formation.

Methods: In this review, we focus on key regulators of cristae structure, including the mitochondrial contact site and cristae organizing system, optic atrophy-۱, mitochondrial calcium uniporter, and ATP synthase, which function in the dynamic remodeling of cristae. We summarized their contribution to sustaining functional cristae structure and abnormal cristae morphology, including a decreased number of cristae, enlarged cristae junctions, and cristae as concentric ring structures. These abnormalities directly impact cellular respiration and are caused by dysfunction or deletion of these regulators in diseases such as Parkinson's disease, Leigh syndrome, and dominant optic atrophy. Identifying the important regulators of cristae morphology and understanding their role in sustaining mitochondrial morphology could be applied to explore the pathologies of diseases and to develop relevant therapeutic tools.

Results: the space between the two membranes is called the intermembrane space (IMS), and the inner membrane is divided into three specialized zones, namely the inner boundary membrane (IBM), cristae junctions (CJs), and cristae. Cristae are bag-like structures formed by the folding of IMM and provide places of residence for complexes I–V of OXPHOS. The MICOS is a complex of a plethora of proteins that staples the cristae together at the junctions.many factors participate in the regulation of cristae morphology. Depending on their location, these proteins can be divided into two categories: members located in CJs (ATP synthase) and those at the tip of cristae (MICOS, OPA۱, and MICU۱). When these proteins are disrupted or disturbed, their effects on mitochondrial cristae morphology differ significantly. Loss or dysfunction of proteins located in CJs leads to aberrant

cristae morphology, such as wider cristae junctions, decreased cristae number, or loss of cristae. Abnormal mitochondrial cristae morphology is also observed in many diseases, including Parkinson's disease (PD), Leigh syndrome, and dominant optic atrophy (DOA), because different proteins regulate the executive functions of the cristae architecture in their pathological processes. PD is a progressive neurodegenerative disease that affects peripheral organs as well as the central nervous system. PARK is a family of genes that encodes proteins such as α-syn, LRRK٢, VPS٣٥, Parkin, PINK١, and DJ١, whose mutations lead to monogenetic PD and thus play an important role in the pathogenesis of PD.

Conclusion: Mitochondrial cristae are functional compartments that ultrastructure can be altered under different conditions. As mentioned above, although many mitochondrial-shaping proteins are known to be involved in cristae remodeling, a well-developed, comprehensive network of their respective roles and interactions requires further exploration. It is noteworthy that how multiple metabolic requirements of different cell types are met by the cristae remodeling. In some diseases, more than one factor is altered in mitochondrial cristae remodeling. The primary and secondary roles between them and how these roles need to be proven should be addressed in future studies.

Keywords: Mitochondria Cristae ultrastructure OPA١ MICOS MICU١

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Model of neuropathic pain in Drosophila and Drosophila larvae using cisplatin (Research Paper)

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Introduction: Neuropathic pain, a debilitating condition affecting up to ١٠٪ of the population, significantly impacts quality of life, contributing to stress, anxiety, depression, and disruption of daily routines. This type of pain arises from various factors, including diabetes, radiculopathy, nerve damage, and the use of anticancer drugs. Notably, chemotherapy-induced neuropathic pain, particularly associated with platinum-based agents like cisplatin, poses a significant clinical challenge. While cisplatin remains a crucial therapeutic option for various cancers, its use is often limited by the development of neuropathic pain. The precise mechanism underlying cisplatin-induced neuropathic pain remains elusive, highlighting the urgent need for further research. To facilitate such investigations, the establishment of an animal model utilizing cisplatin is essential to unravel the underlying mechanisms and explore potential therapeutic interventions.

Methods: In this study, wild-type Drosophila melanogaster and Drosophila third instar larvae were used to create a neuropathic model due to their physiological similarity to humans. Concentrations of ١٠٠ mg/L and ٢٠٠ mg/L of cisplatin were added to the Drosophila culture medium, and after ٦ days of feeding, the flies were isolated from the culture medium for the Hotplate test, and the duration of the flies' establishment on the hot plate It was recorded at temperatures of ٤١ to ٥٠ degrees Celsius. (n=١٠) for Drosophila larvae, the larvae were placed on ٣ cc of physiological serum on a hot plate, and the number of their movements during one minute was The temperature was observed and recorded from ٣٥ to ٤١ degrees (n=١٠).

Results: One-way analysis of variance was performed using Graphpad prism١٠ software. The cisplatin group with a concentration of ١٠٠ mg/liter was not significantly different from the control group. (pANOVA>٠,٠٥) The ٢٠٠ mg/liter cisplatin group had a significant difference with the control group and the cisplatin group with a concentration of ١٠٠ mg/liter. (PANOVA< ٠,٠٥). In Drosophila larvae, there was no significant difference between the ١٠٠ mg/L cisplatin group and the larval control group at any of the tested temperatures. (pANOVA>٠,٠٥) The larvae of ٢٠٠ mg/L cisplatin group were significantly different from the control group at temperatures of ٣٨ and ٤١ degrees. Being on the hot plate died.

Conclusion: The results show that ١٠٠ mg/L cisplatin does not cause neuropathic pain in adult Drosophila and its larvae, and ٢٠٠ mg/L cisplatin causes neuropathic pain and hyperalgesia at all tested temperatures in larvae and Drosophila matures.

Keywords: Urtica dioica, Drosophila melanogaster, stinging nettle, neuropathic pain, CIPN

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Modeling Neurological Diseases Using Endogenous Pluripotent Stem Cells (Research Paper)

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Introduction: Neurological diseases pose significant challenges due to their complex pathophysiology and limited treatment options. Traditional models often fail to capture the intricacies of human disease. Endogenous pluripotent stem cells, derived from somatic tissues, present a promising alternative for modeling these conditions. This article reviews recent advancements in ePSC technology and its application in studying various neurological disorders, including Alzheimer's disease and Parkinson's disease.

Methods: Cell Line Development: Endogenous pluripotent stem cells (ePSCs) were derived from somatic tissues of patients diagnosed with various neurological disorders. The reprogramming process involved using non-integrative methods to minimize genomic alterations. ۲. Differentiation Protocols: ePSCs were differentiated into neural progenitor cells and subsequently into specific neuronal subtypes using defined growth factors and culture conditions tailored for each lineage. ۳. Characterization: The differentiated cells were characterized using: - Immunocytochemistry: To assess the expression of neural markers (e.g., βIII-tubulin, MAP۲). - Gene Expression Analysis: Quantitative PCR was performed to evaluate the expression levels of genes associated with neurological diseases. Functional Assays: Electrophysiological recordings and calcium imaging were conducted to assess neuronal functionality.

Results: Key findings reveal that ePSCs can differentiate into various neural lineages and exhibit disease-relevant characteristics. For instance, ePSC-derived neurons from Alzheimer's patients showed increased amyloid-beta accumulation, while those from Parkinson's patients displayed impaired mitochondrial function. These results underscore the validity of ePSCs as a tool for studying the underlying mechanisms of neurological diseases

Conclusion: Endogenous pluripotent stem cells represent a powerful resource for modeling neurological diseases, offering insights into their pathogenesis and potential therapeutic interventions. Future research should focus on refining ePSC technologies and expanding their applications to a broader range of neurological disorders.

Keywords: Endogenous Pluripotent Stem Cells Neurological Diseases

MOF-based immunosensors for the determination of carcinoembryonic antigen: A concise review

(Review)

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Introduction: Carcinoembryonic antigen (CEA) as a crucial for glycoprotein cell adhesion during fetal development serves as a specific tumor marker for pancreatic, breast, and colon cancers. Elevated levels of CEA above ٥ ng mL-١ in serum/plasma indicate an increased risk of these diseases. In the existence of CEA antigen identified as a tumor marker, the body produces antibodies (Abs) to help fight them. Accurate and rapid determination of CEA is essential for effective cancer treatment and clinical diagnosis. Hence, the advancement in selective and sensitive CEA determination is significant in clinical medicine. Metal organic frameworks (MOFs) are porous crystalline materials that have mostly received consideration for high-efficiency signal probes due to their large specific surface area, high porosity, and adjustable size and morphology. In this regard, immunoassay strategies using antigen-antibody interactions are crucial for precise measurement of target molecules in biochemical fields. This article discusses recent advancements in MOF synthesis methods and functionalization mechanisms with antigen/antibody for CEA immunoassays, employing electrochemical, electrochemiluminescent, and colorimetric techniques.

Methods: New ideas are provided for the development of efficient and novel immunoassay strategies due to the remarkable properties of MOF-Ab materials. Based on the type of detection, various immunosensors such as colorimetric, electrochemical, and electrochemiluminescent (ECL) immunosensors are constructed and their main features are summarized.

Results: In recent years, immunosensing techniques utilizing MOF-derived nanocomposites have gained popularity due to their rapid detection, high sensitivity, and selectivity, particularly in CEA monitoring. Thereinto, current techniques for the MOF's synthesis and MOF-derived nanocomposites and their employment as detection platforms in immunosensors for CEA determination, are thoroughly discussed.

Conclusion: Immunosensors based on MOF-derived composites are still in the early stages of development, with advancements primarily observed in laboratory settings. It is crucial to further develop ECL, electrochemical, and optical immunoassays utilizing MOFs for practical applications with minimal user intervention. Future research efforts should prioritize the design of immunosensors and data transfer mechanisms to ensure both effectiveness and ease of use.

Keywords: Immunoassay; Metal organic framework; Synthesis and application; Biomedical analysis

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Molecular biology of human breast carcinoma metastasis (tumor progression) (Review)

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Introduction: Breast cancer is the most common malignancy in women worldwide. Metastasis is the leading cause of high mortality in most cancers. Breast cancer comprises five molecular subtypes that have distinct prognosis and treatment strategies. These five subtypes include: luminal A (ER+, PR+, Ki٦٧ < ٢٠٪), luminal B (ER+, PR+ or PR-, Her٢+ or Her٢-, Ki٦٧ > ٢٠٪), triple-negative (ER-, PR-, HER٢-), and HER٢-enriched breast cancer (ER+, PR+), (HER٢+). The absence of receptors on the surface of tumor cells of breast cancer is one of the signs of aggressive status and poor prognosis. The most aggressive subtypes include HER٢ neu-positive and triple-negative breast cancer (TNBC). Although predicting the early stage of breast cancer before metastasis can increase the survival rate, breast cancer is often discovered or diagnosed after metastasis has occurred. The progressive expansion of cells at a location distant from the source tumor is referred to as metastasis. Cells can spread throughout the body through the lymphatic system, blood vessels, or cavities. the molecular biology of human breast cancer metastasis was the goal of this investigation.

Methods: This review study used scientific databases such as Science Direct, Springer, Google Scholar, and PubMed about title of investigating Molecular biology of human breast carcinoma metastasis (tumor progression).

Results: Malignant and metastatic tumors can be distinguished in more subtle ways. Several morphologic characteristics, such as less differentiated cytology, vascularity, necrosis, mitotic index, aneuploidy, and nuclear: cytoplasmic ratio is used by pathologists to describe malignancy. An invasion of cells via a basement membrane and/or metastasis are undeniable signs of cancer. There are some exceptions to every other trait used to classify a tumor as malignant. When the wild-type expression of tumor suppressor genes is reinstated in a cancer cell, the gene's ability to develop a tumor is strongly inhibited. Therefore, by definition, metastasis ought to be prevented as well. On the other hand, metastasis suppressor genes solely prevent the development of metastases. Cells that are still tumorigenic but no longer metastatic would result from re-activating a metastasis suppressor gene.

Conclusion: Studies revealed a correlation between the onset and/or progression of breast cancer and the differential expression of over ١٥٠ genes. However, to date, only six human metastasis-suppressor genes NME١ KiSS١, KAI١, CAD١, BRMS١, and MKK٤—have been shown to exhibit functional activity utilizing in vivo metastasis. Complex genetics underlie metastasis in general and breast cancer in particular.

Keywords: Breast Carcinoma, Metastasis, Tumor, malignant

Molecular docking based investigation on the emetine as EGFR inhibitor in colorectal cancer

(Research Paper)

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Introduction: Colorectal cancer is one of the most common malignancies in the world that needs serious attention. One of the causes of this cancer is the dysregulation of the epidermal growth factor receptor (EGFR), which plays an important role in functioning cell division, differentiation, apoptosis, and migration. Therefore, in this study, emetine with potential anticancer activity was investigated for its binding affinity to the EGFR receptor in colorectal cancer.

Methods: The EGFR protein ٣D structure was retrieved from the Protein Data Bank, and the molecular docking was carried out using AutoDock software. The ٣D structures of emetine and erlotinib (control compound) were obtained from Pubchem and converted into PDB format by AutoDock software. Then, these compounds were docked into the active site of EGFR (PDB ID: ١M١٧) by AutoDock software.

Results: Molecular docking results showed that the emetine compound had a good binding towards EGFR protein by forming two hydrogen bonds with KV٢١ and EV٣٨. Also, the emetine compound was presented for computational ADMET and Lipinski analysis.

Conclusion: Emetine has a high potential to inhibit the EGFR enzyme and can show promising results in colorectal cancer treatment after further studies.

Keywords: Colorectal cancer, EGFR, Emetine, Molecular Docking

Molecular Docking Study of Telmisartan and Valsartan with miR-۲۷a-۵p: Insights into Therapeutic Efficacy for Diabetic Neuropathy (Research Paper)

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Introduction: Initial explorations into the diabetes-centric drug interactions were performed. Diabetes was queried using the DrugBank database, and Telmisartan and Valsartan were identified as candidate drugs for the treatment of this disease. Their respective ۳D structural files were obtained from the PubChem website. Two ligands were separately optimized using the Chimera software to prepare the drugs for further analysis. A literature review showed that miR-۲۷a-۵p had a significant role in the pathophysiology of diabetes and its expression levels were found to be higher in diabetic patients. The sequence of the said microRNA was retrieved from the web servers of miRDB and UNAFold, and the final file was prepared for docking operations. Further employment of the ViewerLite program was done to get rid of the attached water molecules to the miRNA molecule since the docking operations require the absence of additional molecules and the removal of any inappropriate bonds. The receptor, which in this case is miR-۲۷a-۵p, was prepared in Discovery Studio for docking by adding polar hydrogens-add polar option. After that, the docking of both Telmisartan and Valsartan individually with miR-۲۷a-۵p was performed through the use of AutoDock software in order to gain the output.

Methods: Initial explorations into the diabetes-centric drug interactions were performed. Diabetes was queried using the DrugBank database, and Telmisartan and Valsartan were identified as candidate drugs for the treatment of this disease. Their respective ۳D structural files were obtained from the PubChem website. Two ligands were separately optimized using the Chimera software to prepare the drugs for further analysis. A literature review showed that miR-۲۷a-۵p had a significant role in the pathophysiology of diabetes and its expression levels were found to be higher in diabetic patients. The sequence of the said microRNA was retrieved from the web servers of miRDB and UNAFold, and the final file was prepared for docking operations. Further employment of the ViewerLite program was done to get rid of the attached water molecules to the miRNA molecule since the docking operations require the absence of additional molecules and the removal of any inappropriate bonds. The receptor, which in this case is miR-۲۷a-۵p, was prepared in Discovery Studio for docking by adding polar hydrogens-add polar option. After that, the docking of both Telmisartan and Valsartan individually with miR-۲۷a-۵p was performed through the use of AutoDock software in order to gain the output.

Results: Moreover, the docking simulations have shown that through an open Guanine ۱۸, the receptor has a strong hydrogen bond with Telmisartan. In the same direction, a strong hydrogen bond was formed between the receptor and Valsartan through the same open nucleotide. Additionally, miR-۲۷a-۵p also forms one hydrogen bond and one Pi-Pi bond with Valsartan through

Cytosine ١٠. In addition, in the case of Telmisartan, the receptor did form a phosphoanionic bond. Moreover, Telmisartan interacted through the phospho-anion bond with Guanine ٩ of miR-٢٧a-٥p.

Conclusion: These results with Valsartan show that it interacts with miR-٢٧a-٥p at Cytosine ١٠, but the interaction with Telmisartan has an added potential of multiple bonding, conferring a higher binding affinity with the mi-RNA and hence a higher therapeutic efficacy. Thus, the medicines are also not recommended to be administered together due to possible drug interactions. Telmisartan emerges as the drug of choice for the treatment of diabetes.

Keywords: Diabetic Neuropathy (DN); Telmisartan; Valsartan; miR-٢٧a-٥p; Drug Interactions

Molecular Insight into Wip١ phosphatase (PPM١D) Importance in Cancers (Review) (Review)

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Introduction: One of the hallmark features of cancers is their genomic instability, which is associated with an increased propensity for DNA damage accumulation. The DNA damage response (DDR) related proteins leading to the cell cycle arrest were inactivated due to dephosphorylation by some phosphatases, so the cell cycle returned to its pre-stress state (normal conditions). PPM١D (Protein phosphatase ١D), also known as wild-type p٥٣-induced phosphatase ١ (Wip١) or protein phosphatase ٢C delta (PP٢Cδ), is one of the most important Ser/Thr DDR phosphatases and exerts suppression of several signaling pathways within DDR (as a negative regulator) through affecting the activity of its downstream targets i.e., tumor suppressors in a p٥٣-dependent manner. The role of Wip١ in the proliferation of stem cells and the regulation of T- and B-cell maturations and inflammation was also proposed. Therefore, Wip١ is known as a growth-promoting phosphatase and may be an oncoprotein. The encoding gene (PPM١D) is located on chromosome ١٧q٢٣. In many high-risk human cancers, such as liver, ovarian, breast, lung, skin, pancreatic, brain, and different types of blood cancers, the PPM١D gene plays an oncogenic role. Studying and investigating the molecular mechanism of Wip١ and its role in cancer is important because these studies ultimately can clarify the etiology of cancer, and also open the way to introduce new candidates for cancer diagnosis, prognosis, and even treatment.

Methods: This study was conducted using the studies published in databases such as PubMed, Google Scholar, and Sci-hub from ١٩٩٦ to ٢٠٢٤. The search focused on key terms such as 'wip١ phosphatase,' 'PPM١D gene,' 'DNA damage response', and 'human tumorigenesis.' The content aimed to comprehensively collect information related to common human cancers from a molecular perspective, particularly emphasizing the oncogenic role of cellular phosphatases.

Results: Different types of cellular stress such as single-stranded DNA (ssDNA) and DNA double-strand breaks (DSBs) activated the ATR/CHK١ as well as ATM/ CHK٢ pathways, respectively. In fact, the role of ATM and ATR is phosphorylation and activation of the effector checkpoint kinases i.e., CHK٢ and CHK١. Consequently, the p٥٣ protein is modified post-translationally by ATR/CHK١ and ATM/CHK٢, leading to its stabilization and oligomerization. The protein P٥٣ as a tumor suppressor is an important molecule that interconnects DDR, cell cycle checkpoints, and also cell fate decisions. In addition, this protein stimulates the expression of WIP١ and Mdm٢ as its negative regulators. WIP١ inactivates the p٥٣ pathway after accumulating sufficient protein levels and terminates the DDR. WIP١ also dephosphorylates MDM٢ which leads to its stabilization and the degradation of P٥٣. It can be said that the main role of WIP١ is to inhibit the stability of P٥٣ by increasing the stability of MDM٢. WIP١, like other members of the PPM/PP٢C family, is a monomeric enzyme (٦٠٥ amino acids) that requires divalent cations, primarily Mg٢+ or Mn٢+, for catalytic effectiveness. The PPM١D

structure includes a large flap subdomain with ٧٦ residues (P٢١٩-D٢٩٥) adjacent to the active site. The flap region consists of two short α-helices (α٣ and α٤) and three short β-strands (β٩, β١٠, and β١١) followed by an irregular loop. In the crystal structure of PPM١D, extra electron density was observed for an unidentified atom between the nitrogen of the Lys٣٣٦ side chain and the sulfur of Cys٣٤٦, with ١٠٠٪ occupancy. Competitive modifications suggest this atom is oxygen, indicating a covalent cross-link that connects Lys٣٣٦ and Cys٣٤٦ through a nitrogen-oxygen-sulfur (NOS) bridge. The formation of the Lys٣٣٦-Cys٣٤٦ NOS cross-link may preserve PPM١D activity under high oxidative potential conditions, such as in cancer cells or following exposure to ionizing radiation.

Conclusion: Since WIP١ acts as an important negative regulator of p٥٣ and a terminator of DDR, its overexpression inhibits p٥٣ function and contributes to tumorigenesis, while loss or downregulation of this protein can significantly delay tumor growth in mice. Therefore, the use of RNA interference drugs affecting this pathway can reactivate the p٥٣ pathway and inhibit proliferation in tumors with p٥٣. It is hoped that with further studies on the PPM١D gene, more successes in cancer treatment or control will occur in the future.

Keywords: DNA damage response, Phosphatase, PPM١D gene, Tumor suppressor, WIP١

Molecular Insights into Thyroid Malignant Tumors: Implications for Diagnosis and Personalized Treatment (Review)

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Introduction: Thyroid malignant tumors represent a heterogeneous group of disorders marked by significant genetic and phenotypic variability, resulting in diverse clinical presentations and prognostic outcomes. The distinction between well-differentiated cancers, such as papillary thyroid carcinoma (PTC) and follicular thyroid carcinoma (FTC), and more aggressive forms like poorly differentiated and anaplastic thyroid carcinoma necessitates a deep understanding of their molecular foundations. This knowledge is crucial for refining diagnostic approaches and informing targeted therapeutic interventions that can substantially improve patient outcomes.

Methods: This narrative review synthesizes findings from an extensive analysis of recent peer-reviewed literature focused on the genetic and molecular characteristics of thyroid cancers. Key molecular features, including oncogenic mutations, gene expression profiles, and emerging biomarkers, were evaluated for their implications in diagnosis, prognosis, and therapeutic modalities.

Results: Our analysis underscores several pivotal genetic alterations associated with thyroid tumors: _TERT Promoter Mutations: Frequently associated with aggressive variants of PTC, these mutations serve as critical prognostic indicators (Xing et al., ٢٠١٤). _BRAF Mutations: Notably, the BRAF V٦٠٠E mutation significantly influences treatment outcomes, supporting its role as a therapeutic target (Namba et al., ٢٠١٦). _RAS Mutations and PAX٨-PPAR Gamma Rearrangements: Common in FTC, these alterations play vital roles in tumor progression and prognostic evaluation (Tufano et al., ٢٠١٥). _Anaplastic thyroid carcinoma is characterized by a high mutational burden, including mutations in TP٥٣, BRAF, and TERT, which often confer resistance to conventional therapies, highlighting the urgent need for innovative treatment strategies (Liu et al., ٢٠١٨). _Emerging molecular biomarkers, such as microRNAs and circulating tumor DNA (ctDNA), have proven invaluable for non-invasive diagnostics and monitoring disease progression. Specific microRNA expression profiles correlate with tumor aggressiveness and therapeutic resistance, indicating their potential as targets for novel therapeutic interventions (Kumar et al., ٢٠١٩). _Comprehensive genomic profiling has revealed alterations in pathways regulating cell proliferation, apoptosis, and immune evasion, thereby identifying new therapeutic targets that can be leveraged in precision medicine.

Conclusion: As our understanding of molecular alterations in thyroid cancers evolves, integrating these insights into clinical practice holds significant promise for enhancing prognostic accuracy and facilitating the development of personalized therapeutic interventions. This review emphasizes the critical role of molecular diagnostics in refining the management of thyroid cancer and highlights the potential for pioneering treatment strategies tailored to the unique molecular characteristics of

individual tumors. Future research should prioritize the translation of these molecular insights into clinical protocols to optimize patient outcomes and advance the field of targeted therapies.

Keywords: Thyroid cancer, molecular diagnostics, TERT mutations, BRAF mutations, personalized treatment, bioma

Multi-cancer early detection tests: A new paradigm in cancer screening (Review)

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Introduction: Multi-cancer early detection (MCED) tests can detect many different cancers through a single blood test. An example is the Galleri® test, which uses cfDNA methylation patterns, and an extracellular vesicle protein-based blood test. Thus, this type of testing reveals cancers that are at an early, more treatable stage, which then reduces mortality rates, and consequently, enhances patients' outcomes.

Methods: This review presents findings from several MCED tests. The research included a thorough analysis of ١٠ journal articles, where direct attention was paid to test methodologies, clinical trials, and statistical analyses. The authors of the studies provided key data points and a summary that included information about sensitivity, specificity, and the influence on early-stage cancer detection rates.

Results: The Galleri® test showed an overall sensitivity of ٥٥٪ through more than ٥٠ cancer types with a false-positive rate of less than ١٪. Another test based on an extracellular vesicle protein showed a sensitivity of ٧١,٢٪ and specificity of ٩٩,٥٪. This test could detect many cancers at early stages, leading to a reduction of ٧٧ to ١٠٠ deaths per ١٠٠,٠٠٠ individuals annually. These tests would be superior to the current single-cancer screening methods in terms of positive prediction value (PPV), especially when combined with machine learning algorithms. It is shown that this approach led to ٩٥,٥٪ sensitivity and ٩٥٪ specificity in detecting lung, liver, and colorectal cancers.

Conclusion: MCED testing is not only a new and fascinating way to detect a variety of cancers but also a procedure that would have a positive impact on cancer screening as patients would only need to take a blood test to discover a possible diagnosis. These tests that can detect multiple types of cancer at once would thus contribute to the early detection of cancer and the resulting higher survival rate of the patients. Their use in clinical settings may not only take the place of current methods but might also play a significant role in the reduction of cancer incidence.

Keywords: MCED, Cancer screening, Circulating tumor DNA, Extracellular vesicles, Liquid biopsy

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Multimodal Elastography: Synergistic Approaches for Advanced Tissue Characterization (Review)

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Introduction: Elastography, the imaging of mechanical tissue properties, has emerged as a powerful tool for characterizing pathological conditions and evaluating tissue health. While individual elastography modalities, such as magnetic resonance elastography (MRE) and ultrasound elastography, have demonstrated clinical utility, the combination of complementary modalities through multimodal elastography approaches has the potential to provide unprecedented insights into tissue biomechanics.

Methods: To review recent developments in multimodal elastography, a comprehensive search was conducted across several databases, including PubMed, Scopus, and Web of Science. The search strategy involved combinations of keywords such as "multimodal elastography," "multimodal imaging," "magnetic resonance elastography," "ultrasound elastography," "optical elastography," "data fusion," and "tissue biomechanics." The search was limited to peer-reviewed articles published in English within the last five years. Additionally, reference lists of relevant articles were manually examined to identify additional studies of interest.

Results: Multimodal elastography leverages the strengths of different imaging modalities to overcome the limitations of individual techniques. For example, the high spatial resolution of ultrasound elastography can be fused with the excellent soft tissue contrast and whole-body coverage of MRE, enabling comprehensive characterization of pathologies throughout the body. Additionally, the integration of optical elastography with MRE or ultrasound enables high-resolution microscopic elasticity mapping correlated with macroscopic observations. These strategies have shown promise in diverse applications, such as improving the specificity of liver fibrosis staging, characterizing heterogeneous tumors, and evaluating neurodegenerative disorders.

Conclusion: Despite the potential benefits, multimodal elastography faces challenges in data acquisition, registration, reconstruction, and interpretation. Ongoing research efforts are focused on developing robust frameworks for data fusion, establishing standardized protocols, and validating multimodal biomarkers through clinical studies. In summary, multimodal elastography combines the strengths of multiple imaging modalities, offering a powerful and comprehensive approach to tissue characterization. As this field continues to evolve, multimodal elastography is poised to provide new insights into tissue biomechanics and enable advanced diagnostic and therapeutic applications.

Keywords: Elastography, multimodal imaging, magnetic resonance elastography, ultrasound elastography,

Multiplex Gene Editing in Primary T Cells: A Non-Viral Approach to CAR Expression (Review)

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Introduction: CAR T-cell therapy has revolutionized cancer treatment for blood cancers, relying on viral vectors to deliver genetic material to T-cells. However, these vectors can cause secondary cancers through random genome integration, and while successful in blood cancers, they have yet to achieve similar results with solid tumors due to factors such as limited tumor homing, persistence, and exhaustion. To improve CAR T cell therapy, researchers have investigated methods like preventing T cell exhaustion and creating allogeneic CAR T cells. Strategies to prevent exhaustion include blocking inhibitory receptors or using CRISPR/Cas۹ to alter T cell genes. Allogeneic CAR T cells provide convenience as off-the-shelf products but face issues like graft-versus-host disease (GVHD) and immune rejection. In this study, researchers aimed to tackle these issues by creating CAR T cells with multiple genetic modifications. They used CRISPR/Cas۹ to insert a GD۲-CAR transgene into the TRAC locus while disrupting the TRAC, β۲M, and PDCD۱ loci. This approach was intended to reduce GVHD and T-cell rejection, prevent CAR exhaustion, and enhance T-cell persistence by promoting stem-cell memory phenotypes.

Methods: T cells were isolated from leukopaks, activated, and cultured with specific cytokines. For genetic modification, plasmids carrying a GD۲-tNGFR-CAR sequence were prepared for CRISPR/Cas۹ insertion, followed by nucleofection of T cells with the RNP mixtures and HDR template. The modified T cells were then expanded, cryopreserved, and later thawed. Flow cytometry was used to analyze CAR, TCR, and other markers. In vitro cytotoxicity was assessed using GD۲+ neuroblastoma cells and AkaLUC-GFP CHLA-۲۰ cells. ddPCR quantified translocations, and GUIDE-seq assessed off-target effects. Data were analyzed with Prism, Excel, FlowJo, and Illustrator.

Results: Manufacturing of Non-Viral, TRAC-B۲M-PD۱ Triple-Knockout GD۲ CAR T Cells: Multiplex-edited CAR T cells were designed targeting TRAC, B۲M, and PD۱. A HDR donor template containing a third-generation anti-GD۲ CAR transgene and a tNGFR tag was integrated into the TRAC locus. Human primary T cells were isolated, activated, and nucleofected with RNPs knocking out TRAC, B۲M, and PD۱ and knocking-in the dsDNA CAR donor template. TRAC-B۲M-PD۱ triple-knockout GD۲ CAR T cells were expanded and cryopreserved. Low Translocation Rate and Off-Target Editing: Simultaneous multiplex editing of T-cells can introduce chromosomal abnormalities. ddPCR and GUIDE-seq were employed to assess the frequency of these events. Low rates of translocations and off-target editing were observed, indicating high efficacy and fidelity in more than ۹۹٪ of T cells. Favorable Memory Phenotypes: Higher amounts of naive and central memory T-cells in pre-infusion CAR T products have been correlated with increased persistence and potency. This phenotype can be characterized by the expression of surface markers like CD٤٥RA and CCR۷. Over ٥۰٪ of TRAC-B۲M-PD۱ triple-knockout GD۲ CAR T cells had a naïve or central memory phenotype. High in Vitro Potency: The potency of triple-knockout GD۲-CAR T cells was investigated by measuring cytotoxicity

after co-culture with the GD۲+ neuroblastoma cell line, CHLA-۲۰. TRAC-B۲M-PD۱ triple-knockout GD۲ CAR T cells showed high cytotoxicity against CHLA-۲۰ target cells, suggesting that the knockout of PD-۱ may increase the potency for GD۲ CAR T cells against neuroblastoma.

Conclusion: This study demonstrates the feasibility and safety of using multiplex editing with CRISPR/Cas۹ to manufacture allogeneic GD۲ CAR T cells with minimal chromosomal abnormalities and off-target editing. The engineered T cells exhibited high cytotoxicity against GD۲+ human neuroblastoma cells in vitro and displayed favorable memory phenotypes. The simultaneous disruption of TRAC, B۲M, and PD-۱ in CAR T cells effectively prevents exhaustion, enhances anti-tumor efficacy, and limits GVHD and host rejection. The non-viral gene delivery strategy used in this study offers potential advantages in terms of scalability and manufacturing efficiency. Future research should focus on further optimizing the editing process to minimize off-target effects and translocations, exploring alternative editing strategies, and investigating the in vivo potency of these engineered T cells in various GD۲-expressing indications. Additionally, efforts to improve the stem cell memory profile and optimize cryopreservation protocols are essential for the successful translation of allogeneic CAR T cell therapies.

Keywords: chimeric antigen receptor T cells, multiplex gene editing, CRISPR/Cas۹, chromosomal translocation

Mycology **(Review)**

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Introduction: Mushrooms form a very wide collection of about one hundred thousand species, some of which are extremely different in appearance and size. Some of these are microscopic and others like Polypores and Lycoperdon Borista are very large. This group of small and big creatures form a world, each of which chooses a suitable environment according to their nature. Fungi, unlike bacteria and water algae that do not have a true nucleus (protocaryotes), all have a clear nucleus (eucayotes). This opinion is close to the red and green algae of flowering plants and animals. Mushrooms are classified as plants and phytophytes in the classification of living organisms. They are considered chlorophyll. Nutrition and ways of life of mushrooms: Due to the lack of chlorophyll, these organisms are not able to use the carbon in the air through photosynthesis and are always heterotrophic towards this element. This nature of heterotrophy and lack of independence causes them to be divided into three groups: ۱- Saprophytes ۲-parasites ۳- Symbiotes They divide

Methods: Fungi living on dead organic matter are called saprophytes. A group of these umbrella fungi may obtain the nutrients they need from living materials by living in a parasitic way, and the other group has a facultative state, that is, they can live in a saprophytic or parasitic state. Other capped fungi also live in symbiosis with plants, which are called micro-organisms. Two corrections (mushroo toadstool) are used for caped mushrooms. Umbrella mushrooms belong to the order (aphyllophorales & agaricale) of the basidiomycetes. And their edible group is called (mushroom) and poisonous mushrooms (toadstool). Mushroom life: Mushroom is a type of plant whose asexual organ called mycelium or thread which consists of microscopic thin filaments or hypha is not often seen. What we know as mushroom means the cap set and the base of the reproductive system of this plant. The special set that produces and holds spores is called hymenium. The spore is a very fine particle that is more or less round and its diameter does not exceed a few thousandths of a millimeter. Spores can be considered mushroom seeds. Each milligram of mushroom spore contains about twenty million particles, and a whole mushroom produces several billion spores during its lifetime. ۱- Basidiomycetes: (basidiomycotes) whose spores are formed outside of the baside. ۲- Ascomycetes: (ascomysetes) (including morels) whose spores are produced inside a long appendage called asgue. Vegetative structure of mushrooms: The reproduction of the fungus is done by the sprouts from the resistant mycelium and spores. Resistant mycelium, which consists of microscopic thin filaments or hyphae, often produce buds when the right conditions are provided and give birth to a new fungus. This mycelium is mostly endowment and sometimes colored and sometimes sinks into the soil or support. From the weaving of the spore, which is the complete organ of reproduction, the primary mycelium-forming thread is produced. As a result of multiplication, the primary mycelium first forms the secondary or resistant mycelium and then the carpophore. When talking about mushroom, it means the visible part of the plant, i.e. the set (cap + base) that is used,

and in scientific language, these two parts are collectively called carpophore, which is actually the fruit of the plant. The plant itself, i.e. its asexual part, is a collection of thin filaments with a diameter of three thousandths to ten thousandths of a millimeter. These tangled filaments are called mycelium or mycelium in the scientific language and in the language of mushroom growers, they are called mycelium. The mycelium is the asexual organ of the fungus that absorbs nutrients from the bed in which it is located to grow, and the reproductive organs produce a plant. The carpophore consists of a cap and a base. In most cases, there are organs on the lower surface of the cap where spores or spores can be produced as: ١- Blade or lamelle: Agaricaceae family that includes Shami mushroom. ٢- Tube: bolets mushrooms ٣- Auguillon: hyclnes ٤- Simple folds: (chanterelles) ٥- Smooth: trumpet of the dead (trom pettesdelamort) Tal building The thallus of mushrooms is generally made of thin and branched filaments called mycelium, whose longitudinal growth is terminal and their branches are lateral and terminal. In ascomycetes and basidiomycetes, the mycelium filaments generally have a transverse wall and the cells have one, two or more nuclei, in which case they are referred to as hyphae. In each wall between two cells, there is one or more synapses that connect the cytoplasm of the two cells to each other. These cells are called dikaryotic if they contain a dikaryote, i.e. two nuclei of different sexes. In phycomycetes and zygomycetes, the mycelium strands without a transverse wall are called syphot.

Results: Due to the great importance and health measures, it is necessary to recommend the following items: ١- The location of the mushroom cultivation units in the area where there is no possibility of contamination by some chemical compounds. At the same time, the air of the place should be free of toxic and polluting compounds. ٢- The floor of the compost production halls should be cemented and tiled and roofed ٣- The raw materials for preparing compost must be completely fresh and mixed together in the right proportion ٤- Pasteurization and preparation steps of compost should be done at the optimal temperature in the whole cycle. During these steps, the compost should not acquire the necessary conditions for the growth and spread of the pathogen. ٥- The workers who work in the compost preparation area should refrain from entering the seed inoculation halls and other breeding halls without changing their shoes and clothes. ٦- Spawn and seeds used in inoculation must be completely fresh and free of contamination. ٧- It is necessary to wash and disinfect all the necessary equipment in the process of inoculation of seeds and spawn. ٨- The cover soil mixture should be properly pasteurized at a temperature of ٦٠ to ٦٥ degrees Celsius for ٥ to ٦ hours. ٩- People who enter the cultivation halls to harvest must use clean work clothes and gloves. ١٠-Residues from the previous harvest must be completely collected and removed from the halls. ١١- In irrigation water, it is better to use chlorine in the amount of ١٥٠ micrograms per milliliter to prevent the occurrence of bacterial diseases. ١٢- Remove the infected bags from the halls quickly or treat the infected parts with ٢٪ formalin to make it (anti-infectious). ١٣- Bags filled with compost should remain completely closed to prevent possible contamination during transportation. ١٤- The remaining compost should not be placed near the breeding halls. Other methods of controlling green mold disease include reducing humidity, reducing the amount of carbon dioxide (ventilation), increasing air ventilation, using clean and pollution-free materials, preparing cover soil in which there are no traces of rotten and dead wood tissues. He mentioned

increasing soil pH by covering uncontaminated areas with sodium hypochlorite salt or sodium bicarbonate or Triof solution. In the chemical method, as the results of the studies in the previous section showed, fungicides can be used.

Conclusion: Due to the great importance and health measures, it is necessary to recommend the following items: ١- The location of the mushroom cultivation units in the area where there is no possibility of contamination by some chemical compounds. At the same time, the air of the place should be free of toxic and polluting compounds. ٢- The floor of the compost production halls should be cemented and tiled and roofed ٣- The raw materials for preparing compost must be completely fresh and mixed together in the right proportion ٤- Pasteurization and preparation steps of compost should be done at the optimal temperature in the whole cycle. During these steps, the compost should not acquire the necessary conditions for the growth and spread of the pathogen. ٥- The workers who work in the compost preparation area should refrain from entering the seed inoculation halls and other breeding halls without changing their shoes and clothes. ٦- Spawn and seeds used in inoculation must be completely fresh and free of contamination. ٧- It is necessary to wash and disinfect all the necessary equipment in the process of inoculation of seeds and spawn. ٨- The cover soil mixture should be properly pasteurized at a temperature of ٦٠ to ٦٥ degrees Celsius for ٥ to ٦ hours. ٩- People who enter the cultivation halls to harvest must use clean work clothes and gloves. ١٠-Residues from the previous harvest must be completely collected and removed from the halls. ١١- In irrigation water, it is better to use chlorine in the amount of ١٥٠ micrograms per milliliter to prevent the occurrence of bacterial diseases. ١٢- Remove the infected bags from the halls quickly or treat the infected parts with ٢٪ formalin to make it (anti-infectious). ١٣- Bags filled with compost should remain completely closed to prevent possible contamination during transportation. ١٤- The remaining compost should not be placed near the breeding halls. Other methods of controlling green mold disease include reducing humidity, reducing the amount of carbon dioxide (ventilation), increasing air ventilation, using clean and pollution-free materials, preparing cover soil in which there are no traces of rotten and dead wood tissues. He mentioned increasing soil pH by covering uncontaminated areas with sodium hypochlorite salt or sodium bicarbonate or Triof solution. In the chemical method, as the results of the studies in the previous section showed, fungicides can be used.

Keywords: parasitology Mycology. Mushroom growth process. Types of mushrooms. Characteristics of mushrooms.

Nano Phytosomes : An Innovative Herbal Approach for Targeted Tumor Therapy (Review)

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Introduction: Cancer is a predominant life-threatening illness that is addressed by numerous modalities such as surgery, radiation, and chemotherapy. Chemotherapy is the preferred technique for cancer care, although it encounters certain constraints. Significant challenges identified in contemporary chemotherapy include pronounced side effects, limited therapeutic indices, and multidrug resistance. The graph of treatment resistance in cancer is rising concerning therapeutic efficacy. The ۲۵٪ rise in disease burden may be attributable to resistance mutations in cancer during therapy. Prolonged conventional treatment induces acquired resistance. Traditional therapies have failed to target cancer cells precisely and need the use of nanocarriers or bioengineering for polychemotherapy. Phytochemicals are natural compounds that provide an alternative treatment strategy to reduce resistance. Phytochemicals are extracted, separated, and purified from dietary fibers or natural plants. Natural extractives operate via many mechanisms and provide optimal efficacy against resistant cancer. Phytochemicals are regarded as potential chemotherapeutics and chemopreventive agents; nevertheless, their clinical applicability may be uncertain due to inadequate bioavailability and stability. Various strategies have been used to produce efficient vehicle systems to address these challenges. Phytosome technology emerges as a possible method to improve bioavailability and address other obstacles.

Methods: This review provides details of the formulation approach for phytosomes and elucidates their chemical and biological features. The technological efficacy is assessed with a compilation of significant patented innovations related to phytosomes. It also emphasizes essential facts, production, characterization, proprietary methods, commercial products available in the market, and uses of phytosomes for innovative administration of herbal medications in targeted tumor therapy. The data compiled in this study was sourced from several scientific sources, including PubMed, MDPI, ScienceDirect, and Google Scholar.

Results: The significant implications of phytochemical and chemotherapeutic combination treatment may emerge in the future, but the investigation of phytosomes is still in its infancy and requires more examination.

Conclusion: Targeting tumor tissues in oncotherapeutics has garnered increasing global interest during the last three decades. The urgent need to mitigate the negative effects of medications underscores the demand for breakthroughs in targeted treatments and superior alternatives to traditional chemotherapies. Phytosomes are innovative medication delivery systems created by

conjugating phospholipids with hydrophilic herbal components or bioactive phytochemicals. It is beneficial for administering the herbal treatment at a specified pace, targeting the place of action, and reducing harmful effects. Enhancement of drug bioavailability, The distribution of the medicine is regulated by incorporating it into a carrier system or by modifying its molecular structure. Vesicular drug delivery methods typically function as passive targeting carriers by circumventing the immune system. In tumor treatment, phytosomes above ٤٠ kDa and within a nanometric size range of ١٠٠–١٢٠٠ nm aggressively target malignant cells owing to the improved penetration and retention impact. Passive targeting enhances the bioavailability of medications, while active targeting precisely directs the pharmaceuticals to the site of action; both are integrated into phytosomes to deliver bioactive substances.

Keywords: Phytosome, Cancer, Targeted therapy, Herbal medicine

Nano-carrier based targeted delivery of aflibercept to retinoblastoma cells (Research Paper)

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Introduction: Retinoblastoma is the most common intraocular malignancy in children, with an incidence of approximately ١ in ١٧,٠٠٠ live births worldwide. Mutations in the retinoblastoma gene (RB١), located on chromosome ١٣q١٤,٢, are responsible for this condition. It is a curable cancer if diagnosed in a timely manner. However, the mortality rate remains high in developing countries, and advanced tumors can limit the possibility of globe salvage. Although chemotherapy is an effective treatment for retinoblastoma, many affected children suffer from undesirable side effects. Therefore, there is a pressing need to design a new drug delivery system that is more efficient and has fewer side effects. In recent years, a novel nano-carrier containing MiRGD peptides and graphene quantum dots (GQDs) has been developed, based on the structural differences between cancerous and normal cells. Since αv integrins are overexpressed in tumor cells, the iRGD motif in the peptide facilitates deep penetration into cancerous tissues by binding to them. Other motifs enhance the delivery of both hydrophobic and hydrophilic drugs. The non-toxic GQDs assist with non-invasive biological tracking and improve drug binding to the peptides. Consequently, this nano-carrier is deemed suitable for delivering Aflibercept, an anti-VEGF drug, to prevent the activation of angiogenesis.

Methods: In order to extract the MiRGD peptide, E. coli BL٢١ containing the expression vector (pET٢٨a) was cultured in ٢xYT medium supplemented with kanamycin and IPTG as an inducer of protein expression. Then, the bacterial cells were harvested by centrifugation, and the cell pellets were resuspended in lysis buffer. A Ni-NTA column chromatography was employed to purify the MiRGD peptide, and impurities were removed using buffers with a urea-imidazole gradient. Following the examination of the peptide's purity by SDS-PAGE, the purified peptide was desalted by dialysis against PBS buffer. Graphene quantum dots (GQDs) were synthesized by dissolving citric acid and urea in water using a hydrothermal method. The solution was then autoclaved, and ethanol was added. After centrifugation, the solution was dried and redispersed in deionized water. The UV/Vis

and fluorescence spectra of the synthesized GQDs and Aflibercept were examined using a Cytation reader. Dynamic Light Scattering (DLS) was performed to determine the ζ-potential of GQDs, the MiRGD peptide, and Aflibercept. Fourier-transform infrared spectroscopy (FTIR) was conducted to identify the bands related to the surface functional groups present on the GQDs. After assembling the complexes of the drug, GQDs, and varying concentrations of MiRGD, the ζ-potential and UV/Vis spectrum of the complexes were investigated.

Results: The MiRGD peptide band was observed on a ١٥٪ Tris-glycine SDS-PAGE gel, with a molecular weight of approximately ٩,٦ kD. The UV/Vis spectrum of the MiRGD peptide, examined at various wavelengths, revealed a peak at ٢٠٧ nm. Similarly, the UV/Vis spectrum of the synthesized graphene quantum dots (GQDs) showed two peaks at ١٩٩ nm and ٣٣٨ nm. The fluorescence spectrum of the synthesized GQDs was analyzed at different excitation wavelengths, with the maximum emission observed at ٤٤٠ nm. Aflibercept's UV/Vis absorption spectroscopy, conducted at various wavelengths, displayed a peak at ٢١٦,٥ nm, while the fluorescence spectrum of the drug revealed a peak at ٤٢٠ nm. The ζ-potential measurements of GQDs, Aflibercept, and the peptide were found to be −٢٣,٣ mV, +٤,٧٠ mV, and +٦,٥٧ mV, respectively. FTIR spectroscopy of GQDs demonstrated an absorption band in the range of ٣٠٠٠-٣٥٠٠ cm−١, indicating the presence of amino and hydroxyl groups on the surface of the GQDs. The bands at ١٧٠٠ cm−١ correspond to the vibrational absorption of C=O, and the band at ١٤٠٠ cm−١ is related to the bending vibrations of C=C. The UV/Vis spectrum of the complexes illustrated peaks between ٢٠٠ and ٢٢٠ nm. The ζ-potential of the complexes ranged from ١٠ to ١٢ mV.

Conclusion: In conclusion, there is a pressing need for a new targeted drug delivery system for the treatment of retinoblastoma. A novel nano-carrier containing MiRGD peptide and graphene quantum dots (GQDs) has been developed for this purpose. This study aims to investigate the effect of this nano-carrier on retinoblastoma. So far, the MiRGD peptide and GQDs have been prepared and characterized. Additionally, aflibercept, an anti-angiogenesis drug, has also been characterized and will be incorporated into the complex. The assembly and characterization of the complex, which includes MiRGD, the drug, and GQDs, have been completed. The next step will involve investigating the effects of these complexes on a retinoblastoma cell line.

Keywords: Retinoblastoma, graphene-quantum-dots, drug-delivery, nanoparticle, nano-carrier

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Nanobodies in Medical Biotechnology; Applications and Advances in Therapeutic and Diagnostic Innovations (Review)

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Introduction: Nanobodies, also known as single-domain antibodies (sdAbs), are a relatively new class of antibody fragments that are derived from heavy-chain-only antibodies naturally found in Camelidae species. These small, robust molecules have become powerful tools in medical biotechnology due to their unique structural and functional properties. Their small size (~١٥ kDa), high stability, and ability to bind to epitopes that conventional antibodies cannot access make nanobodies particularly well-suited for a wide range of therapeutic and diagnostic applications. This unique structure not only enhances their stability and solubility but also enables the engineering of bispecific and multispecific formats, expanding their potential in complex therapeutic scenarios. Additionally, their ease of production in microbial systems allows for large-scale manufacturing, making them attractive alternatives to conventional antibodies. Nanobodies are generated through immunization of Camelidae species or via phage display technology, where a large library of synthetic nanobodies is screened for binding to a specific antigen. The selected nanobodies are then characterized for their binding affinity, specificity, and stability. Nanobodies can be conjugated with drugs, toxins, or radioisotopes to target specific cells, such as cancer cells, with high precision for therapeutic applications. In diagnostic applications, nanobodies can be linked to fluorescent, radioisotope, or enzymatic markers to detect biomarkers in various diseases, including infectious diseases, cancer, and neurological disorders.

Methods: The terms “Nanobodies and their applications” were searched in PubMed, Science Direct, and Google Scholar, the selected articles were critically evaluated.

Results: Promising results have emerged from preclinical and clinical trials for nanobody-based therapeutics. For illustration, nanobody-drug conjugates have demonstrated heightened targeting of cancer cells with reduced off-target effects, resulting in enhanced efficacy and safety profiles. Nanobodies have been integrated into various diagnostic tools, such as biosensors and imaging methods, delivering exceptional sensitivity and specificity in detecting disease biomarkers. Moreover, their diminutive size and capacity to penetrate biological barriers like the blood-brain barrier make nanobodies an attractive option for treating disorders of the central nervous system, opening up new avenues for research and development.

Conclusion: Nanobodies exhibit superior tissue penetration due to their small size, enabling them to effectively target solid tumors and other hard-to-reach areas. This is because they can bind to unique epitopes, including those in enzyme active sites or those hidden within protein complexes, which further enhances their utility in both therapeutic and diagnostic applications. Furthermore, the ease of genetic manipulation allows for the development of multifunctional nanobody constructs, such as multispecific nanobodies, which can simultaneously target multiple antigens and improve treatment outcomes in complex diseases. Despite these advantages, challenges remain, particularly with regard to the immunogenicity of nanobodies in humans. Although they originate from camelids, which could potentially trigger immune responses, strategies such as the humanization of nanobodies and the use of human-derived nanobody libraries are being explored to mitigate this issue. Additionally, the development of resistance to nanobody-based therapies, as observed with other biologics, is an area that requires ongoing research and monitoring. Nanobodies represent a transformative innovation in medical biotechnology, offering significant advantages over traditional antibodies for both therapeutic and diagnostic applications. Their small size, high stability, and ability to access unique epitopes make them ideal candidates for a wide range of medical applications, ranging from targeted drug delivery to sensitive diagnostic assays. Continued research and development in this field is expected to further enhance the utility of nanobodies, address current challenges, and expand their role in precision medicine.

Keywords: Nanobodies, single-domain antibodies, medical biotechnology, therapeutic applications, drug delivery

Nanocarrier-Based Intranasal Drug Delivery for Psychiatric Disorders: A Review of Novel Approaches to Overcome the Blood-Brain Barrier (Review)

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Introduction: Psychiatric disorders present significant challenges in delivering therapeutics to the brain due to the presence of the blood-brain barrier (BBB) and limitations associated with traditional routes of administration. The BBB, a highly selective semipermeable border of endothelial cells, prevents many drugs from reaching their targets in the central nervous system. This barrier has long been a major obstacle in the treatment of various psychiatric conditions, including mood disorders, anxiety, schizophrenia, and other mental illnesses. In recent years, the nose-to-brain channel, also known as intranasal delivery, has emerged as a promising approach to overcome these barriers. This method offers a direct pathway to the brain, bypassing the BBB and potentially improving the efficacy of psychiatric treatments. Intranasal delivery has garnered significant attention in the field of neuropharmacology due to its non-invasive nature and potential for rapid drug absorption. The advent of nanotechnology has further enhanced the potential of intranasal delivery. Nanocarriers, including polymeric nanoparticles, liposomes, and nanoemulsions, offer unique advantages for delivering therapeutic agents to the brain via the intranasal route. These nanocarriers can protect drugs from degradation, enhance their solubility, and facilitate their transport across biological membranes, potentially leading to improved bioavailability and therapeutic outcomes in psychiatric disorders.

Methods: his review employed a comprehensive literature search strategy to gather relevant information on nanocarrier-based intranasal drug delivery for psychiatric disorders. The methodology involved conducting preliminary searches on major scientific databases, including PubMed, ScienceDirect, Web of Science, and Google Scholar. Key search terms and phrases included "psychiatric disorders," "intranasal delivery," "nose-to-brain drug delivery," "nano formulations for intranasal delivery," "nanocarriers in psychiatric treatment," "blood-brain barrier," and combinations thereof. The search was limited to articles published in English, with a focus on recent publications to ensure the most up-to-date information was included. The review process involved screening titles and abstracts to identify relevant studies, followed by a full-text review of selected articles. Studies discussing various types of nanocarriers, their applications in intranasal delivery for psychiatric disorders, and their potential advantages over traditional drug delivery methods were included. Additionally, articles exploring the mechanisms of nose-to-brain transport and the challenges associated with this delivery route were considered.

Results: The review highlights several key findings regarding nanocarrier-based intranasal drug delivery for psychiatric disorders: Advantages of Intranasal Delivery: The intranasal drug delivery pathway emerges as a non-invasive, reliable, and efficient method for targeting the brain. By bypassing the BBB, this route offers potential advantages in terms of rapid onset of action and

reduced systemic side effects compared to traditional oral or intravenous administration. Types of Nanocarriers: Various novel nanocarrier-based formulations have shown promise for intranasal delivery of psychiatric medications. These include: a) Polymeric nanoparticles: Biodegradable polymers that can encapsulate drugs and protect them from degradation. b) Liposomes: Lipid-based vesicles that can enhance drug solubility and permeability. c) Nanoemulsions: Submicron-sized emulsions that can improve drug absorption. d) In-situ gels: Formulations that gel upon contact with nasal mucosa, prolonging drug residence time. e) Hydrogels: Networks of hydrophilic polymers that can control drug release. Application in Psychiatric Disorders: Nanocarrier-based intranasal delivery systems have shown potential in the treatment of various psychiatric conditions, including: a) Mood disorders: Enhanced delivery of antidepressants and mood stabilizers. b) Anxiety disorders: Improved targeting of anxiolytic medications. c) Schizophrenia: Better delivery of antipsychotic drugs to the brain. d) Other psychiatric illnesses: Potential applications in ADHD, addiction, and neurodegenerative disorders with psychiatric symptoms. Mechanisms of Action: The review discusses the potential mechanisms by which nanocarriers enhance drug delivery via the intranasal route, including: a) Increased drug solubility and stability b) Enhanced mucoadhesion and residence time in the nasal cavity c) Improved transport across the nasal epithelium d) Targeted delivery to specific regions of the brain Challenges and Future Directions: While promising, the review also identifies several challenges that need to be addressed for the widespread adoption of nanocarrier-based intranasal delivery in psychiatric treatment, including: a) Optimization of nanocarrier formulations for specific drugs and disorders b) Evaluation of long-term safety and efficacy in clinical trials c) Development of standardized production methods for consistent nanocarrier quality d) Regulatory considerations for approval of novel nanoformulations.

Conclusion: Nanocarrier-based intranasal drug delivery presents a promising approach for overcoming the challenges associated with treating psychiatric disorders. By bypassing the blood-brain barrier and offering targeted delivery to the brain, this method has the potential to revolutionize the treatment of various mental health conditions. The use of nanocarriers such as polymeric nanoparticles, liposomes, and nanoemulsions can enhance the efficacy of psychiatric medications while potentially reducing systemic side effects. However, further research is needed to fully realize the potential of this approach. Clinical trials are necessary to establish the safety and efficacy of nanocarrier-based intranasal formulations in psychiatric populations. Additionally, optimization of nanocarrier designs for specific drugs and disorders will be crucial for maximizing therapeutic outcomes. As research in this field progresses, nanocarrier-based intranasal delivery may offer new hope for patients with psychiatric disorders who have not responded adequately to traditional treatment methods. This innovative approach has the potential to improve drug targeting, enhance bioavailability, and ultimately lead to better clinical outcomes in the field of psychiatry.

Keywords: Nose-to-Brain drug delivery, psychiatric disorders, nano drug delivery systems

Nanoparticles in Colorectal Cancer: A Review of Diagnostic and Therapeutic Innovations (Review)

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Introduction: Colorectal cancer (CRC) represents one of the most commonly occurring malignancies globally and remains a principal contributor to cancer-related fatalities. Despite the advancements achieved in traditional therapeutic modalities, including surgical intervention, chemotherapy, and radiotherapy, obstacles such as pharmacological resistance and adverse effects continue to impede therapeutic efficacy, particularly in advanced disease stages. The utilization of nanoparticles (NPs) in the therapeutic landscape of CRC presents a compelling alternative by optimizing drug delivery mechanisms, augmenting diagnostic capabilities, and enhancing treatment specificity. This article provides a comprehensive review of the contemporary advancements in the application of nanoparticles for CRC therapy, informed by recent empirical findings from four pivotal studies.

Methods: This review encapsulates recent progress in the application of nanoparticles for the diagnosis and treatment of colorectal cancer (CRC). To facilitate a more profound comprehension of this subject, we executed a meticulous literature review employing databases such as PubMed, Google Scholar, and NCBI. This investigation yielded ١٤ relevant publications concerning various nanoparticle types, elucidating their capacity to enhance imaging modalities, augment drug delivery systems, and amplify the efficacy of therapeutic interventions, including phototherapy and immunotherapy.

Results: Diagnostic Enhancement: Nanoparticles, including quantum dots (QDs) and gold nanoparticles (AuNPs), have exhibited considerable potential in augmenting both molecular and conventional imaging methodologies. Real-time detection of CRC tumors was made possible by quantum dots, and gold nanoparticles boosted the signal visibility in neoplastic tissues using surface-enhanced Raman techniques. Progress in Drug Delivery Techniques: Nanoparticles, especially liposomal and polymeric variants, have demonstrated notable improvements in the areas of drug solubility, stability, and targeted release strategies. For example, cetuximab-functionalized nanoparticles have proven effective in selectively administering chemotherapeutic agents to CRC cells, thereby minimizing off-target effects. Overcoming Drug Resistance: Nanoparticles engineered for co-delivery of multiple pharmacological agents have shown promising outcomes in overcoming drug resistance associated with CRC treatment. This includes the concurrent delivery of "٥-FU" and "irinotecan," which resulted in enhanced therapeutic efficacy through improved drug accumulation within tumor sites. Studies have looked into nanoparticles and their ability to improve photothermal therapy (PTT) and photodynamic therapy (PDT) by acting as transporters for photosensitizing materials. These therapeutic strategies involve light-mediated activation to induce cytotoxicity in cancer cells. Also, nanoparticles are being employed to better the transport of immunotherapeutic

agents, such as checkpoint inhibitors, aimed specifically at tumor areas, thereby amplifying the immune response to CRC cells.

Conclusion: Nanoparticles present substantial promise in advancing both the diagnostic and therapeutic paradigms of colorectal cancer. They improve imaging modalities, optimize drug delivery, and provide innovative strategies for addressing drug resistance. Additionally, nanoparticles demonstrate encouraging outcomes in enhancing phototherapy and immunotherapy for CRC. However, issues linger, encompassing the adaptation of preclinical milestones into clinical settings, maintaining biocompatibility, and optimizing processes for large-scale production. Ongoing research and clinical trials are imperative to fully exploit the potential of nanoparticles in CRC therapy, thereby offering renewed hope for enhanced patient prognoses.

Keywords: Nanoparticles, Colorectal Cancer, CRC

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Nanotechnology in cancer immunotherapy: Enhancing efficacy and reducing side effects (Review)

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Introduction: Cancer immunotherapy has experienced a revolution in the last decade, and there is an increasing interest in combining it with nanotechnology to enhance the efficacy and reduce the side effects. The delivery of cytokines by polymeric nanoparticles, the targeting of immune checkpoints by lipid-based nanoparticles, or antigen presentation facilitated by metallic nanoparticles are some examples. Various nanotechnologies have substantially reduced systemic toxicity and enhanced therapeutic efficacies in different cancer types.

Methods: This study is based on an assessment of ۸ journal articles dealing with the use of nanotechnology in cancer immunotherapy through a systematic review. The data were extracted to understand the basic principles of nanoparticle applications, including the types of particles, how they behave, and their potential effects on the effectiveness and side effects of cancer immunotherapy. Major findings were synthesized and analyzed.

Results: Nanoparticles improve cancer immunotherapy by improving drug delivery, reducing systemic toxicity, and increasing immune response specificity. Polymeric nanoparticles loaded with cytokines can activate the immune system, lipid-based nanoparticles encapsulate mRNAs encoding tumor-associated antigen proteins, and metallic nanoparticles like Au and Fe_3O_4 nanoparticles present antigens to dendritic cells and induce robust anti-tumor immunity. This has led to better patient outcomes and fewer side effects.

Conclusion: Cancer-specific nanoparticle technologies from companies such as BIND Therapeutics or Merrimack Pharmaceuticals have shown promise in targeted delivery. Nanoparticles are very beneficial for drug applications to improve stability while decreasing the systemic toxicity of the drug and increasing the concentration at the tumor sites. Nevertheless, certain problems such as the proper control of protein encapsulation, biosafety, and effective clinical translation are still there. Continuous progress in the area of nanotechnology and clinical research is very important for the development of efficient and customized cancer therapies.

Keywords: Nanotechnology, Cancer Immunotherapy, Efficacy, Side Effects, Drug Delivery

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Neurological Diseases Diagnosis with Electrical Impedance Tomography (Review)

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Introduction: Most brain diseases have high mortality and disability rates. For instance, cerebral edema is a common response to various forms of brain injury and stroke has a sudden onset and rapid progression, so they need quick and timely identification. Advanced diagnostic techniques such as computed tomography (CT) scans and magnetic resonance imaging (MRI) are used. However, these techniques are limited due to size, cost, and the risk of exposure to ionizing radiation in CT scans. In addition, the ultrasound device cannot be used because, due to the particular structure of the skull, ultrasonic rays cannot penetrate it. Hence, A new and secure imaging system is required. An innovative medical imaging method called electrical impedance tomography (EIT) measures the voltage across the human skin while delivering a safe excitation current, and it reconstructs the image using a predetermined imaging algorithm. Additionally, EIT is beneficial because it is a small, portable device, non-invasive, radiation-free, and can be used for functional imaging. It also has great potential for the early detection of intracranial conditions in patients with brain diseases. In this review, we investigated the use of EIT for diagnosing brain abnormalities.

Methods: The Web of Science, Science Direct, PubMed, and Google Scholar databases were searched up to July ٢٠٢٤, utilizing various keyword combinations: stroke, electrical impedance tomography, edema, brain diseases, neurological diseases, and tissue impedance.

Results: Impedance spectra analysis revealed significant differences between normal, ischemic, and hemorrhagic brain tissue. The characteristic frequency-dependent changes in impedance enabled the differentiation of tissue types. EIT has shown promise in imaging and diagnosing stroke, with the potential for early detection and monitoring of thrombolysis. Moreover, EIT has been shown to detect functional brain changes associated with ischemia, with studies reporting significant impedance increases in ischemic brain tissue. Another study on stroke in anesthetized rats found that cerebral ischemia led to a ٦٠٪ increase in impedance, while cortical electrodes detected a ١٠–٢٠٪ increase. Researchers demonstrated the feasibility of utilizing a generic head mesh for EIT imaging in post-traumatic stroke monitoring, eliminating the need for patient-specific models. Furthermore, they incorporated a Jacobian matrix-based electrode movement correction method to enhance image quality. The progression of brain edema is closely linked to the brain's water content, which is indicated by the intracranial pressure. Studies have shown the potential of EIT for real-time monitoring and differentiation of cerebral edema types in the brain. Investigators have explored the possibility of using EIT to track changes in brain water content associated with brain edema. It has been shown that EIT could be a useful non-invasive imaging technique for early detection of cerebral edema and assessing the effects of mannitol dehydration.

Conclusion: EIT has made significant advancements in brain imaging, which is expected to aid in the early detection and identification of neurological diseases, ensuring timely patient treatment.

Keywords: stroke, "electrical impedance tomography", edema, and "neurological diseases"

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Neuroplasticity and Cognitive Rehabilitation in Psychiatric Disorders (Research Paper)

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Introduction: The relationship between neuroplasticity and cognitive rehabilitation has garnered significant attention in the field of psychiatry. Neuroplasticity refers to the brain's ability to reorganize itself by forming new neural connections throughout life, which can be harnessed through targeted cognitive interventions. This review aims to explore the efficacy of various cognitive rehabilitation methods in promoting neuroplastic changes across different psychiatric disorders, including depression, schizophrenia, and PTSD.

Methods: A systematic literature review was conducted, focusing on studies that investigated cognitive rehabilitation techniques and their impact on neuroplasticity in psychiatric populations. Databases such as PubMed, PsycINFO, and Scopus were searched using keywords related to cognitive rehabilitation, neuroplasticity, and specific psychiatric disorders. Inclusion criteria encompassed peer-reviewed articles published within the last two decades that reported empirical findings on cognitive interventions and neuroplastic outcomes. Additionally, qualitative analyses were performed to synthesize findings from different studies, focusing on the efficacy of cognitive rehabilitation methods in promoting neuroplastic changes. The review also examined the role of factors such as age, duration of illness, and comorbid conditions in influencing treatment outcomes.

Results: The findings indicate that cognitive rehabilitation methods, including CBT, mindfulness-based interventions, and cognitive training exercises, consistently promote neuroplastic changes in individuals with psychiatric disorders. Improvements were observed in cognitive functions such as memory, attention, and emotional regulation. Age and duration of illness emerged as significant moderators of treatment efficacy, with younger individuals and those with a shorter duration of illness showing more pronounced neuroplastic changes. Comorbid conditions also influenced outcomes, highlighting the need for tailored interventions.

Conclusion: Cognitive rehabilitation methods hold substantial promise for fostering neuroplasticity and improving mental health outcomes in individuals with psychiatric disorders. The evidence underscores the importance of personalized treatment approaches that consider individual differences in age, illness duration, and comorbidities. Future research should continue to investigate the mechanisms underlying these neuroplastic changes and explore innovative cognitive interventions to enhance recovery in diverse psychiatric populations. Integrating neuroplasticity-focused strategies into clinical practice may ultimately lead to more effective treatments and improved quality of life for individuals facing mental health challenges.

Keywords: Nouroplastisity, disorders

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Neuroprotective Effect of Cornus mas (cornelian cherry) on Global Cerebral Ischemia/Reperfusion Injury in Rats (Research Paper)

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Introduction: Ischemic stroke usually initiates inflammation and oxidative stress leading to neuronal death. Growing attention is currently being paid to the use of neuroprotective agents in ischemic strokes. Cornelian cherry (Cornus mas L.) fruits are abundant in iridoids and anthocyanins—compounds with potent antioxidant and anti-inflammatory activity. The study aims to evaluate the neuroprotective effect of Cornus mas L. extract (CME) on the cerebral ischemia/reperfusion injury (CIRI) model in rats and explore its potential anti-neuroinflammatory properties.

Methods: Fifty rats were randomly divided into five groups: sham, ischemia-reperfusion (I/R), ٣٠ mg/kg CME, ٦٠ mg/kg CME, and ١٢٠ mg/kg CME. We used Middle cerebral artery occlusion (MCAO) to induction a rat CIRI model, different doses of CME were intraperitoneally injected ٢٤ h after ischemia, for ١٤ days. Histopathology assays were used to evaluate neurological damage and some inflammatory (Nitrite level ($NO_٢^-$)), oxidative stress (malondialdehyde (MDA), and antioxidant power (ferric reducing antioxidant power (FRAP)) parameters were determined in the serum and hippocampus of rats by kit assay.

Results: The results of Hematoxylin and eosin staining showed that CME (٣٠, ٦٠, and ١٢٠ ml/kg) dose-dependently improved the $CA_٣$ diameter of the post-stroke pyramidal cell layers of the hippocampus but $CA_١$ diameter was improved cell layers in ٦٠ ml/kg dose. CIRI significantly increased MDA and NO and decreased FRAP in the hippocampus and the serum levels in the ischemia group. However, the CME significantly declined the levels of MDA and NO and increased FRAP in the hippocampus and the serum levels in post-treatment groups.

Conclusion: Based on the findings, we concluded that CME has a neuroprotective potential against CIRI through antioxidant and anti-inflammatory properties and protects neurons against ischemic death.

Keywords: Cornelian cherry, Ischemic stroke, Oxidative stress, inflammatory

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New insights in Prostate Cancer Treatment : Targeted Drug Delivery systems and Nano lipids

(Review)

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Introduction: Prostate cancer (PC) is expected to be the second most common cancer in males and is a significant health concern, especially among elderly patients. Based on the heterogenic manner of the disease, there is a substantial need to develop new therapeutic options to overcome the limitation in specificity of conventional chemotherapeutic drugs and for the early detection of precancerous cells in prostate cancer. Nano-lipids (NLs) have become influential in targeted drug delivery systems and cancer treatment. One step ahead, innovations in NL engineering are accomplished by modifying their surface to improve their pharmacokinetic and pharmacodynamic properties. Surface-modified NLs have shown a remarkable ability to improve diagnosing and treating protocols, especially when it leads to the targeted administration of anticancer medications. Surface modifications have been designed to allowance new properties and functions, such as hydrophilicity/hydrophobicity, surface charge properties, roughness, adhesion, or adding optical and magnetic properties, to the surface of materials together in a controlled way to enable programmed drug release over time.

Methods: In this review, we attempted to comprehensively study the mechanisms of how PC cells exhibit resistance to chemotherapy, radiation, and ADT (androgen-deprivation therapy) because of activating tumor-endorsing signaling pathways. Herein, we elucidate current developments of Nanotechnology in drug delivery systems and advancements of NL surface modification, their synthesis methods, and how these modifications enhance the specificity and efficacy of drug delivery, decrease systemic toxicity, and overcome multi-drug resistance.

Results: Modifying NL surfaces improves their biocompatibility and reduces their toxicity, enhancing treatments and positively impacting the quality of life. Potential future applications include combination therapies and controlled release profiles, and increased production offers the potential for more effective and widespread treatments for prostate cancer.

Conclusion: Continuing research and investigation are crucial for improving the treatment methods of PC. This can be achieved through the development of surface-modified NLs. It is important to keep studying NL design, surface modifications, and targeted delivery systems to enhance effectiveness, minimize side effects, and improve patient outcomes. By collaborating with researchers, physicians, and the industry, we can swiftly implement these advancements in clinical practice and effectively address the significant challenges of this disease.

Keywords: Nano-lipids, Drug delivery, Prostate cancer, surface modification

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Non-Coding RNAs key players for overcoming drug resistance in Breast Cancer (Review)

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Introduction: Breast cancer is the most prevalent malignancy among females worldwide, with approximately ۲,۳ million new cases diagnosed annually. It typically originates in the ductal carcinoma or lobular carcinoma and can be categorized into non-invasive and invasive forms. Chemotherapy is the most widely used treatment for breast cancer (BC) and is known to improve patient survival rates. Common chemotherapy drugs for BC include Trastuzumab, Doxorubicin, Cisplatin agents, and Tamoxifen. However, resistance to chemotherapy remains a major challenge, as cancer cells can develop resistance, leading to tumor growth and metastasis. Factors contributing to this resistance encompass tumor heterogeneity, genetic mutations, the tumor microenvironment, metabolic reprogramming, and epigenetic alterations. It has recently reported in various resources that epigenetic emerges critical role in drug resistance. One of the recent approaches to overcome epigenetic aroused chemoresistance is through relevant molecular pariticles including long non-coding RNAs (lncRNAs), micro RNAs (miRNAs), and circular RNAs (circRNAs). Investigations in the field of the aforementioned particles have revealed their critical involvement in treatment through various molecular mechanisms, such as inhibiting apoptosis, autophagy and maintaining the stemness of breast cancer stem cells (BCSCs). In this context, we studied various therapeutic agents in which have been used commonly in breast cancer therapies and the chemoresistance phenomenon has been investigated over these drugs with a specific focus on miRNAs, lncRNAs, circRNAs to brighten this vague occurrence for future researches in order to provide an adequate resource regrading most commonly used drugs and non-coding RNAs.

Methods: In this review article, a comprehensive search strategy across multiple academic databases has been employed including PubMed, Google Scholar, Scopus, ResearchGate, Web of Science, and Science Direct. To achieve this goal, the search focused on a combination of keywords: "breast cancer," "epigenetic," "chemotherapy," "drug resistance," "chemoresistance", ”circRNAs”, "LncRNA," and "miRNA." This approach aimed to comprehensively explore the existing body of knowledge and emerging research trends surrounding these critical areas.

Results: In our study we studied the chemoresistance phenomenon in breast cancer in four most commonly used drugs including Doxorubicin, Cisplatin, Tamoxifen, and Trastuzumab. lncRNAs, miRNAs and cirRNAs as major players in this phenomenon have been studied. Regarding this occurrence we could find totally ۵۰ specific lncRNAs, miRNAs and circRNAs that were reported as interferers for inducing drug resistance and drug sensitivity. It is worth mentioning that in our study there was a small proportion of increased drug sensitive phenomenon that was about ۲۵٪ of all

reports. This specific occurrence indicates that the aforementioned non-coding RNA are mostly interfere in drug resistance. While evaluating this topic it was shown that the effect of circRNAs on chemoresistant breast cancer emerges the least numbers of studies which shows that this critical field need to be evaluated more efficiently specifically concerning the Cisplatin and Trastuzumab drug resistant breast cancer. Based on our findings, there were numbers of pathways were shown to play critical roles in drug resistance. Among these pathways, BCL٢, mTOR, and EMT/TGFB signalling pathways had the most repetition compared to all other signalling path ways that indicates their importance in this field. Other important finding was that some non-coding RNAs were repeated in different studies including miR-٢٠٠ that used to be involved in Tamoxizen drug resistance (in two different pathways) and Doxericibin drugresistant breast cancer. In this regard, lncRNA UCA١, ZEB١ gene, and IGF١R gene, and UBE٢D٢ gene which shows their critical role in drug resistance and can be counted as potential topics for further evaluations.

Conclusion: Breast cancer (BC) remains the most prevalent malignancy and a leading cause of cancer-related mortality among women. Drug resistance poses a significant challenge, contributing to the failure of breast cancer treatments in clinical practice. This phenomenon is complex, involving numerous factors, stages, and genes. In this review, we have highlighted the discovery, development, and advancement of miRNAs, lncRNAs, and circRNAs as promising therapeutic agents for breast cancer. Despite considerable funding and research efforts, this area of translational research is still in its infancy. Moreover, our analysis revealed that certain pathways exhibited higher recurrence rates. Additionally, several interfering factors were found to be significantly more prevalent than others, suggesting that these factors may play a critical role in the progression of breast cancer and warrant further investigation in future studies.

Keywords: Non-coding RNAs, Drug resistance, Breast cancer, Epigenetic, Chemotherapy

Novel Applications of Extracellular Vesicles in Cancer Identification and Therapy: Investigating Bioengineered and Biomarker-Based Methods (Review)

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Introduction: Extracellular vesicles (EVs) including exosomes and microvesicles have emerged as critical players in cancer biology due to their role in intercellular communication, carrying bioactive molecules that contribute to tumor progression, metastasis, and therapy resistance. Studies have shown that EVs from cancer cells enhance processes like angiogenesis and immune evasion that support the spread of cancer to parts of the body. Moreover EVs are also involved in regulating the system and the non invasive liquid biopsy approach utilizing EVs has proven effective in tracking tumor development and treatment outcomes particularly for brain tumors. These tiny vesicles offer an avenue for cancer therapy as they can be loaded with various substances, like proteins, short RNAs or chemotherapy drugs. Lately there has been a rising interest in using EVs derived from plants as alternatives for delivering anti cancer drugs due to their unique characteristics and compatibility, with the human body system. Recent advances in bioengineering have further expanded their therapeutic potential, which allow for the development of hybrid or fully synthetic EVs for targeted drug delivery and precision medicine.

Methods: This review discusses the recent research from various studies conducted between ٢٠١٩ and ٢٠٢٤ on how EVs play a role, in diagnosing and treating cancer. The studies focused on carcinoma (HCC) esophageal cancer (EC) and EVs derived from platelets to explore the diagnostic and treatment capabilities of EVs. The approach involved analyzing findings related to EV biomarkers profiling, using bioengineered EVs for delivering drugs, and imaging in vivo with nanocarriers based on EVs.

Results: Extracellular Vesicles may serve as markers for early cancer detection, according to research, particularly for rapidly progressing tumours like hepatocellular carcinoma (HCC). lung cancer and prostate cancer By battling treatment resistance and focussing on cancer stem cells, bioengineered and plant-based EVs have demonstrated enhanced capacities to administer medication efficiently. Emerging as novel diagnostic and therapeutic tools are platelet-derived EVs and EVs laden with microRNA. Furthermore, research on animals has indicated promise in the use of EVs to deliver RNA-based treatments.

Conclusion: Extracellular Vesicles show potential for detecting and treating cancer by providing ways to identify biomarkers without invasive procedures and delivering drugs effectively. Ongoing exploration of engineering EVs and how they influence signaling pathways could bring about approaches to customized cancer treatment. Future investigations need to address existing

obstacles such as establishing methods for isolating EVs and ensuring scalability for use, in medical settings.

Keywords: Extracellular vesicles, cancer biomarkers, bioengineered vesicles, drug delivery, cancer therapy

Novel Biomarkers for Early Detection of Cardiovascular Diseases (Review)

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Introduction: Cardiovascular diseases (CVD) are the leading cause of morbidity and mortality worldwide, accounting for about ٣١٪ of deaths annually. Early detection of CVD is essential for effective management and prevention of severe complications like heart attacks and strokes. Traditional biomarkers, such as troponins and natriuretic peptides, play significant roles in diagnosing heart conditions but often lack the sensitivity and specificity required for early diagnosis, especially in asymptomatic patients. Recent advancements in molecular biology and technology have led to the discovery of novel biomarkers that enhance early detection and risk stratification. This article reviews these emerging biomarkers, their detection methods, and potential clinical applications, highlighting their importance in improving cardiovascular health outcomes.

Methods: A comprehensive literature review was conducted using databases such as PubMed, Google Scholar, and ScienceDirect, focusing on studies published between ٢٠١٥ and ٢٠٢٤. Selected articles were analyzed for the types of biomarkers discussed, their detection methods, and potential clinical implications, providing a thorough understanding of the current landscape in cardiovascular biomarker research.

Results: Several promising biomarkers for early detection of cardiovascular diseases were identified. MicroRNAs are small, non-coding RNA molecules that regulate gene expression. Circulating microRNAs (miRNAs), such as miR-١, miR-١٣٣, and miR-٢٠٨, have been linked to myocardial injury. Elevated levels of these miRNAs are associated with acute coronary syndromes and heart failure, indicating their potential for early diagnosis and risk assessment. Their unique expression patterns provide valuable insights into the pathological processes occurring in the heart, facilitating earlier diagnosis and tailored interventions. Novel lipid profiles have also emerged as significant biomarkers. Research has focused on identifying lipid and small RNA biomarkers linked to inflammation and cardiovascular diseases. Increased levels of ceramides, a type of sphingolipid, correlate with higher cardiovascular risk, highlighting the importance of lipid profiling in early detection. This innovative approach allows for identifying high-risk patients, paving the way for timely preventive measures and personalized treatment strategies. The development of optical sensor technology has revolutionized the detection of cardiovascular biomarkers in non-invasive body fluids, such as blood and saliva. These sensors provide real-time monitoring and valuable diagnostic insights. By enabling simultaneous detection of multiple biomarkers, they can provide a comprehensive view of a patient's cardiovascular status, improving overall diagnostic capabilities and patient compliance. Established biomarkers like B-type natriuretic peptide (BNP) and its precursor NT-proBNP remain critical in heart failure diagnostics. Recent studies have developed novel assays targeting glycosylation-free regions of NT-proBNP, enhancing diagnostic accuracy. These advancements could lead to better assessments of heart failure severity and guide treatment

decisions more effectively, ensuring that patients receive the appropriate interventions in a timely manner. Soluble ST۲ is recognized for its role in risk stratification in heart failure. It is associated with myocardial fibrosis and remodeling, and its levels correlate with disease severity and prognosis. The incorporation of ST۲ into clinical guidelines reflects its utility in improving patient outcomes through better risk assessment. Additionally, high-sensitivity C-reactive protein (hs-CRP) and fibrinogen have shown promise in cardiovascular risk assessment. Elevated levels of these proteins indicate inflammation, a key factor in atherosclerosis. Combining these protein markers with novel biomarkers can lead to a more comprehensive approach in evaluating cardiovascular risk, improving overall patient care and management. The integration of machine learning techniques in biomarker discovery is transforming the identification of new cardiovascular biomarkers. Machine learning algorithms can analyze large datasets of clinical and biomarker information, enhancing predictions of cardiovascular events and enabling personalized treatment strategies.

Conclusion: The exploration of novel biomarkers for the early detection of cardiovascular diseases represents a significant advancement in cardiology. Emerging biomarkers offer promising avenues for improving diagnosis and patient management. Integrating machine learning techniques enhances the potential for precision medicine, allowing for tailored treatment strategies based on unique biomarker profiles. As these biomarkers move from research to clinical practice, they can transform cardiovascular care by enabling earlier detection and improved risk assessment. Ongoing validation is crucial to realizing their potential and reducing the burden of cardiovascular diseases. The future of diagnostics lies in applying these biomarkers to ensure patients receive effective, personalized care. By embracing these advancements, the healthcare community can enhance patient outcomes and mitigate the impact of cardiovascular diseases on public health, leading to healthier populations and improved quality of life.

Keywords: Cardiovascular Diseases, Novel Biomarkers, Early Detection

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Novel Irinotecan-SMO affinity: Comparing with Glasdegib in AML's Hedgehog pathway via Molecular Docking (Research Paper)

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Introduction: Acute myeloid leukemia (AML) is a multifactorial type of cancer characterized by the rapid growth of abnormal white blood cells. Amongst several pathways implicated in the development of AML, dysregulation of the hedgehog pathway can be a hallmark as it's a crucial signaling system in cell differentiation and proliferation. Recent studies suggest that the aberrant activation of the Hedgehog pathway is linked to the evolution and progression of leukemia, particularly leading to uncontrolled cell growth. One key player in the Hedgehog pathway is the Smoothened (SMO) protein, which regulates downstream signaling. Glasdegib is shown to inhibit tumor growth by targeting the Hedgehog pathway via blocking the activity of SMO in AML. Furthermore, Irinotecan known as a chemotherapeutic agent, exerts its antitumor effects by inhibiting the activity of topoisomerase I. Also, Irinotecan is an effective treatment option for leukemia, not yet been discovered whether it affects the hedgehog pathway or not. The objective of this study is to evaluate the affinity of Irinotecan to SMO protein in comparison with Glasdegib and to hypothesize the probable association of Irinotecan through the hedgehog pathway in leukemia.

Methods: In this research, at first, the SMO protein structure was downloaded from the Uniprot website, then necessary preparations, including adding charge and hydrogen ions, were performed using Chimera software. The three-dimensional structures of Irinotecan and Glasdegib were obtained from the PubChem website. The binding site of the SMO protein was determined using Deepsite. [Center; X: -١٣,٩٢٦, Y: -٢٩,٨٠٠, Z: -١٢,١١٩٧ and Dimensions (Angstrom); X, Y, Z: ٢٥,٠٠] Finally, the molecular docking process was conducted using AutoDock Vina in PyRx ٠,٨ to assess the binding status of Irinotecan and Glasdegib to SMO protein.

Results: Following the completion of the docking process of Irinotecan and Glasdegib with SMO protein, using PyRx software, the achieved results are summarized below. For each Model, the data represents their binding affinity, RMSD lower bond and RMSD upper bound, respectively: Irinotecan: Model #١: [-٧,٨, ٠,٠, ٠,٠] Model #٢: [-٧,٥, ٧,٩٣, ١١,٧٦] Model #٣: [-٧,١, ٢,٦٦٨, ١١,٦٨٤] Glasdegib: Model #١: [-٦,٣, ٠,٠, ٠,٠] Model #٢: [-٦,٢, ٦,٠٢١, ٨,٥٣٨] Model #٣: [-٦,٢, ٥,٦٥, ١٠,٠٧٣]

Conclusion: Based on the findings from the molecular docking analysis of Irinotecan and Glasdegib with SMO protein, it was determined that both drugs exhibit negative binding energy. Additionally, Irinotecan showed a stronger affinity compared to Glasdegib. According to the data presented in this research, it is likely that Irinotecan is involved in regulating the SMO protein, potentially offering a novel pathway of this drug for AML treatment. Nevertheless, further investigation is still needed to determine if Irinotecan has got a role in inhibiting SMO protein even greater than Glasdegib.

Keywords: Irinotecan, Hedgehog pathway, SMO protein, Glasdegib, AML

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Novel polysaccharides: a path to safety (Review)

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Introduction: The surface of cells is enveloped by a compact coating of glycans, referred to as the cellular glycocalyx. The intricate glycans within the glycocalyx are implicated in diverse biological occurrences such as bacterial pathogenicity and safeguarding bacteria against environmental stressors. Polysaccharides located on the outer surface of bacterial cells are tremendously conserved and accessible molecules, thus rendering them exceptional targets for immunological purposes. Consequently, bacterial polysaccharides and their repetitive units have been extensively examined as antigens in the advancement of antibacterial vaccines. This review critically examines the recent progress made in the field of bacterial polysaccharide-based vaccinations targeting various pathogenic bacteria that affect the human population.

Methods: A PubMed search was conducted for "glycoconjugate vaccine", "immunization" and "vaccination" in English articles published from ۱۹۲۳ to ۲۰۳۳.

Results: Vaccination is widely regarded as the most efficient and cost-effective platform for combating infectious diseases. Carbohydrates, acting as antigens, are abundant and positioned on the cell surface to be acknowledged by the immune system of the host. They are heavily guarded on bacterial cells and serve as essential pathogenic factors crucial for bacterial survival. Due to this reason, there is immense interest in vaccine preparation technology regarding carbohydrates. Consequently, numerous bacterial polysaccharides have been successfully transformed into vaccines and employed in clinical settings to manage diverse bacterial infections.

Conclusion: Emerging technologies facilitate vaccine development and contribute to the battle against various infections that pose threats to human life. Furthermore, they alleviate the social and economic burden associated with infectious diseases, thereby augmenting human health and well-being.

Keywords: Glycoconjugate vaccine, Capsular polysaccharide, Conjugate Vaccine, Immunization, vaccination

Nutrition, related to stomach cancer. (Review)

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[1]. Dastheib [3]

Introduction: Stomach cancer is an abnormal growth of cells that starts in the stomach, which is a muscular pouch located in the upper half of your abdomen, just below the ribs.

Methods: According to the NCI Trusted Source for Stomach Cancer Symptoms, there are usually no early symptoms of stomach cancer. Unfortunately, this means that until the cancer is at an advanced stage, people usually don't know there's anything wrong. Some of the most common symptoms of advanced stomach cancer include: Nausea and vomiting-Frequent heartburn-Loss of appetite, sometimes accompanied by sudden weight loss-Constant bloating-Early satiety (feeling full after eating only a small amount of food)-bloody stool-Jaundice-extreme fatigue-Stomach pain that may be worse after eating-Swelling or fluid accumulation-Low number of red blood cells-Dull discomfort in the abdomen, usually above the navel

Results: Stomach cancer is treated with one or more of the following: Chemotherapy-radiotherapy-surgery-immunotherapy such as vaccines and drugs Your exact treatment plan depends on the origin and stage of the cancer. Age and general health can also play a role. Apart from treating cancer cells in the stomach, the goal of treatment is to prevent the cells from spreading. Stomach cancer, if left untreated, may spread to the following: Lungs-lymph nodes-bones-liver

Conclusion: If stomach cancer is diagnosed in the early stages, you are more likely to recover. Most people who survive stomach cancer have a local diagnosis. This means that the stomach was the main source of cancer. Cancer is difficult to diagnose and stage when the origin is unknown. This also makes cancer treatment more difficult. It is also more difficult to treat stomach cancer in the later stages. If your cancer is more advanced, you may want to participate in a clinical trial. Clinical trials help determine whether a new medical procedure, device, or other treatment is effective in treating certain diseases and conditions. You can go to Shiraz Campus Cancer Institute to diagnose and treat stomach cancer as soon as possible.

Keywords: cancer Stomach cancer

Obesity and inflammation (Review)

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Introduction: Since obesity rates have increased rapidly in recent decades, it is now referred to as a global epidemic. The World Health Organization (WHO) estimates that negative health effects from obesity cause at least ٢,٨ million deaths annually. The prevalence for both metabolic and non-metabolic diseases, including type ٢ diabetes (T٢D), insulin resistance, hyperglycemia, dyslipidemia, cardiovascular disorders, fatty liver, high blood pressure, and cancer, is higher in obese individuals. Continuous obesity triggers mild inflammations in the body, which can elevate one's susceptibility to a variety of illnesses. Fat position, the state of the immune system, genetics, and even the type of adipose tissue (AT) all possess a significant impact on the inflammation induced by obesity. The passage of immune cells such as neutrophils, eosinophils, and macrophages into inflammatory tissues is one of the key characteristics of inflammation. Based on current studies, as peri-adipocytes, or fat cells, increase, they may begin to release chemotactic signals that attract macrophages. The necrotic fat cells often serve as the immune system's trigger in cases of chronic obesity. Due to their necrosis in obesity-related conditions, these cells stimulate immune system components such as macrophages to produce a cytokine known as tumor necrosis factor-alpha (TNF-α). Long-term obesity can lead to changes in the number of macrophages as well as distinct phenotypes. Under normal circumstances, they can polarize in this manner from the M٠ or M٢-like phenotype to the inflammatory or M١ phenotype, and they may enhance the inflammation in AT through the release of additional inflammatory cytokines such as TNF-α, IL-١β, and IL-٦. Insulin resistance may develop as a result of this cytokine's prolonged secretion, which is one of the factors contributing to type II diabetes (T٢D). Investigation has indicated that the generation of inflammatory mediators such as IL-٦ and IFN-γ may stimulate mast cells, which in turn induce inflammation in the visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) of obese humans and mice. Obese individual's SAT and VAT comprise neutrophils, which are likewise active in peripheral blood.

Methods: The research's keywords were "inflammation and obesity," "obesity-linked inflammation," and "inflammatory mechanisms in obesity." These terms can be found in well-known obesity-related databases, websites, and journals such as PubMed/Medline, Google Scholar, Elsevier, and Nature. The required information was then extracted and analyzed from these sources of information.

Results: Although obesity is prevalent, it is a very treatable and preventable condition. This disease causes mild inflammation, which over time may increase a person's risk of developing conditions like atherosclerosis, type II diabetes, high blood pressure, liver problems, and even cancer. It's fascinating to note that tertiary lymphatic tissues can be induced in obesity-related inflammation by

recruiting immune system cells to the site. Obesity may raise the number of ILC١s in SAT, which may then stimulate M١-like macrophages and enhance inflammation in AT through the production of IFN-γ. On the other hand, ILCϒs are normally found in the VAT and SAT of humans and mice, decrease with obesity and may be crucial for maintaining eosinophils and Mϒ-like macrophages as well as appropriate AT homeostasis.

Conclusion: Despite common belief, the inflammation induced by fat is manageable, even though it can be quite hazardous. It is now widely known that chronic inflammation, especially in AT, has a role in the etiology of TϒD and its consequences. Inflammatory pathways are an appealing target for the treatment of metabolic diseases because of the connection between obesity, AT inflammation, and metabolic disease. Obesity may produce inflammation, although its inhibitors may help lessen it. Major inflammatory cytokines such as TNF-α and IL-١β are generated in obesity. Additionally, medications with anti-inflammatory capabilities, such as metformin in different dosages, salsalate, and thiazolidinediones (TZDs), may help lessen inflammation caused by obesity.

Keywords: inflammation and obesity, obesity-linked inflammation, inflammatory mechanisms in obesity

Obesity and Mesenchymal Stem Cell's Mitochondria Dysfunction (Review)

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Introduction: Mesenchymal stem cells (MSCs) are adult stem cells found in several types of tissues. They carry out a natural repair system within the body. MSCs have unique features, including being easy to isolate and their ability to migrate to injured areas. They exhibit anti-inflammatory and anti-apoptotic properties in damaged tissues and can modulate the immune response through paracrine signaling. Additionally, they have an antimicrobial effect. MSCs can also activate other local stem cells and promote angiogenesis. MSCs have become a major focus in recent research because of their biological importance and potential clinical uses. Obesity is a worldwide issue that considerably damages healthcare systems economically and is linked to higher rates of cardiovascular diseases and deaths. Obesity declines the immunomodulatory capabilities of MSCs. However, the exact mechanisms behind this impairment are still unclear. The viability, compatibility, self-renewal, and differentiation potential of MSCs depend heavily on the health and performance of their mitochondria. These organelles not only generate cellular energy but also regulate key cellular functions such as the production of reactive oxygen species (ROS), cell proliferation, survival, and apoptosis.

Methods: A comprehensive article search was conducted using the PubMed database to identify relevant studies about mitochondrial changes in obese MSCs. Keywords such as "obesity" and "mesenchymal stem cells" and "mitochondrial dysfunction" were used to find articles published between ٢٠٢٠ and ٢٠٢٤.

Results: Obesity causes alterations in the hydroxymethylation and mRNA profiles of genes related to mitochondria in MSCs derived from human adipose tissue.

Conclusion: These findings could help in creating new strategies using epigenetic modulators and mitoprotective drugs to maintain the therapeutic effectiveness of MSCs in obese individuals. Additional research is required to develop and test methods for managing the obesity-related epigenetic environment of MSCs in living organisms.

Keywords: Obesity Mesenchymal Stem Cell MSC Mitochondrial Dysfunction

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Omega-٣ fatty acids for breast cancer prevention and survivorship (Review)

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Introduction: Breast cancer is a kind of cancer that begins as a growth of cells in the breast tissue. After skin cancer, breast cancer is the most common cancer diagnosed in women in the United States. The use of ω-٣ PUFAs, eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) has been shown to minimize chemotherapy side effects and improve progression-free survival as well as the overall survival of patients with breast cancer.

Methods: In this study, ١٠ articles published from ٢٠٢٠ to ٢٠٢٤, which were in the form of quantitative studies, original research and systematic review were examined. Entry criteria included: Availability of full text and articles published between ٢٠٢٠ and ٢٠٢٤, and exit criteria included: Case report studies. The study used the keywords: Omega-٣ fatty acids, breast cancer, prevention.

Results: The exact cause of most breast cancers isn't known. Researchers have found things that increase the risk of breast cancer. These include hormones, lifestyle choices and things in the environment. If increasing EPA and DHA relative to arachidonic acid is effective in reducing breast cancer risk, likely mechanisms include reduction in pro inflammatory lipid derivatives, inhibition of nuclear factor-κB-induced cytokine production, and decreased growth factor receptor signaling as a result of alteration in membrane lipid rafts. EPA and DHA supplementation is also being explored in an effort to help prevent or alleviate common problems after a breast cancer diagnosis, including cardiac and cognitive dysfunction and chemotherapy-induced peripheral neuropathy.

Conclusion: The insulin-sensitizing and anabolic properties of EPA and DHA also suggest supplementation studies to determine whether these omega-٣ fatty acids might reduce chemotherapy-associated loss of muscle mass and weight gain. We will briefly review relevant omega-٣ fatty acid metabolism, and early investigations in breast cancer prevention and survivorship.

Keywords: Omega-٣ fatty acids, breast cancer, prevention

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Omics and data analysis of ALL cancer data and selection of new generation chemotherapy drugs

(Research Paper)

Majid Mesgartehrani,[1,*] Parnian Hossainzadeh,[2] Mohammad mahdi Eslami,[3] Saeid Mirlohi,[4]

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٢.
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Introduction: Acute lymphoblastic leukemia (ALL) is a type of blood cancer caused by genetic mutations in lymphoid stem cells, leading to the uncontrolled proliferation of these cells. This disease is one of the most common types of blood cancer in children. With advancements in omics techniques, it has become possible to more accurately analyze these mutations and identify single nucleotide polymorphisms (SNPs) that can affect patients' response to treatment and the occurrence of side effects. This study aims to optimize the selection of next-generation chemotherapy drugs based on the genetic profile of ALL patients.

Methods: The NCBI database was used to identify common SNPs based on two factors: citation and population data. Subsequently, drug information and the side effects of the chemotherapy drugs available in Iran for ALL were extracted. Finally, the data were analyzed and evaluated using the pharmacogenetics software "Mega Gene."

Results: The results showed that some common SNPs not only play a role in the development of ALL but can also influence the severity and type of side effects associated with chemotherapy. SNPs such as rs٦٣٧٥١٢٢١, rs١٢١٩١٢٦٦٤, and rs١١٥٩٧٨٢ may increase the risk of side effects like nausea, anorexia, and inflammation.

Conclusion: These findings underscore the importance of conducting genetic tests before starting chemotherapy to select drugs with fewer side effects and greater efficacy for each patient.

Keywords: Omics , Acute lymphoblastic leukemia (ALL) , Pharmacogenetics , SNP , Chemotherapy

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Omics Data Analysis and New Generation Chemotherapy Drug Selection in Pancreatic Cancer

(Research Paper)

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Introduction: Pancreatic cancer is one of the deadliest forms of cancer, and its diagnosis and effective treatment remain challenging. Utilizing omics approaches and data analysis can enhance our understanding of genetic mechanisms and aid in selecting appropriate chemotherapy drugs.

Methods: In this study, SNPs associated with pancreatic cancer were gathered from the NCBI database. For the analysis of polymorphisms and identification of genetically based side effects, the pharmacogenomic software MegaGen was employed.

Results: The findings indicated that three polymorphisms, rs٢٨٨٩٧٧٥٣, rs١٠٤٢٥٢٢, rs١٨٠٥٧٩٤, and rs٣٠٢٧٢٣٤, play a significant role in the development of pancreatic cancer. Additionally, the polymorphism rs٦٣٧٥١٢٢١ was identified as having the greatest impact on the genetic side effects of chemotherapy drugs such as Alvoxal, Erloxha, and Oncozar.

Conclusion: The results underscore the importance of examining genetic polymorphisms in the diagnosis and effective treatment of pancreatic cancer. Identifying these variations can lead to the selection of drugs with fewer side effects and greater efficacy. Genetic testing prior to drug administration, especially for common genes like MLH١, is essential. By identifying polymorphisms, optimal treatments with minimal side effects can be chosen for patients.

Keywords: Polymorphisms, Pancreatic Cancer, Pharmacogenomics, Chemotherapy Side Effects, Data Analysis

Omics, data analysis of gastric cancer, and selection of a new anticancer drug (Research Paper)

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Introduction: Gastric cancer (GC) is known to be among the most prevalent types of cancer and a leading cause of cancer-related death in Iran. Currently, therapeutic strategies, selection of chemotherapy drugs, and treatment modalities in Iran are mainly based on the tumor histology type. This uniform strategy often leads to drug resistance, metastasis, and adverse therapeutic outcomes. In recent years, the dramatic advances in genomics and bioinformatics fields have allowed for personalized cancer treatment. The cancer patient's exclusive genomic profile can now be identified in most countries using methods such as flow cytometry and new-generation sequencing (NGS). This valuable information allows for a more accurate selection of chemotherapy drugs and the design of targeted therapeutic strategies. The personalization of treatment based on the genomic profile can promise a better therapeutic response, reduction of side effects, and prolonged life of patients.

Methods: This study mainly aims to establish an all-inclusive database of GC patients' genomic profiles, aiming at the personalized treatment and prediction of the patient's response to various treatments, particularly concerning drug side effects. Through a comprehensive analysis of genomic and clinical data, this research seeks to identify genetic biomarkers related to response to treatment and the incidence of side effects in GC patients. To achieve the study goals, the comprehensive NCBI genomic database was used as a rich source of genetic information, and the genomic data of GC patients were extracted and analyzed from this database. The data were more accurately analyzed using the specialized pharmacogenetic software (Mega Gene), which allows for analyzing gene polymorphisms and predicting their impacts on drug metabolism and side effects.

Results: The comprehensive analysis of GC patients' genomic data has manifested the pivotal role of gene polymorphisms in the development and progression of this disease. This article represents a wide range of multifactorial genes involved in GC pathogenesis. Our results indicate that the RS٤٩٨٧٠٤٧ polymorphism in the BRCA٢ gene is associated with an increased risk of breast and ovarian cancers. Similarly, the RS٨٠٣٥٧٩٠٦ polymorphism in the BRCA١gene is linked to an elevated risk of neoplasm of ovary and pancreatic cancers, and the RS١٨٠٠٠٥٦ polymorphism in the ATM gene is related to a heightened risk of breast and carcinoma of colon cancers. These results demonstrate specific patterns of tumor metastasis and spread in GC patients.

Conclusion: Based on our results, it can be concluded that evaluating GC patients' genomic profile, particularly the polymorphisms detected in this study, can help predict the risk of developing other cancers and play an effective role in selecting the chemotherapy drug type. Moreover, genetic tests

are necessary to examine polymorphisms in common genes, including FTO, JAK۲, TYR, and MLH, before prescribing the drugs for GC patients. This helps physicians to select a drug with minimal side effects based on each patient's genetic profile, thereby improving treatment effectiveness.

Keywords: Next-generation-sequencing; Flowcytometry; Personalized medicine; Gastric cancer; Genomic profile.

Oncolytic Viruses: The Rising Stars for Cancer Treatment (Review)

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Introduction: Cancer is becoming a leading concern worldwide by the rate of global death. Not only, early detection and new methods of treatment increased remission expectancy but also, the cancer death rates have decreased by ٣٣٪ from ١٩٩٠s to the recent years due to many accepted therapies for cancer, such as chemotherapy, radiotherapy, targeted therapy, surgery, hormonal therapy and immunotherapy. However, they have limited efficacy for advanced cancer patients. During ١٩٩٠s, patients with virus-infected cancer showed tumor remission for a short time which led to Oncolytic Viruses (OVs) have become the rising stars. This new innovative form of immunotherapy can infect and demolish cancer cells selectively, while saving normal cells from damage. Early case reports illustrate the effect of natural form of viruses on tumor cells. But by develop of genetic engineering and viral gene research, Oncolytic Viruses have become a promising approach for cancer treatment.

Methods: The infection mechanism of OVs depends on the type of virus infecting the tumor cells and the antiviral immune response of the host immune system will determine the success of oncolytic virotherapy. By adhering to the cancer cells, OVs use several lytic pathways to stimulate immune system. The virus uses the tumor cell's protein translational machinery to block protein synthesis. The replication of viral nucleic acid and viral protein synthesis cause progeny virus particles which lyse tumor cells and release. The lysed cells release chemokines and cytokines that let the immune system to detects the lysed cells and provoke pathways to recognize other tumor cells. During the tumor cell apoptosis, the released tumor antigens, such as tumor-associated antigens (TAAs), damage-associated molecular patterns (DAMPs), and pathogen-associated molecular patterns (PAMPs), attract cytotoxic T lymphocytes, dendritic cells, natural killer cells, and macrophages to induce tumor-specific immune response. Furthermore, the release of cytokines can attract an immune response to nearby tumor cells without the apoptosis function. OVs can also decrease the oxygen and nutrients percentages by disrupting the blood vessels which connected to tumors.

Results: To date, many OVs have entered into early-phase clinical trials, such as adenoviruses, herpes viruses, measles viruses, coxsackie viruses, polioviruses, reoviruses, poxviruses, and Newcastle disease viruses, but OVs will exhibit a series of complicated and exact mechanisms of action when they are employed in cancer therapy. In some cases, the immune system can detect the OVs and defeat the viruses before they reach the target tumors. On the other hand, the virus can escape from the immune system, and causing inflammation elsewhere, which is also a cause of concern.

Conclusion: In conclusion, the OVs has the potential to be a highly effective way to treat cancer; however, there are still limitations and difficulties with virotherapy that can be solved by additional research and clinical trials. Further knowledge of the therapeutic activity mechanism, identification of biomarkers, and conducting clinical trials with combination therapies will enhance the therapeutic application of OV for various cancers. Immunotherapy aims for a sustainable full response or recovery; thus, we need to prioritize various OVs and develop methods to choose the most promising ones for cure.

Keywords: Oncolytic virus, Cancer, Immunotherapy, Treatment

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Optical Microscopy Imaging: Unveiling the Molecular Landscape of Biological Systems (Review)

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Introduction: Optical microscopy imaging has emerged as a powerful tool for visualizing and tracking individual molecules or nanoparticles within biological environments. This technique offers high temporal and spatial resolution, enabling researchers to study biological processes and detect biomolecules with unprecedented detail. The application of optical microscopy imaging has revolutionized various fields, including molecular detection and single-particle tracking.

Methods: A comprehensive literature search was conducted using various databases, including PubMed, Semantic Scholar, arXiv, and NCBI PMC. The search terms included "optical microscopy imaging," "super-resolution microscopy," "single-molecule tracking," "photothermal microscopy," "nonlinear optical microscopy," "photoacoustic microscopy," and "supercontinuum radiation." Relevant articles published in peer-reviewed journals were carefully reviewed and analyzed.

Results: Several optical microscopy techniques have been developed and employed in bio-analytical assays. Total internal reflection fluorescence microscopy (TIRFM), super-resolution optical microscopy (SRM), and dark-field optical microscopy (DFM) are among the widely used techniques. These methods utilize principles such as fluorescence, absorption, and scattering to generate high-resolution images of biological samples. Photothermal microscopy has also been explored for label-free detection of individual nanoabsorbers, overcoming limitations of fluorescence-based detection. Other techniques like nonlinear optical microscopy, photoacoustic microscopy, and supercontinuum radiation have further expanded the capabilities of optical microscopy imaging.Optical microscopy imaging has been successfully applied in various fields, enabling the study of biological processes and the detection of biomolecules with high spatial and temporal resolution. These techniques offer several advantages, including non-invasive and non-destructive imaging of biological samples, real-time observation of live cells and tissues, and label-free detection capabilities. However, challenges such as the need for high-quality optics, precise control over imaging conditions, and the potential for photobleaching or photodamage to the sample need to be addressed.

Conclusion: Optical microscopy imaging has become an indispensable tool in bio-analytical assays, providing researchers with a powerful means to study biological systems and improve diagnostic capabilities. The development of new techniques and methods, coupled with ongoing efforts to address existing challenges, will further enhance the sensitivity, resolution, and applicability of optical microscopy imaging in various fields.

Keywords: Optical microscopy, super-resolution microscopy, fluorescence microscopy, single-molecule imaging,

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Optimized Transdifferentiation of Fibroblasts: A Robust Approach to Alzheimer's Disease Modeling

(Research Paper)

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Introduction: Transdifferentiation of human adult fibroblasts into mature neurons offers a promising and efficient method for generating patient-specific neuronal cells for neurodegenerative diseases like Alzheimer's. This approach is precious for disease modeling, mechanistic studies, and drug screening. Unlike induced pluripotent stem cells (iPSCs), which undergo rejuvenation and lose aging characteristics, transdifferentiated neurons retain the donor's aging signatures, providing a more accurate model of age-related diseases. Although transdifferentiation can be challenging, especially with increasing passage numbers, it avoids the need for an intermediate pluripotent stage, making it faster and more cost-effective. Transdifferentiated cells also maintain genetic diversity, reflecting the natural mosaicism of the original fibroblast population.

Methods: In this study, we optimized existing protocols to efficiently generate mature neurons from fibroblasts of elderly Alzheimer's patients, regardless of passage number. These neurons retained age-related characteristics and exhibited functional capabilities similar to native neurons. For this purpose, human dermal fibroblasts were obtained from skin biopsies of six Alzheimer's patients. Lenti-X ٢٩٣ cells were transfected with a lentiviral vector containing Ascl١ and Brn٢ transcription factors, along with shRNA against REST and packaging vectors pMD٢.G and psPAX٢. Three days post-transduction, human dermal fibroblasts were cultured in an induction medium containing dual SMAD inhibition factors, growth factors, and VPA. On day ١٢, cells were passaged using ROCKi and accutase onto plates coated with PO/FN/Lam. Seven days later, a secondary induction medium containing LM-٢٢A٤, GDNF, NT٣, AA, and db-cAMP was applied.

Results: By day ٢٥, a significant yield of neurons, accounting for approximately ٥٠٪ of the total cells, was achieved. Western blot, real-time PCR, and immunocytochemistry analyses confirmed the expression of neuronal markers such as MAP٢ and TAU, confirming their mature neuronal identity. The conversion process was consistent across different cell lines, including those from older donors and those that had undergone multiple passages.

Conclusion: This protocol offers an efficient method for generating induced neurons (iNs) from human adult dermal fibroblasts, regardless of passage number. Our results demonstrate the feasibility of producing neurons from individuals aged ٥٠-٧٩ with high efficiency, providing a valuable tool for Alzheimer's disease research.

Keywords: Cell Reprogramming; Neurogenesis; Aging; Neuronal Differentiation; Lentiviral Vectors

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Optimized Transgene-Free Reprogramming of Human Fibroblasts into Functional Neurons using Small Molecules (Research Paper)

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Introduction: Neuronal transdifferentiation plays a vital role in the progress of regenerative medicine and the modeling of neurodegenerative diseases. Current methods utilize transcription factors, which raise safety concerns and limit their clinical use. Our study addresses these challenges by introducing an optimized transgene-free method that directly converts human fibroblasts into functional neurons using a small molecule cocktail, bypassing the neural progenitor state. In this study, we reprogrammed human dermal fibroblasts obtained from the skin biopsy of a ٦٧-year-old Alzheimer's patient into mature neurons.

Methods: To generate neuronal cells from human fibroblasts, ٥٠٠٠ fibroblasts were seeded per well in Nunc® Lab-Tek® II chambered coverglass coated with PLO/Lam and maintained in a fibroblast culture medium for one day. To promote cell differentiation and survival, conditioned media from mixed glial cell cultures (mGCM) and neural conditioned medium (NCM) were employed. Primary microglia were isolated from mixed glial cell cultures of neonatal mouse brain tissue to prepare these media, and neural stem cells were isolated from the postnatal cerebellum. Neural induction medium consisting of a ١:١:١ mixture of NCM, mGCM, and Neurobasal supplemented with N-٢, B-٢٧, db-cAMP, and bFGF, along with a small molecule cocktail containing Valproic acid, CHIR٩٩٠٢١, Repsox, Forskolin, SP٦٠٠١٢٥, GO٦٩٨٣, and Y-٢٧٦٣٢. This cocktail was refreshed every four days for ٨ days. Subsequently, cells were switched to a neuronal maturation medium containing the same basal components supplemented with BDNF, GDNF, NT٣, AA, db-cAMP, N-٢, and B-٢٧ and cultured for an additional two weeks.

Results: Finally, we successfully obtained human chemical-induced neuronal cells (hciNs) that expressed neuronal markers, including Tau and Tuj١. After fine-tuning the technique, we managed to generate functional neurons without introducing exogenous genes.

Conclusion: Our findings offer a safer, more efficient platform for personalized medicine and disease modeling in neurodegenerative diseases.

Keywords: Regenerative Medicine, Primary Culture, Conditioned Medium, Transdifferentiation, Neurodegenerative

Optogenetics: Battling cancer with light (Review)

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Introduction: Gene and cell therapies are widely recognized as future cancer therapeutics but poor controllability limits their clinical applications. Optogenetics, the use of light-controlled proteins to precisely spatiotemporally regulate the activity of genes and cells, opens up new possibilities for cancer treatment Normal cancer treatment involves drugs that are often harmful to the body. The optogenetics technique involves injecting a gene into cells that make a light-sensitive protein. Next, they shine a laser on these cells to alter their behaviors. Different proteins will result in different behaviors. Breast and skin cancers may be most ideal for this kind of treatment because they are easy to target with a laser, according to Levin.

Methods: Here, we introduce optogenetic approaches in cancer research, their clinical potential and challenges of incorporating optogenetics in cancer therapy. We critically discuss beneficial combinations of optogenetic technologies in cancer.

Results: optogenetics approaches can provide us with outstanding tool to extend our understanding of how cells perceive, respond, and behave in meeting with complex signals, particularly in terms of cancer evasion from the anticancer immune system functions

Conclusion: If this approach works on humans, it would place scientists closer to developing alternative drug-free treatment methods. Similarly, this method works differently than many cancer drugs, which commonly kill cells. Reverting the cell back to its original state by hitting it with light may be the cancer treatment of the future. Optogenetics merely reverts the cell back to its normal, or non-dividing, state. Standard cancer drugs that target dividing cells are not ۱۰۰ percent effective, and they often have harsh side effects. This drug-free treatment technique may be a healthier alternative to treating a volatile disease.

Keywords: Optogenetics, Cancer

Oral mucosal tissue engineering (Review)

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Introduction: Tissue engineering of oral mucosa combines cells, materials and engineering to produce a three-dimensional reconstruction of oral mucosa. It is meant to simulate the real anatomical structure and function of oral mucosa. Tissue engineered oral mucosa shows promise for clinical use, such as the replacement of soft tissue defects in the oral cavity.[1] These defects can be divided into two major categories: the gingival recessions (receding gums) which are tooth-related defects, and the non tooth-related defects. Non tooth-related defects can be the result of trauma, chronic infection or defects caused by tumor resection or ablation (in the case of oral cancer). Common approaches for replacing damaged oral mucosa are the use of autologous grafts and cultured epithelial sheets.

Methods: Autologous grafts are used to transfer tissue from one site to another on the same body. The use of autologous grafts prevents transplantation rejection reactions. Grafts used for oral reconstruction are preferably taken from the oral cavity itself (such as gingival and palatal grafts). However, their limited availability and small size leads to the use of either skin transplants or intestinal mucosa to be able to cover bigger defects.[2]Other than tissue shortage, donor site morbidity is a common problem that may occur when using autologous grafts. When tissue is obtained from somewhere other than the oral cavity (such as the intestine or skin) there is a risk of the graft not being able to lose its original donor tissue characteristics. For example, skin grafts are often taken from the radial forearm or lateral upper arm when covering more extensive defects. A positive aspect of using skin grafts is the large availability of skin. However, skin grafts differ from oral mucosa in: consistency, color and keratinization pattern. The transplanted skin graft often continues to grow hair in the oral cavity.Cell culture techniques make it possible to produce epithelial sheets for the replacement of damaged oral mucosa. Partial-thickness tissue engineering uses one type of cell layer, this can be in monolayers or multilayers. Monolayer epithelial sheets suffice for the study of the basic biology of oral mucosa, for example its responses to stimuli such as mechanical stress, growth factor addition and radiation damage. Oral mucosa, however, is a complex multilayer structure with proliferating and differentiating cells and monolayer epithelial sheets have been shown to be fragile, difficult to handle and likely to contract without a supporting extracellular matrix. Monolayer epithelial sheets can be used to manufacture multilayer cultures. These multilayer epithelial sheets show signs of differentiation such as the formation of a basement membrane and keratinization.[1]

Results: To obtain the best results, the type and origin of the fibroblasts and keratinocytes used in oral mucosa tissue engineering are important factors to hold into account. Fibroblasts are usually taken from the dermis of the skin or oral mucosa. Kertinocytes can be isolated from different areas of the oral cavity (such as the palate or gingiva). It is important that the fibroblasts and keratinocytes are used in the earliest stage possible as the function of these cells decreases with time. The

transplanted keratinocytes and fibroblasts should adapt to their new environment and adopt their function. There is a risk of losing the transplanted tissue if the cells do not adapt properly. This adaptation goes more smoothly when the donor tissue cells resemble the cells of the native tissue.

Conclusion: Although it has not yet been commercialized for clinical use clinical studies have been done on intra- and extra-oral treatments with full-thickness engineered oral mucosa. Full-thickness engineered oral mucosa is mainly used in maxillofacial reconstructive surgery and periodontal peri-implant reconstruction. Good clinical and histological results have been obtained. For example, there is vascular ingrowth and the transplanted keratinocytes integrate well into the native epithelium. Full-thickness engineered oral mucosa has also shown good results for extra-oral applications such as urethral reconstruction, ocular surface reconstructi١. K. Moharamzadeh et al (٢٠٠٧), Tissue-engineered Oral Mucosa: a Review of the Scientific Literature, JDR Journal of Dental Research ٢. Ulrich Meyer et al (٢٠٠٩), Fundamentals of Tissue Engineering and Regenerative Medicine, p. ٣٦٨, ISBN ٩٧٨-٣-٥٤٠-٧٧٧٥٤-٠on and eyelid reconstruction.[١]

Keywords: Oral, Mucosal,Tissue engineering

Oropouche Virus: An Emerging Threat in Tropical Regions (Research Paper)

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Introduction: The Oropouche virus (OROV) is a tropical viral infection primarily transmitted by biting midges (Culicoides paraensis) and some mosquito species. First identified in 1900 near the Oropouche River in Trinidad and Tobago, this virus has since become a significant public health concern in several countries in South and Central America, including Brazil, Panama, and Peru. Recent outbreaks have also been reported in Cuba, highlighting its expanding geographical reach. The virus is known for its ability to cause large outbreaks, affecting thousands of individuals in urban and rural settings. Understanding the epidemiology, transmission dynamics, and clinical manifestations of Oropouche virus is crucial for developing effective prevention and control strategies.

Methods: This study synthesizes data from recent epidemiological reports, clinical studies, and public health records to provide a comprehensive overview of the transmission, symptoms, and prevention strategies for Oropouche virus. The information was gathered from reputable sources, including the Centers for Disease Control and Prevention (CDC), World Health Organization (WHO), and peer-reviewed journals. Data collection involved a systematic review of literature published in the last decade, focusing on studies that reported on the incidence, vector ecology, clinical features, and public health interventions related to Oropouche virus. Additionally, case studies from recent outbreaks were analyzed to identify patterns and risk factors associated with the spread of the virus.

Results: Transmission The primary vectors for Oropouche virus are biting midges, particularly Culicoides paraensis, and some mosquito species. The virus is also found in natural reservoirs such as sloths, non-human primates, and birds. Human infection occurs through the bite of an infected midge or mosquito. The virus has shown the ability to adapt to different vectors, which may contribute to its spread in various regions. Symptoms Oropouche virus infection typically presents with an abrupt onset of fever, severe headache, chills, muscle and joint pain, and sometimes a rash. Other symptoms may include photophobia, dizziness, retroorbital pain, nausea, and vomiting. In severe cases, the virus can cause neuroinvasive diseases such as meningitis and encephalitis. Symptoms usually last between 2 to 7 days, but in some cases, they can recur weeks later. The recurrence of symptoms can complicate diagnosis and management, making it essential for healthcare providers to be aware of the virus's clinical presentation. Prevention Currently, there are no vaccines or specific treatments available for Oropouche virus. Prevention relies heavily on personal protective measures to avoid bites from infected midges and mosquitoes. Recommended strategies include using insect repellents, wearing long sleeves and pants, and sleeping under bed nets. Environmental control measures, such as reducing standing water where midges and mosquitoes breed, are also crucial. Public health campaigns focusing on educating communities about the importance of these preventive measures can significantly reduce the incidence of Oropouche virus infections.

Conclusion: The Oropouche virus represents a growing threat in tropical regions, with its ability to cause significant morbidity and its potential for widespread outbreaks. Given the lack of vaccines and specific treatments, emphasis must be placed on preventive measures and public health education to mitigate the impact of this virus. Further research is needed to develop effective vaccines and treatments and to better understand the virus's epidemiology and pathogenesis. Collaborative efforts between governments, healthcare providers, and researchers are essential to address the challenges posed by Oropouche virus and to protect vulnerable populations in affected regions. Strengthening surveillance systems and improving diagnostic capabilities are also critical steps in early detection and response to outbreaks, ultimately reducing the public health burden of Oropouche virus.

Keywords: Oropouche virus, transmission, symptoms, prevention, tropical regions

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Ovarian Drilling, a Notable Medical Approach to Treat PCOS (Review)

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Introduction: PCOS is the most common endocrine disorder in women who are at the age of fertility. Its main cause is not well-known. Its main characteristics are hyperandrogenism, raised Luteinizing hormone : Follicle stimulating hormone (LH:FSH) ratio and ovulatory dysfunction (irregular or stopped ovulations). Therefore, PCOS can cause infertility. This problem may be managed by changing lifestyle. There are also treatments for PCOS-related infertility. Such as medications to induce ovulation. Clomiphene citrate, aromatase inhibitors (such as letrozole) and gonadotropin are among these medications. There are also remedial methods to overcome this kind of infertility. One of them is ovarian drilling and is performed via laparoscopy (under general anesthesia) or transvaginal hydrolaparoscopy (under general or spinal anesthesia). During this procedure, a specialist operates a surgery to make some punctures in the tissue of ovaries. This procedure destructs some of the follicles, thereby lowering plasma levels of androgens and inhibin. This ultimately results in an increase of plasma FSH level and helps ovulation to occur.

Methods: The search for collecting information was conducted across electronic databases, including PubMed, Google Scholar and StatPearls. We explored available English-language articles that are related to the subject of our article.

Results: According to research that was conducted in France and published in ٢٠١٩, ٢٨٩ infertile women with PCOS underwent ovarian drilling surgery and ١٣٧ of them achieved at least one pregnancy after drilling (٧١ were spontaneous), and ٤٨ of them achieved at least two (٢٧ were spontaneous). The Rotterdam criteria were applied to define PCOS and ٢٦٨ women had polycystic ovaries with a mean antral follicle count (AFC) of ٥٠,٥ . Some possible risks of the procedure are adhesion, problems caused by anesthesia, internal bleeding and infection. The probability of occurrence of ovarian hyperstimulation syndrome (OHSS) and multiple pregnancies caused by this procedure is notably lower than that of medications.

Conclusion: There are women who struggle with infertility caused by PCOS and medications failed to cure their problem. There are also other infertile PCOS patients who tend not to be treated with medications because of their possible side effects, such as OHSS and multiple pregnancies. In these cases, ovarian drilling can be a good attempt to overcome the infertility and increase the chance of getting pregnant.

Keywords: PCOS, ovarian drilling, infertility, pregnancy

Overcome challenges in perfusion culture system for manufacturing of recombinant human interferon β-۱a by Chinese hamster ovary cells (Research Paper)

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Introduction: Recombinant human interferon β-۱a is a protein product that is obtained by the recombinant method and is used in the treatment of condyloma acuminatum and relapsing forms of multiple sclerosis (MS disease) and reduces the frequency of disease recurrence and relieves the patient's weakness and disability. In order to produce rh-IFN β-۱a protein, Chinese hamster ovary cells are transformed with human beta interferon gene and used in the industrial production process. IFN β-۱a is expressed by the host in a perfusion production system using serum-free culture medium in a stirred bioreactor and secreted in the culture medium. In the early stages, there were many challenges such as the lack of cell growth and viability, clogging of the spin filter, the challenge of increasing the amount of host DNA. To solve this problems, various optimizations were performed to select optimal conditions for cell growth and protein expression. In this work, the perfusion cell line of producing rh-IFN β-۱a was studied to overcome challenges mentioned.

Methods: ۱- Lack of proper cell growth in the logarithmic phase In the early stages of setting up, one of the challenges ahead was the lack of proper cell growth and the doubling time was longer than expected, so that the maximum cell density obtained was about ٦ million cells per cc. With this cell density, the amount of the final product was less than expected, and the cost of the finished product was higher than expected. To solve this problem, various experiments were conducted with various culture mediums to select the optimal culture medium for growth. ۲- Temperature shift in order to changing in cell growth phase and enhance protein expression Various parameters have been used to slow down cell growth. Mild hypothermia is probably the most well-known environmental factor that can improve the performance of mammalian cell culture processes. Temperature performance between ۳۰ and ۳٤ degrees Celsius has shown that by stopping the cell in the G۰/G۱ phase, it affects the cell cycle, cell growth is inhibited, and the amount of glucose or amino acid consumption tends to decrease. One of the most widely used strategies is to reduce the culture temperature in order to change the behavior of the cell so that instead of cell proliferation, the target protein has a higher expression. ۳- Clogging of the perfusion system during the production process due to the adhesion of the host cell to the spin filter: In cell culture, perfusion is a process that uses a method to keep cells in a bioreactor while continuously exchanging culture medium. Fresh medium replenishes nutrients and carbon sources, while cellular waste and medium depleted of nutrients are removed. In the perfusion system, spin filters are used as a fixed substrate for cell maintenance. The physical parameters used for cell maintenance are particle size and density. In spite of the advantages of perfusion system, there are several problems that which occurred in these systems. The increase in titers and live cell density, makes the downstream purification steps more challenging because with

the increase of the titer, the amount of DNA released in the environment increases. The sedimentation of cell DNA in the cell holding system (spin filter) occurred frequently.

Results: ١- Optimization of cell growth With the changes made on the culture medium, the results showed that the cell density can be increased more than twice by choosing the optimized medium. The changes applied in the formulation were not only in the basic culture medium, but also with changes in the amount of glutamine and glucose, as well as the addition of poloxamer in order to reduce shear stress on the cell and helped the cell growth to show an acceptable doubling time. ٢- Temperature shift optimization to enhance protein expression In the production process, by lowering the temperature from ٣٧ to ٣٢ degrees, it was observed that the percentage of cell survival dropped suddenly, so that after about ٤٨ hours, the survival rate reached less than ٤٠٪. On the other hand, lowering the temperature to higher temperatures such as ٣٣ and ٣٤ degrees did not have the expected effect on increasing the expression of interferon β-١a. In order to overcome this challenge, we used the strategy of reducing the temperature step by step. This step change in temperature significantly increased the percentage of survival at ٣٢ degrees and helped to prolong the period of cell stagnation and in other words, the period of product production by the cell became wider. ٣- Modification of spin filter to prevent clogging The reliable and efficient spin filter not only prevents the cells from leaving the reactor during the harvest process, but also fulfills some of the important requirements of the system's performance, including avoiding product retention, preventing shear stress, sufficient aeration to the cells, and preventing sedimentation and clogging.

Conclusion: In conclusion to solve the problems mentioned above, various optimizations were performed to select optimal conditions for cell growth and protein expression. The changes applied on the culture medium and supplements, such as changes in the amount of glucose, adding poloxamer in order to reduce the shear stress on the cells, helped the cell growth to show an acceptable doubling time. In the other hand, the modifications applied in structure of the spin filter fulfill the requirements of the system's performance, including avoiding product retention, preventing shear stress, sufficient aeration, and prevent of spin filter clogging. In addition, step by step changes in temperature shift increased the percentage of cell viability and changed cell growth phase to expression phase significantly.

Keywords: Interferon β-١a, Perfusion bioreactor challenge, CHO cells, Temperature shift, spin filter clogging

Overview of CAR-T-Cell Therapy in Non-Small Cell Lung Cancer (Review)

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Introduction: The use of CAR-T-cell therapy signifies a pioneering tactic in the fight against cancer. This article investigates the existing scenario and potential innovations in CAR-T-cell therapy, stressing non-small-cell lung cancer (NSCLC). However, obstacles such as antigen specificity, immunosuppressive tumor microenvironments, and toxicity management persist.

Methods: A systematic literature review was undertaken, concentrating on contemporary research and clinical trials pertinent to CAR-T-cell therapy in NSCLC. Information was gathered from scholarly journals were available on PubMed and Google Scholar, and pertinent literature to evaluate the architecture, development, and utilization of CAR-T cells.

Results: The genetic composition of CAR-T cells is carefully structured to manifest receptors that specifically correspond to tumor-associated antigens (TAAs). The design of CAR-T cells involves an extracellular domain for attaching to antigens, a hinge or spacer segment, a domain that crosses the membrane, and internal domains that are key for signaling. Recent advancements in the development of CAR generations have significantly improved T-cell activation and longevity. Regarding non-small cell lung cancer (NSCLC), several antigens have surfaced as targets: EGFR, MSLN, MUC1, PSCA, CEA, PD-L1, and CD80/CD86. Each of these antigens poses distinct challenges and opportunities for optimized targeting. Clinical investigations have demonstrated the potential effectiveness of CAR-T cells against these specific targets, albeit the aspects of safety and efficacy continue to be subjects of rigorous inquiry. Prominent challenges encompass on-target but off-tumor toxicity, neurological toxicity, cytokine release syndrome, and the phenomenon of tumor antigen escape. Approaches to mitigate these challenges involve the selection of antigens that are deemed safer, the optimization of CAR constructs, and the enhancement of T-cell infiltration and persistence within the tumor microenvironment.

Conclusion: The introduction of CAR-T-cell therapy indicates a key improvement in the care of non-small cell lung cancer (NSCLC), with a host of innovative practices now being examined closely. Ongoing scholarly inquiry and clinical trials remain imperative to surmount prevailing obstacles and to augment the therapeutic efficacy and safety profiles of CAR-T cells for patients afflicted with NSCLC. As novel methodologies and technological advancements materialize, the prospective landscape of CAR-T-cell therapy appears auspicious, instilling optimism for enhanced clinical outcomes in the context of NSCLC.

Keywords: NSCLC, CAR T Cell Therapy, Tumor-Associated Antigens

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Overview of Irritable Bowel Syndrome (Review)

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Introduction: Irritable bowel syndrome (IBS) is a chronic disorder of bowel function characterized by altered bowel function and abdominal pain associated with bowel function. Patients typically present to primary care physicians with various combinations of four main symptoms: abdominal discomfort or pain, diarrhea, constipation, and bloating. IBS is commonly attributed to disturbances in gut-brain interactions. In general, it is important to identify patients with physical disorders such as tension-type headache or arthralgia and psychological symptoms of anxiety or depression, because early use of behavioral psychotherapy, hypnotherapy, or central nervous system modulators can help reduce the severity of IBS. To diagnose IBS, tests are performed that differentiate it from a series of diseases such as colon cancer and celiac disease. Also, after diagnosis, a series of first-line treatments are prescribed to the patient.

Methods: In this article, we tried to gather information about irritable bowel syndrome and its symptoms and diagnosis from Science Direct and PubMed databases.

Results: History of rectal bleeding, weight loss, nocturnal diarrhea; Symptoms indicating physical or mental disorders such as anxiety or depression; And blood screening tests such as hemoglobin and C-reactive protein increase the diagnostic performance of symptom-based criteria for IBS. There is no single or specific diagnostic test for IBS, however tests to rule out organic diseases such as colon cancer, inflammatory bowel disease, or celiac disease according to colon cancer screening guidelines or the presence of warning signs such as decreased weight or rectal bleeding, is recommended.

Conclusion: First-line treatments for IBS are fiber and osmotic laxatives such as saline or polyethylene glycol ۳۳۵۰ laxatives for constipation, loperamide for diarrhea, and antispasmodics such as hyoscine for abdominal pain. Although there is no single or specific diagnostic test for IBS, if patients do not respond to first-line treatments for initial symptoms of diarrhea, constipation, or pain or discomfort, a careful reevaluation of the history and physical examination may indicate the need for additional tests to identify Show curable. These tests include anorectal manometry and balloon evacuation, colonic transit, and tests for biochemical causes of diarrhea including sugar malabsorption, bile acid diarrhea. Finally, the main strategies for treating IBS patients are diet, psychotherapy, drug therapy, and microbial treatments.

Keywords: Irritable bowel syndrome, Symptoms, Diagnosis, Treatment

patient blood management in oncology patients (Review)

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Introduction: Anemia is a common problem in patients with cancer. The prevalence of anemia in patients with cancer varies according to clinical factors, including the type of malignancy, stage, duration of disease, and chemotherapy regimen, so the prevalence of anemia in cancer patients ranges from ٣٠ to ٩٠. Current guidelines recommend the active correction of anemia in cancer patients by erythropoiesis-stimulating agents (ESA) and iron supplementation. Red blood cell (RBC) transfusion is reserved for patients who are hypovolemic or patients with chronic anemia unresponsive to iron supplementation. However, there are some side effects which are PRBC transfusion promotes a systemic inflammatory response in patients and increases postoperative complications. The implementation of the patient blood management (PBM) program was suggested in ٢٠١٠ to reduce RBC transfusion and maintain the quality of transfusions. The PBM program has been standardized as routine practice in the USA and most European countries, as well as in a few Asian countries. This study aims to evaluate whether the introduction of our PBM can affect the appropriateness of transfusion therapy in cancer patients.

Methods: The present review was conducted through electrical scientific databases, including Google Scholar and PubMed, by searching with keywords including oncology and blood management. After reviewing these articles, a general conclusion was extracted from all the articles.

Results: The results suggest that transfusions negatively impact cancer patient outcomes by supporting tumor growth and metastases. The number of patients receiving RBC transfusion, as well as the amount of transfused RBC, decreased after the specific guideline for cancer patients was implemented. The efficacy of transfused RBC increases from ٣٨٪ to ٧٥٪ in the postoperative but rises from ٣٨٪ to ٧١٪ in the perioperative period of cancer patients. No difference was detected in the rate of complications, but the rate of anastomosis leakage decreased. The implementation of PBM also decreases the transfusion rate. The mean number of RBC units each patient received reduced from ١,٨ to ١,٣ in postoperative, and the transfusion rate was halved from ١٦,٣٪ to ٨,٣٪ in postoperative.

Conclusion: According to the above, the implementation of a PBM program was associated with a decrease in the total transfusion rate and an increase in the optimal transfusion rate. It was also associated with a reduction in postoperative complications. approximately all the studies mentioned the advantage of PBM, so we can try it and if it works, we can use it to improve health.

Keywords: Patient blood management PBM Cancer Anemia

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Pelvimetry in Cephalopelvic Disproportion (CPD) (Review)

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Introduction: Cephalopelvic Disproportion (CPD) is a condition where the baby's head or body is too large to fit through the mother's pelvis. This can happen when the baby is too big, the pelvis is too small, the baby is in a wrong position, or the relationship between the baby and the pelvis is incorrect .CPD is rare, but often diagnosed when a women's labor fails to progress, the cervix has stopped dilating, or the baby does not descend through the pelvis. When an accurate diagnosis of CPD has been made, the safest type of delivery for mother and baby is a cesarean.Possible causes of cephalopelvic disproportion (CPD) include:Large baby due to:Hereditary factors-Diabetes-Postmaturity (still pregnant after the due date has passed)-Multiparity (not the first pregnancy)-Abnormal fetal positions-Small pelvis-Abnormally shaped pelvis.Complications of CPD include an increased risk of cesarean section and shoulder dystocia with a vaginal delivery as well as an increased risk of postpartum bleeding.Most women with CPD have a successful pregnancy outcome after a cesarean delivery and there is no evidence to suggest that CPD affects a baby after its birth. Statistics suggest that about one out of ٣ cesarean sections are the result of some form of CPD. Another study shows that ٦٥ percent of women who received a diagnosis of cephalopelvic disproportion in an earlier pregnancy went on to deliver vaginally in subsequent pregnancies. In fact, many of these women had larger babies on subsequent pregnancies than with the CPD baby.

Methods: There are four main types of pelvic shapes in women, each with unique characteristics that can influence childbirth:١-Gynecoid Pelvis: This is the most common type, accounting for about ٥٠٪of women. It has a round and wide shape, which is ideal for childbirth, making vaginal delivery easier.٢-Android Pelvis: Resembling a male pelvis, this type is heart-shaped or triangular and narrower. It can make vaginal delivery more challenging, often requiring a cesarean section.٣-Anthropoid Pelvis: This pelvis is long and oval-shaped, providing more room front to back. While it can facilitate vaginal birth, it may lead to longer labor.٤-Platypelloid Pelvis: The least common type, it is wide and flat. This shape can make vaginal delivery more difficult.

Results: Pelvimetry is the measurement of the female pelvis, primarily to assess its size and shape in relation to childbirth. This can help determine if the pelvis is adequate for a vaginal delivery or if there might be complications such as cephalopelvic disproportion, where the baby's head is too large to pass through the pelvis.There are different methods of pelvimetry:١-Clinical Pelvimetry: This involves a physical examination where the healthcare provider manually assesses the dimensions and shape of the pelvis.٢-Radiographic Pelvimetry: This uses imaging techniques like X-rays, CT scans, or MRI to measure the pelvis more precisely.However, the routine use of pelvimetry has decreased because many studies suggest that it doesn't significantly change the management of labor and delivery.The choice of pelvimetry method often depends on the clinical situation:١-Suspected Cephalopelvic Disproportion (CPD).٢-Previous Obstetric History.٣- Fetal Position and Size.٤- Maternal Health Conditions.

Conclusion: Clinical pelvimetry steps typically involved:١-Preparation:The healthcare provider explains the procedure to the patient and obtains her consent. The patient is then positioned comfortably, usually lying on her back with her knees bent and feet apart.٢- Assessment of Pelvic Inlet: - Diagonal Conjugate: The provider measures the distance from the lower border of the pubic symphysis to the sacral promontory using their fingers.Obstetric Conjugate:This is estimated by subtracting ١,٥ to ٢ cm from the diagonal conjugate.٣- Assessment of Midpelvis:Ischial Spines: The provider palpates the ischial spines to determine their prominence and the distance between them. This helps assess the transverse diameter of the midpelvis.٤- Assessment of Pelvic Outlet: Subpubic Angle: The angle formed by the pubic bones is assessed. A wider angle is generally more favorable for vaginal delivery.Intertuberous Diameter: The distance between the ischial tuberosities is measured, which indicates the width of the pelvic outlet.٥- Overall Pelvic Shape: The provider evaluates the overall shape of the pelvis (gynecoid, android, anthropoid, or platypelloid) based on the findings from the above assessments.Clinical pelvimetry is a useful tool, but its routine use has declined due to the availability of more precise imaging techniques and the understanding that many women can have a successful vaginal delivery regardless of pelvimetry results.

Keywords: Cephalopelvic Disproportion -clinical pelvimetry-childbirth-gynecoid-MRI-CT-Radiographic Pelvimetry

Personalized Medicine: Strategies for prognosis and treatment of breast cancer (Review)

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Introduction: Breast cancer is known as one of the most common cancers in the world. Today, prognosis of this disease and timely treatment is possible using molecular methods. Also, personalized methods can be an effective method in the rapid diagnosis of breast cancer. Increased accuracy and confidence in determining the treatment method, it leads to a more definite result in improving the disease. Therefore, the purpose of this research is to investigate the results of personalized breast cancer treatment.

Methods: In this review article, clinical information related to personalized medical treatments and breast cancer has been extracted from reliable scientific sources and articles.

Results: Results: Clinical studies have shown that breast cancer is characterized by estrogen receptor (ER), progesterone receptor (PR) and Ki-٦٧ (a prognostic and predictive protein marker) biomarkers. There are also hormone receptor tests:, potential for helper chemotherapy), and human epidermal receptor ٢ (HER٢), to diagnose this cancer. But due to the errors in these methods for diagnosis and current treatment methods, the quality of life of these patients has decreased, and the development of personalized medicine with techniques such as gene expression profiling in optimizing the selection of drugs for treatment and improving the quality of life These patients have a significant impact.

Conclusion: Breast cancer has always been challenging, and misdiagnosis and treatments done with past methods have many side effects. Therefore, personalized medicine has improved the process of prognosis, prevention and treatment in these patients due to its extraordinary potential in determining the personal genetic causes of the

Keywords: Personalized Medicine, Breast Cancer, Cancer Prognosis, Cancer Treatment.

Personalized Treatment Optimization in Psychiatry: A Review of Therapeutic Drug Monitoring, Pharmacogenomics, and Biomarker Testing (Review)

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Introduction: Personalized treatment optimization in psychiatry addresses the critical challenge of suboptimal effectiveness and variable patient responses to psychiatric medications, potentially revolutionizing mental health care. Mental disorders such as depression, bipolar disorder, and schizophrenia affect millions of people worldwide, causing significant personal suffering and societal burden. Traditional approaches to psychiatric treatment often involve a trial-and-error process, where medications are prescribed based on general guidelines and adjusted according to patient response. This method can lead to prolonged periods of inadequate symptom control, increased risk of side effects, and poor treatment adherence. The concept of personalized treatment optimization aims to tailor pharmacological interventions to individual patients based on their unique genetic, physiological, and environmental factors. By leveraging advanced analytical techniques and genetic testing methodologies, clinicians can potentially predict which medications are most likely to be effective for a given patient while minimizing the risk of adverse effects. This approach holds the promise of improving treatment outcomes, reducing the time to achieve symptom remission, and enhancing overall quality of life for individuals with mental health disorders.

Methods: This review examines three primary approaches to personalized treatment optimization in psychiatry: therapeutic drug monitoring, pharmacogenomics, and biomarker testing. Each of these methods contributes valuable information to guide clinical decision-making and treatment planning. Therapeutic drug monitoring involves measuring the concentration of psychiatric medications in a patient's blood or plasma. This technique allows clinicians to ensure that drug levels are within the therapeutic range, optimizing efficacy while minimizing toxicity. Advanced analytical methods such as liquid chromatography and mass spectrometry are employed to accurately quantify drug concentrations. These techniques offer high sensitivity and specificity, enabling precise measurements of multiple drugs and their metabolites simultaneously. Pharmacogenomics focuses on identifying genetic variations that influence an individual's response to psychiatric medications. This approach involves analyzing specific genes associated with drug metabolism, transport, and targets. Genetic testing methodologies, including polymerase chain reaction (PCR) and next-generation sequencing, are used to detect relevant genetic polymorphisms. By understanding a patient's genetic profile, clinicians can predict how they might metabolize certain medications and adjust dosages accordingly. Biomarker testing involves measuring biological indicators that can provide insights into a patient's disease state, treatment response, or risk of adverse effects. In psychiatry, biomarkers may include neurotransmitter levels, inflammatory markers, or neuroimaging findings. Various analytical techniques, such as enzyme-linked immunosorbent assays (ELISA),

electroencephalography (EEG), and functional magnetic resonance imaging (fMRI), are employed to assess these biomarkers.

Results: The review of current evidence supporting personalized approaches in clinical practice reveals promising findings across various psychiatric disorders. In depression, studies have shown that therapeutic drug monitoring can improve treatment outcomes by ensuring adequate drug concentrations and guiding dose adjustments. Pharmacogenomic testing has demonstrated potential in predicting antidepressant response and side effect risk, with some genetic variants associated with increased likelihood of remission or adverse reactions. For bipolar disorder, therapeutic drug monitoring has proven particularly valuable in managing lithium therapy, a medication with a narrow therapeutic index. Genetic testing has identified polymorphisms that may influence response to mood stabilizers and antipsychotics commonly used in bipolar treatment. Biomarker research has explored the use of inflammatory markers and neuroimaging findings to predict treatment response and differentiate bipolar subtypes. In schizophrenia, personalized treatment optimization has shown promise in managing antipsychotic therapy. Therapeutic drug monitoring helps clinicians maintain optimal drug levels, particularly for clozapine, which requires careful monitoring due to its side effect profile. Pharmacogenomic studies have identified genetic variants associated with antipsychotic response and metabolic side effects. Biomarker research in schizophrenia has explored the use of neuroimaging and cognitive measures to predict treatment outcomes and guide medication selection.

Conclusion: While personalized treatment optimization shows considerable promise in enhancing therapeutic outcomes and minimizing adverse effects in psychiatry, further research is needed to establish its clinical utility and cost-effectiveness across various disorders. The integration of therapeutic drug monitoring, pharmacogenomics, and biomarker testing into clinical practice has the potential to significantly improve patient care by enabling more precise and individualized treatment strategies. However, several challenges must be addressed before personalized treatment optimization can fully transform the mental health treatment landscape. These include the need for larger, well-designed clinical trials to validate the efficacy of personalized approaches, the development of standardized testing protocols and interpretation guidelines, and the education of healthcare providers on the appropriate use and interpretation of personalized treatment data. As evidence accumulates and technologies advance, these approaches may become increasingly integrated into standard psychiatric care. The future of personalized treatment optimization in psychiatry holds the potential to revolutionize mental health care, offering hope for improved outcomes and quality of life for individuals living with mental health disorders. Ongoing research and clinical implementation efforts will be crucial in realizing this potential and shaping the future of psychiatric treatment.

Keywords: Biomarker, Pharmacogenetic, Therapeutic Drug Monitoring, Psychiatry, Personalized Medicine

Phage Therapy: An Emerging Alternative to Antibiotics for Treating Infections (Review)

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Introduction: Antimicrobial resistance (AMR) is a significant global health concern, responsible for over ۱,۲ million deaths in ۲۰۱۹. As bacteria evolve to resist traditional antibiotics, alternative treatments are becoming increasingly necessary. One such alternative is phage therapy, which uses bacteriophages—viruses that specifically target and kill bacteria. Unlike antibiotics, which have broad-spectrum effects, phages are highly specific, targeting only certain bacterial strains. This specificity makes phage therapy a potential tool to combat multidrug-resistant (MDR) bacteria. Although not yet widely adopted, phage therapy shows considerable promise, particularly for infections where antibiotics have proven ineffective. This article explores the mechanisms, applications, and challenges of phage therapy as an alternative to antibiotics.

Methods: This review is based on recent studies and clinical trials related to phage therapy. Sources such as PubMed and Google Scholar were used to locate research on phage therapy's role in treating infections caused by MDR bacteria. Emphasis was placed on studies where biofilm-related infections were examined, as biofilms often play a significant role in antibiotic resistance.

Results: Phage therapy leverages the natural ability of bacteriophages to specifically target and eliminate bacteria. When a bacteriophage encounters its host bacterium, it attaches to the bacterial cell surface, injects its genetic material, and commandeers the bacterial machinery to replicate itself. This process culminates in the lysis (destruction) of the bacterial cell, releasing new phages that can infect surrounding bacteria, thereby reducing the overall bacterial population. Numerous clinical studies highlight the efficacy of phage therapy in treating infections resistant to conventional antibiotics. For example, a notable case involved a patient suffering from a severe Staphylococcus aureus infection, which was resistant to multiple antibiotic treatments. After exhausting traditional options, the patient was treated with a personalized phage cocktail. This innovative approach led to significant clinical improvement and full recovery, underscoring phage therapy's potential as a tailored intervention for stubborn infections. Another critical study focused on phage therapy's effectiveness against Pseudomonas aeruginosa, a pathogen notorious for forming biofilms that protect bacteria from antibiotics. Phage treatment not only reduced bacterial loads but also effectively disrupted the biofilm structure, which is often a significant barrier to treatment success. The ability of phages to penetrate and dismantle biofilms provides a crucial advantage over traditional antibiotics, enhancing the overall effectiveness of phage therapy and offering a promising complementary strategy to improve outcomes for patients with chronic infections. Phage therapy also demonstrates a significant adaptability advantage. While bacteria can develop resistance to both antibiotics and phages, phages can evolve in response to bacterial defenses. This co-evolutionary dynamic is crucial for maintaining phage therapy's efficacy. For instance, if bacteria develop resistance to a particular phage, using a different phage or a combination of phages can

effectively combat the resistant bacterial strain, thereby prolonging treatment success and providing a dynamic response to evolving bacterial threats. Despite these promising results, challenges remain in the broader application of phage therapy. The specificity of phages may limit their utility in infections involving multiple bacterial species. To overcome this, researchers are actively developing broad-spectrum phage cocktails that can target various bacterial strains. Additionally, regulatory hurdles complicate the approval process for phage therapy, as existing frameworks are not well-suited for living therapeutic agents. These challenges necessitate ongoing research to optimize phage therapy protocols, ensuring its successful integration into clinical practice and expanding treatment options for patients with resistant infections, thereby positioning phage therapy as a crucial alternative in the fight against antimicrobial resistance.

Conclusion: Phage therapy presents significant potential as an alternative to antibiotics, especially in treating infections caused by multidrug-resistant bacteria. Its precision in targeting specific bacterial strains, ability to disrupt biofilms, and adaptability to bacterial resistance mechanisms make it a valuable tool in the fight against antibiotic-resistant infections. However, several obstacles, including host specificity, regulatory challenges, and the potential for resistance, must be addressed before phage therapy can become a mainstream treatment option. As antimicrobial resistance continues to rise, exploring alternatives like phage therapy becomes increasingly important. By harnessing the bactericidal properties of phages, healthcare providers may gain a powerful tool in combating drug-resistant infections. Though still in its early stages, phage therapy has the potential to revolutionize infection treatment and offer hope for patients facing untreatable infections.

Keywords: Phage Therapy, Alternative, Antibiotics

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Phytoconstituents of Momordica charantia have the ability to inhibit the infectivity of human T-lymphotropic virus type-١ (HTLV-١) both in vitro and in vivo (Research Paper)

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Introduction: There is a pressing need to discover a potent therapy for life-threatening diseases associated with HTLV-١. Bitter melon (Momordica charantia), an herbal remedy with recognized antiviral and anticancer attributes, was subjected to testing in this investigation for its impact on HTLV-١ infectivity.

Methods: The alcoholic extract of bitter melon was analyzed using GC-MS. An in vitro assay was conducted by transfecting HUVEC cells with the HTLV-١-MT٢ cell line. These cells were exposed to both alcoholic and aqueous extracts at concentrations of ٥, ١٠, and ٢٠ µg/mL. In vivo experiments involved dividing mice into four groups, three of which were treated with HTLV-١-MT-٢ cells as the test groups and positive control, while PBS served as the negative control. M. charantia extracts were administered both in the presence and absence of the HTLV-١-MT-٢ cells. Peripheral blood mononuclear cells (PBMCs), mesenteric lymph nodes (MLNs), and splenocytes were collected to assess the HTLV-١-proviral load (PVL) using TaqMan-qPCR.

Results: GC-MS analysis revealed the presence of ٣٦ components in M. charantia. The findings demonstrated significant reductions in HTLV-١-PVL when the extract was present in the HUVEC-treated groups (P = ٠,٠٠١). Moreover, the inhibitory effects of the extracts on HTLV-١ infected mice exhibited noteworthy differences in HTLV-١-PVL between the M. charantia treated groups and the untreated group (P = ٠,٠٠١). T-cells in MLNs were found to be significantly more susceptible to HTLV-١ compared to other cells (P = ٠,٠٠١). Notably, there were significant differences in HTLV-١-infected cells between MLNs and splenocytes (P = ٠,٠٠١ and ٠,٠٤٦, respectively). Additionally, the groups treated with aqueous and alcoholic extracts had a substantial impact on HTLV-١-infected PBMCs (P = ٠,٠٠٢ and ٠,٠٠٩, respectively).

Conclusion: It is possible that M. charantia possesses effective antiviral properties. The significant compounds found in M. charantia may have inhibitory effects on the proliferation and transmission of the HTLV-١ oncovirus

Keywords: Antiviral agents · ATLL · HAM/TSP · HTLV-١ · Momordica charantia

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Pirfenidone downregulates eIF٦, P٣١١, and TGF-β expression and improves liver fibrosis induced by Bile duct ligation in Wistar rats; evidence for liver regeneration (Research Paper)

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Introduction: liver fibrosis (LF) is a clinical disorder characterized by Inflammation and extra cellular matrix (ECM) accumulation. Pirfenidone (PFD) is an orally bioavailable pyridone derivative as well as a novel compound with anti-inflammatory and anti-fibrotic effects. The mechanism of its action remains uncertain. This study aims to investigate the influences of PFD on improving LF histologically and through modulation of eIF٦, P٣١١, and TGF-β in rats induced by Bile Duct Ligation (BDL).

Methods: Liver fibrosis was induced in Wistar rats using the BDL model. Animals received daily gavage administration of PFD (٢٠٠ and ٥٠٠ mg/kg) for ٤ weeks. Liver index, hydroxyproline (Hyp) and ALT, AST, and ALP serum levels were calculated. Pathological changes in hepatic tissue were examined using histological staining with haematoxylin and eosin (H&E), Sirius red, and Masson's trichrome staining, as well as immunohistochemical (IHC) analysis to monitor α-SMA and tissue repair markers (Ki-٦٧ and HepPar-١). The mRNA levels of eIF٦, P٣١١, and TGF-β, as well as ECM deposition, HSC activation, and inflammatory mediator genes, were measured by RT-qPCR. We also monitored the protein levels of eIF٦, P٣١١, and TGF-β, which were detected by western blotting.

Results: Compared with the BDL group, PFD dose-dependently reduced Hyp, Liver index and the serum levels of ALT, AST, ALP in rats. Histological staining also showed that PFD reduced the fibrosis score and fibrosis area (٤٠ and ٥٠ percent in doses of ٢٠٠ and ٥٠٠ mg/kg respectively) in tissues. Additionally, PFD dose-dependently modulated BDL-induced hepatic inflammation, ECM accumulation, and HSC activation. Immunohistochemical staining of Ki-٦٧ and HepPar-١ in hepatic tissue revealed that PFD enhanced liver regeneration. Besides, the research confirmed that PFD gradually downregulated elevated levels of eIF٦, P٣١١, and TGF-β in BDL-induced LF.

Conclusion: The findings suggest that PFD might be a potential treatment for LF. PFD can attenuate LF and enhance liver regeneration in a BDL-induced liver injury model, and this effect may be due to modulation of eIF٦, P٣١١ and TGF-β besides improvement in inflammatory response, HSC activation, ECM accumulation, and enhancing its degradation.

Keywords: Pirfenidone, Liver fibrosis, Bile duct ligation, eIF٦, P٣١١

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PNU-٧٤٦٥٤ inhibits colon cancer progression by disrupting the Wnt/beta-catenin pathway

(Research Paper)

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Introduction: Colorectal cancer (CRC) is one of the leading causes of cancer mortality, primarily due to its propensity to metastasize and resistance to conventional therapies. This study investigates the therapeutic potential of PNU-٧٤٦٥٤, a novel inhibitor of the Wnt/β-catenin signaling pathway, in combination with ٥-fluorouracil (٥-FU). We evaluated the antiproliferative effects of PNU-٧٤٦٥٤ on the CT-٢٦ cells and assessed its impact on cell growth, migration, invasion, and apoptosis by various assays. In addition, we used an animal model to analyze the efficacy of PNU-٧٤٦٥٤ alone and in combination with ٥-FU. This study aimed to inhibit colorectal cancer progression through disruption of the Wnt/β-catenin pathway by PNU-٧٤٦٥٤.

Methods: The antiproliferative -effect of PNU-٧٤٦٥٤ was evaluated cell models. The activity of agents on cell growth, migration, invasion, cell cycle, and apoptosis was evaluated by MTT, gene expression, respectively. The oxidant/antioxidant levels were also assessed by determining the level of MDA, SOD, as well as using the DCFH-DA assay. We used an animal model of CRC to investigate PNU-٧٤٦٥٤ activity alone and in combination with ٥-FU followed by histological staining and biochemical and gene expression analyses by RT-PCR and western blot.

Results: PNU-٧٤٦٥٤, a Wnt/β-catenin pathway inhibitor, was investigated for its anti-tumor effects in the colorectal cancer (CRC) models, alone and in combination with ٥-fluorouracil (٥-FU). PNU-٧٤٦٥٤ inhibited cell growth and migration, and enhanced the anti-tumor activity of ٥-FU in CRC cells. Mechanistically, PNU-٧٤٦٥٤ modulated key proteins such as Cyclin D١ and survivin, and reduced migration by affecting E-cadherin expression. In an animal model, the combination of PNU-٧٤٦٥٤ and ٥-FU significantly suppressed tumor growth through induction of reactive oxygen species, down-regulation of superoxide dismutase (SOD), and modulation of inflammatory markers MCP-١, P٥٣, and TNF-α. These findings demonstrate that targeting the Wnt pathway with PNU-٧٤٦٥٤ disrupts CRC cell proliferation and migration while improving the efficacy of ٥-FU, supporting further investigation of this combined therapeutic approach for colorectal cancer treatment.

Conclusion: The study demonstrates that PNU-٧٤٦٥٤, a Wnt/β-catenin pathway inhibitor, reduces tumor growth and enhances apoptosis in colorectal cancer (CRC) cells. It effectively suppresses cyclin D١ expression and exhibits synergistic effects with ٥-fluorouracil (٥-FU) in decreasing cell viability.

PNU-٧٤٦٥٤ also increases oxidative stress by inhibiting superoxide dismutase (SOD) activity, leading to enhanced apoptosis. Additionally, it elevates p٥٣ expression and pro-inflammatory cytokines like TNF-α and MCP-١ in CRC cells. Overall, these findings suggest that PNU-٧٤٦٥٤ targets the Wnt pathway to inhibit cell proliferation and migration while promoting apoptosis, indicating its potential as a therapeutic strategy for CRC treatment. Further research is needed to explore its clinical applications.

Keywords: colorectal cancer, ٥-FU, PNU-٧٤٦٥٤, Wnt/β-Catenin Pathway

Potential Ability of Umbilical Cord-Derived Mesenchymal Stem Cells in The Treatment of Premature Ovarian Failure (Review)

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Introduction: Women of reproductive age may encounter challenges related to infertility or miscarriage, due to conditions such as premature ovarian failure (POF). POF, affecting approximately one percent of women under the age of ٤٠, can lead to infertility. Current data have suggested that utilizing stem cell therapy was the most effective approach for treating POF compared to alternative options. Among the various stem cell types, mesenchymal stem cells derived from the umbilical cord (HUC-MSCs) was a promising choice for treatment due to its features such as relatively low immunogenicity, multipotent, multiple origins, cost-effectiveness, ease of production, and high efficiency.

Methods: In this study, using the keywords of ovarian failure, infertility, umbilical cord-derived mesenchymal stem cells in Scopus, PubMed, Google scholar and Web of Science databases, studies in this field were searched, also using From the keywords of the study, ٩٩ articles were obtained, and according to the intended purpose and the removal of duplicate articles, ٤٨ articles were obtained.

Results: In people facing challenges caused by premature ovarian failure, there are significant effects on mental and physical health. Hormonal therapies are commonly used to reduce symptoms of estrogen deficiency in women with POF, but have not been very successful. Therefore, there is a need for better treatment options to solve this problem and a lot of research has been done to find more effective solutions to treat POF. As a result of numerous researches on the use of mesenchymal stem cells derived from the umbilical cord in the treatment of premature ovarian failure, it seems that these cells can play an important role in improving and regenerating ovarian function. Among the important results of this research, we can mention the increase in the number and function of follicles, the improvement of the reproduction process, and the regular regulation of hormones. These cells appear to be able to restore ovarian function after damage from various things, including chemotherapy. Overall, it seems that umbilical cord-derived mesenchymal stem cells have a potential ability to heal and repair ovaries in the face of premature ovarian failure. These results show that the use of these cells may be an effective and innovative approach in the treatment of this lack of egg production and improve ovarian function and increase fertility opportunities in people with premature ovarian failure.

Conclusion: One of the ways to treat POF is the use of mesenchymal stem cells derived from the umbilical cord, these cells have an extraordinary capacity for repair and regeneration, which helps

them in repairing depleted ovaries. The results of this review article indicate that the use of HUC-MSCs can be considered as a potential treatment method in these patients.

Keywords: Menopause, Premature, Mesenchymal Stem Cells, Infertility.

Potential protective effects of antioxidant agents on ٦-Hydroxydopamine-induced neurotoxicity in PC١٢ cells: A review (Review)

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Introduction: Introduction: Oxidative stress plays a critical role in the pathogenesis of age-related neurodegenerative diseases, particularly Parkinson's disease (PD). The vulnerability of the nervous system leads to distressing symptoms in affected patients, prompting significant research into antioxidant agents as potential therapies. In vitro studies utilizing the neurotoxin ٦-Hydroxydopamine (٦-OHDA) in PC١٢ cells have shown that various antioxidants, such as quercetin glycosides, rutin, and D-psicose, can effectively protect against neurotoxicity. These antioxidants enhance cell viability, increase superoxide dismutase (SOD) activity, and reduce lactate dehydrogenase (LDH) levels. Collectively, these findings suggest that antioxidant therapies may offer promising avenues for alleviating symptoms and slowing disease progression in PD.

Methods: Materials and methods: Electronic databases, including PubMed, Web of Science, Google Scholar, and Scopus, were systematically searched using keywords such as "PC١٢" and "٦-Hydroxydopamine" (٦-OHDA) up to April ٢٠٢٤. The selected articles provided insights into the mechanisms underlying ٦-OHDA-induced neurotoxicity and identified various antioxidant agents that protect PC١٢ cells from this neurotoxin. Data extraction focused on the efficacy of these antioxidants in mitigating neurotoxic effects, contributing to a better understanding of potential therapeutic strategies for neurodegenerative diseases.

Results: Result: In the selected articles, numerous antioxidant agents such as quercetin glycosides, rutin and D-psicose have been employed to safeguard PC١٢ cells against ٦-OHDA-induced neurotoxicity. Increased cell viability assessed using various methods such as MTT, flow cytometry or the TUNEL assays, elevated superoxide dismutase (SOD) activity, and decreased lactate dehydrogenase (LDH) levels in the PC١٢ cells exposed to the antioxidant agents were frequently observed in the results section of the selected articles.

Conclusion: Conclusion: According to the selected studies, antioxidant agents can significantly protect PC١٢ cells against ٦-OHDA-induced neurotoxicity. Nonetheless, more clinical studies are needed to pinpoint the relation between different doses of these agents and the severity of symptoms in PD patients. The selected studies suggest that antioxidant agents can effectively protect PC١٢ cells from the neurotoxic effects of ٦-OHDA, a compound commonly used to induce Parkinson's disease (PD)-like symptoms in cell culture models. However, the authors acknowledge that further clinical research is necessary to determine the specific relationship between varying doses of these antioxidant agents and the severity of symptoms observed in PD patients.

Keywords: Keywords: PC١٢, ٦-OHDA, ٦-Hydroxydopamine, Antioxidant, Oxidative Stress

Potential Therapeutic Implications for Alzheimer's Disease : The Role of ITGAX in Microglial Activation and Neuroinflammation (Research Paper)

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Introduction: Brain aging is a natural physiological process that results in cognitive declines, affecting memory, learning ability, and processing speed. It also increases the risk of neurodegenerative diseases such as Alzheimer's disease (AD), which is characterized by brain atrophy and cell death due to β-amyloid (Aβ) plaques and neurofibrillary tangles (١,٢) Neuroinflammation, mitochondrial dysfunction, and cellular senescence have been identified as major contributors to AD. Microglia, the primary innate immune cells in the brain, play a central role in this process (٣). Also, the GAS–STING signaling pathway, which is responsible for detecting DNA, plays a significant role in chronic inflammation and functional decline associated with aging (٤). Additionally Nicotinamide adenine dinucleotide (NAD+) is crucial for metabolism, mitochondrial function, and genome integrity. Studies indicate that NAD+ depletion may activate the cGAS-STING pathway, contributing to neuroinflammation and cellular senescence in Alzheimer's disease (AD)(٣).

Methods: Given the importance of these processes in AD, the aim of this study is to identify differentially expressed genes (DEGs) that significantly contribute to the development of Alzheimer's disease. Raw microarray data from GSE١٣٥٩٩٩, which includes ٤٨ paired expression datasets from the brains of APP/PS١ AD mice and wild-type (WT) controls, were obtained from the GEO database. Analysis of these two groups was performed using the GEO٢R tool, considering adj.p.value ≤ ٠,٠٥ and logFC ≥ ٠,٤٥. In this study, the STRING database was used to construct the PPI network, which was further analyzed using the Cytoscape application.The gene ITGAX was identified as a hub gene in this study, and further extensive studies were conducted on this gene

Results: ITGAX (Integrin subunit alpha X, also referred to as CD١١c) is associated with immune functions, particularly the activation of microglia, and its expression is predominantly found in microglia within the brain, contributing to neuroinflammation in Alzheimer's disease.(٢) In one study, it also becomes significantly upregulated in aged mice, suggesting increased microglial activation and neuroinflammation associated with aging and neurodegenerative diseases like Alzheimer's.(٤) Additionally, ITGAX has been reported to play a common role between monocytes (blood myeloid cells) and microglia (brain myeloid cells).(٥) To explore whether ITGAX plays a role in the cGAS-STING pathway, we used the STRING database to assess its interactions with key pathway genes, including CGAS, TMEM١٧٣ (STING١), IFNB١, and others. Our analysis revealed potential protein-protein interactions, suggesting that ITGAX may influence immune responses, particularly those regulated by the cGAS-STING pathway, which detects cytosolic DNA and initiates inflammatory

responses. The interactions between ITGAX and genes like CXCL١٠ and IFNB١ indicate possible indirect regulatory roles in immune signaling and cytokine production. Studies show that blocking the STING pathway reduces inflammation in aged human cells, peripheral organs, and the brain, leading to improved tissue function. Single-nucleus RNA sequencing of microglia in a cGAS gain-of-function mouse model demonstrates that cGAS activation promotes inflammatory microglial states, resulting in neurotoxicity, bystander cell inflammation, and cognitive decline. These findings establish cGAS-STING as a major driver of age-related inflammation and neurodegeneration, suggesting that inhibiting this pathway could be a promising therapeutic strategy to prevent neurodegenerative processes associated with aging.(٤) Furthermore, lower NAD+ levels have been observed in various neurodegenerative diseases. In one study, brains of Alzheimer's disease (AD) mice exhibited reduced NAD+ levels and increased inflammation. Treatment with nicotinamide riboside (NR), a precursor to NAD+, reduced neuroinflammation, decreased DNA damage, and prevented cellular senescence. Scientists suggest that the beneficial effects of NR are partly mediated through the cGAS-STING pathway, as NR treatment reduced the DNA damage elevated in AD.(٣)

Conclusion: Our study identifies ITGAX as a critical hub gene involved in neuroinflammation, particularly in the context of Alzheimer's disease. Given its presence in blood, ITGAX may hold potential as a biomarker, as increased expression could indicate heightened inflammatory activity and activation of the cGAS-STING pathway. The strong connection between ITGAX and key components of the cGAS-STING pathway suggests its role in modulating immune responses and contributing to age-related neurodegeneration. Furthermore, NAD+ depletion observed in AD and the beneficial effects of nicotinamide riboside (NR) in reducing inflammation through cGAS-STING inhibition highlight these pathways as promising therapeutic targets. Administering NAD+ supplements could potentially inhibit this pathway, offering a novel strategy to mitigate neuroinflammation and prevent neurodegenerative processes associated with AD and aging. Further research is needed to validate its clinical application.

Keywords: Brain Aging, Alzheimer, ITGAX, CGAS-STING, NAD+

Potentiating the Antimicrobial Effect of Ceftazidime by Thymol Against Klebsiella pneumoniae

(Research Paper)

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Introduction: This study aimed at the antimicrobial effects of thymol/ceftazidime on Klebsiella pneumoniae (K. pneumoniae) bacteria.

Methods: Antimicrobial effects of thymol/ceftazidime were performed first individually and then combined on K. pneumoniae ATCC ١٠٠٠٣١ by the MIC-MBC method. Therefore, the antimicrobial effects of the compounds that had a synergistic impact were performed on ten clinical strains using the MIC-MBC method. The identification of chemical bonds, functional groups, and molecular interactions of the mentioned compounds was investigated using an FTIR device. Checkered method, time killing curve, and biofilm inhibition on K. pneumoniae ATCC ١٠٠٠٣١, investigation of cytotoxicity on red blood cells (RBCs) by hemolysis method and human skin fibroblast cells (Ffk) by MTT method were performed. thymol/ceftazidime had synergistic effects.

Results: The study's findings demonstrated that when applied to K. pneumoniae ATCC ١٠٠٠٣١, the antimicrobial activities of thymol, ceftazidime, and thymol/ceftazidime (A١ compound) were, respectively, ٢٥٦ µg/ml, ٤ µg/ml, and ٤/٢ µg/ml (FICI: ١ µg/ml). The A١ compound exhibited antibacterial activity of ٤-٢٥٦/١-٦٤ µg/ml on clinical strains of K. pneumoniae, respectively. Compared to the individual modes, the combined mode had a longer time curve for eliminating K. pneumoniae. Examination with FTIR showed that these two compounds have C=C conjugated, C≡C compound. Thymol, ceftazidime, and other chemicals have biofilm inhibition rates of ٢٩,٦٩٪, ٢٨,٧١٪, and ٥٨,٤٤٪, respectively against K. pneumoniae bacteria. The toxicity of thymol, cefotaxime, and A١ compound against human RBCs were ٣٦,١٢, ٨,٣٣, and ٨,٣٨, and against human Ffk cells were ١٩,٦٦, ٧,٠٨, and ٩,٠٣ respectively.

Conclusion: This study proved that the thymol/ceftazidime combination could become one of the new drugs for treating K. pneumoniae infections due to its high antimicrobial effects and low toxicity.

Keywords: Klebsiella pneumoniae, Thymol, Ceftazidime, Antimicrobial

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Predicting the Pathogenicity of a Missense Single Nucleotide Polymorphism (rs١٢١٩١٣٢٤٠) in the KRAS Gene Associated with Lung Cancer (Research Paper)

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Introduction: Lung cancer (LC) is caused by the uncontrollable division of lung tissue cells. This cancer is the leading cause of cancer-related death worldwide. Early diagnosis can reduce the number of deaths from LC. Identification of genetic mutations is important for the diagnosis and targeted treatment of lung cancer. Nucleotide changes in many different genes like Kirsten rat sarcoma viral oncogene homologue (KRAS) gene have been found in LC. KRAS is located on chromosome ١٢ and is a member of the RAS family of genes associated with human cancers. KRAS encodes a GTPase that plays a key role in signal transduction cascades and thus, is critical for cell proliferation, survival, and differentiation. The purpose of this study is to investigate the pathogenicity effect of a missense single nucleotide polymorphism (rs١٢١٩١٣٢٤٠) in the KRAS gene using bioinformatics tools.

Methods: In this study, among the identified polymorphisms in the National Center for Biotechnology Information/Single Nucleotide Polymorphism database (NCBI/dbSNP), rs١٢١٩١٣٢٤٠ was selected. In the rs١٢١٩١٣٢٤٠ variant, the amino acid glutamine is replaced by leucine in position ٦١ (p.Gln٦١Leu). We investigated the pathogenicity of this missense variant, the secondary structure of its wild-type and mutated proteins, and the possible effect of amino acid substitution on protein structure and function. For this purpose, we used several bioinformatics servers including PolyPhen-٢, SIFT, PSIPRED, I-Mutant, mCSM-stability, SNPs&GO, PredictSNP and HOPE.

Results: PolyPhen-٢ server indicated that the variant with dbSNP ID rs١٢١٩١٣٢٤٠ (Q٦١L) is probably damaging with a score of ٠,٩٧٧. The score of ٠,٠٠ by the SIFT server showed that this variant has a significant effect on the structure and function of the protein. The secondary structures of wild-type and mutated proteins were compared by the PSIPRED server. According to the PSIPRED result, unlike the amino acid leucine, glutamine was placed in the alpha-helix region of the protein. Also, protein stability increased according to the DDG value in I-Mutant and mCSM-stability servers. Moreover, this variant was predicted as deleterious and disease using PredictSNP and SNPs&GO servers. In addition, the HOPE results indicated that the mutated residue is located in a domain that is important for the binding of other molecules and it might affect the function of the protein.

Conclusion: In this study, the rs١٢١٩١٣٢٤٠ variant in the KRAS gene has been identified from the NCBI/dbSNP. According to the results, the pathogenicity of this variant was confirmed using powerful bioinformatics tools. These results can be examined with experimental studies. Analysis of the SNPs is important for the early diagnosis and targeted treatment of cancer.

Keywords: Single nucleotide polymorphism, rs١٢١٩١٣٢٤٠, KRAS gene, Lung cancer

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Prediction of Immune-Related Genes and pathways in Gastric adenocarcinoma through systems biology approach (Research Paper)

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Introduction: Chronic inflammation is associated with carcinogenesis, especially in digestive organs. The mechanism of this effect, however, has only been partially focused on. This study was conducted with the aim of identifying genetic markers related to immunity and early prognostic pathways and prevention of Gastric cancer (GC).

Methods: This objective was achieved through the analysis of differentially expressed genes (DEGs) from two datasets obtained from the Gene Expression Omnibus (GEO). By doing so, we aimed to identify the hub genes associated with gastric adenocarcinoma that could serve as potential biomarkers and the most prominent pathways for early detection and management of GC. Two GEO datasets (GSE٥٤١٢٩, and GSEV٩٩٧٣), consisting of ٢١ normal and ٣٣ GC samples, were analyzed using the Transcriptome Analysis Console (TAC) software. Functional enrichment analysis of DEGs was performed using Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes database (KEGG). Visualized PPI network analysis was performed by Cytoscape to further identify hub genes. Centrality parameters including degree, betweenness, and closeness were calculated to identify hub genes in the network using Gephi. Among the ١٠٠ selected hub genes, it was used to identify smaller communities that form groups of hub genes, called modules. Then the hub genes were imported to ENRICHR to find the most important pathways.

Results: A total of ١,٤٩٥ common DEGs emerged among the datasets, focusing on significant GC-related pathways. six hub genes (IL٦, FN١, MMP٩, TGFB, COL١A١, and CD٤) are associated with GC through PPI analysis. Based on multilevel systems biology analysis, hub genes in gastric adenocarcinoma showed participation in pathways such as AGE-RAGE signaling pathway in diabetic complications, focal adhesion, Proteoglycans in cancer, and other signaling pathways. Since targeting these genes may have multiple side effects, we decided to target the hub gene in a signaling pathway that specifically affects gastric cancer.

Conclusion: Our findings suggest that the identified hub genes, especially IL٦, FN١, MMP٩, TGFB, COL١A١, and CD٤, play an important role in the inflammatory response in GC. This comprehensive analysis increases our understanding of the molecular mechanisms underlying GC development and may help identify potential therapeutic targets and prognostic markers for GC patients.

Keywords: gastric adenocarcinoma; bioinformatics; gene expression omnibus; inflammatory markers

Preeclampsia and Its Consequences for Fetal Development and Newborn Health (Review)

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Introduction: Preeclampsia is a convoluted hypertensive disorder of pregnancy that typically occurs after ٢٠ weeks of gestation. Affecting ٢-٨٪ of pregnancies globally, it is a major cause of maternal and fetal morbidity and mortality. The condition is defined by new-onset hypertension and proteinuria, or in some cases, other organ dysfunctions. Preeclampsia interferes placental function, leading to imperiled fetal growth and proliferated risk of preterm birth, intrauterine growth restriction (IUGR), low birth weight (LBW), and even perinatal death. Although maternal consequences are often prioritized in clinical care, the outcomes for the fetus are equally severe, with long-term developmental implications. This review aims to synthesize the current understanding of preeclampsia's impact on fetal sequels, exploring both short-term neonatal complications and potential long-term developmental challenges.

Methods: A systematic review was conducted using PubMed, Cochrane, and Scopus databases. Studies published between ٢٠١٠ and ٢٠٢٣ that examined the relevance between preeclampsia and fetal outcomes were included. The search strategy focused on key terms such as "preeclampsia," "fetal outcomes," "preterm birth," "intrauterine growth restriction," and "neurodevelopmental delay." Both observational and interventional studies, including cohort studies, randomized controlled trials, and meta-analyses, were considered for inclusion. Studies involving human subjects and published in English were taken precedence. Amongst of ٢٠٠ articles, ٤٥ studies were deemed relevant based on predefined criteria, including a clear focus on fetal outcomes in pregnancies complicated by preeclampsia.

Results: The review distinguished several key fetal outcomes strongly associated with preeclampsia. Preterm birth was amongst the most common complications, with rates ranging from ٣٠-٥٠٪ in affected pregnancies. Preterm birth, often medically revealed to prevent maternal and fetal complications, significantly contributes to neonatal morbidity, including respiratory distress syndrome (RDS), infections, and long-term developmental delays. Intrauterine growth restriction (IUGR) was reported in approximately ٢٥-٤٠٪ of pregnancies complicated by preeclampsia, primarily due to impaired placental blood flow. This restricted nutrient and oxygen transfer to the fetus results in small-for-gestational-age (SGA) infants and is a key predictor of adverse neonatal outcomes. Low birth weight (LBW), closely related to IUGR, was another prominent finding, with infants exposed to preeclampsia being twice as likely to be born with LBW compared to those from normotensive pregnancies. These infants are often admitted to neonatal intensive care units (NICUs) for closer monitoring and treatment of complications such as hypoglycemia, temperature, and feeding difficulties. Perinatal mortality rates were found to be elevated in pregnancies affected by preeclampsia, with a ٢-٤ times higher risk of stillbirth and neonatal death. These outcomes were particularly common in early-onset preeclampsia (before ٣٤ weeks), where both the severity of the condition and the immaturity of the fetus contribute to adverse outcomes. Long-term follow-up

studies indicated that infants born to mothers with preeclampsia may confront neurodevelopmental challenges, including delays in motor function and cognitive skills. There is growing evidence suggesting that these children may be at higher risk for conditions such as cerebral palsy and attention deficit hyperactivity disorder (ADHD), although the exact mechanisms linking preeclampsia to these outcomes require further investigation.

Conclusion: Preeclampsia poses significant risks to fetal health, fundamentally through mechanisms of placental insufficiency that result in IUGR, preterm birth, and low birth weight. Despite advances in obstetric care, preeclampsia persists a leading cause of adverse fetal outcomes, particularly in low-resource settings where access to timely medical interventions is limited. Future research would concentrate on early detection and management strategies that minimize fetal risks, as well as long-term follow-up of children born to preeclamptic mothers to evaluate and control developmental challenges.

Keywords: Preeclampsia, fetal outcomes, intrauterine growth restriction, preterm birth, developmental delay.

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Preparation and Characterization of AS١٤١١ Aptamer-Targeted Solid Lipid Nanoparticles Containing Lawson for Enhanced Anticancer Efficacy (Research Paper)

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Introduction: Lawsone (LWS), a naphthoquinone-type dye with anticancer properties, faces challenges in aqueous solubility, affecting its medicinal benefits. Solid lipid nanoparticles (SLNs), known to enhance bioavailability of poorly soluble drugs, conjugated with aptamers provide a targeted and effective approach in cancer therapy, minimizing toxicity to healthy tissues. This study aimed to develop chitosan-coated LWS-loaded SLN conjugated with aptamer AS١٤١١ (LWS-SLN-Chit-Apt) for cytotoxicity evaluation against mouse colon adenocarcinoma cells (C٢٦).

Methods: First, the LWS-SLN were prepared using high-shear homogenization and ultrasound methods. Various tests including dynamic light scattering (DLS), differential scanning calorimetry (DSC), scanning electron microscopy (SEM), and fourier-transform infrared spectroscopy (FTIR) were conducted to determine the nanoparticle (NP) properties. The LWS-SLNs were then coated with chitosan and bound with AS١٤١١ aptamer, confirmed by DLS and gel electrophoresis. Cytotoxicity was assessed using the MTT assay on mouse colon cancer (C٢٦) and Chinese hamster ovary (CHO) cell lines, and cellular uptake was measured.

Results: The LWS-SLN and LWS-SLN-Chit-Apt showed a size of ١٦٠ ± ١٤,٨ and ٣٥٠ ± ٢٢,٥ nm, respectively with encapsulation efficiency of ٧٠٪ ± ٤,٣, and continuous drug release over ١٢٠ hours. Higher cellular uptake and cytotoxicity were observed in C٢٦ cells, as nucleolin-positive cells, with AS١٤١١ aptamer-targeted NPs compared to non-targeted NPs, while no significant difference was noted in CHO cells.

Conclusion: Our findings suggest that the LWS-SLN-Chit-Apt formulation is a promising drug delivery system for enhancing the bioavailability of LWS and improving its therapeutic effects against cancer cells. This stable and non-invasive formulation shows promise as a candidate for in vivo and clinical studies.

Keywords: Targeted Drug Delivery, AS١٤١١ Aptamer, Lawson, Solid Lipid Nanoparticle, Colon Cancer.

Prevalence of Extended Spectrum β-Lactamase Escherichia coli, Klebsiella spp. and Proteus spp in bronchoalveolar lavage samples by disk diffusion and molecular methods in Tabriz, Iran (Research Paper)

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Introduction: Resistance to a wide range of common antimicrobials has made the proliferation of extended-spectrum beta-lactamase (ESBL)--producing strains a serious global health concern, complicating therapeutic strategies. The high proportion of ESBL producers among Enterobacteriaceae and the complex molecular epidemiology with different types of ESBL genes are of concern. ESBLs are plasmid-mediated groups of enzymes that hydrolyze penicillins, extended-spectrum cephalosporins, and aztreonam. This study was conducted to identify ESBL production in different Gram-negative bacilli isolated and further identify ESBL producers among Escherichia coli and Klebsiella bacteria by PCR method in Tabriz city.

Methods: A total of ٢٠٠٠ isolates of gram-negative bacilli were isolated by examining more than ٥٠٠٠ Bal culture samples. Then, all the isolated bacteria were identified by microbiology diagnostic methods such as differential media and diagnostic discs. The presence of ESBL positivity was detected using a double disc synergy test (DDST). The discs used in this experiment were ceftazidime and ceftazidime clavulanate. After antibiogram analysis, PCR for beta-lactamase (bla) genes of SHV, TEM and CTX-M family was also performed using primers designed in ٢٥ ESBL isolates of each Escherichia coli, Klebsiella and Proteus species.

Results: Among ٢٠٠٠ Gram-negative bacilli isolated, ٨٢٠ (٤٥,٦٩٪) were ESBL producers. The main source of ESBL production was bronchoalveolar lavage samples, with the highest ESBL production in Klebsiella sp. (٦٥,١٢ %). Resistance to multiple classes of antibiotics was observed among ESBL producers. Among the bacteria that can have EBLS resistance, Proteus was the least of all. Among ESBL-producing genes, the prevalence of bla-CTX-M (٧٠,٣٪) was the highest, followed by bla-TEM (٤٨,٢٪) and bla-SHV (٥٦,٣٪) in the present study. The frequency of ESBL-producing strains among clinical isolates is steadily increasing. Monitoring advanced drug resistance and molecular characteristics of ESBL isolates is essential to guide the appropriate and judicious use of antibiotics.

Conclusion: Gram-negative bacilli that are multidrug-resistant have been increasingly responsible for life-threatening illnesses all over the world. Multiple risk factors were associated with ESBL infections both in the community and hospital setting It must be given importance. Prediction tools

are needed to improve the protocol of appropriate empiric antibiotic selection while preserving antimicrobial stewardship recommendations.

Keywords: Extended-spectrum β-lactamase (ESBL), bronchoalveolar lavage, Double Disk Synergy Test (DDST), Antib

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Prevalence of Helicobacter Pylori by Antibodies titer Using ELISA and Compared to Stool Antigen in Urmia, Iran (Research Paper)

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Introduction: Helicobacter pylori (H. pylori) is one of the most common human infections in the world.(١) This bacterium is also associated with some cases of gastric mucosal lymphoma or maltoma and seems to be a predisposing factor for the development of gastric carcinoma .In developing countries, most children (٨٠٪) are infected by the age of ١٠, while in advanced countries, the prevalence of H. pylori and gastritis increases with age(٢). The aim of this study was to evaluate the antibody titer of IgG and IgM anti-Helicobacter pylori using ELISA method and to investigateits relationship with stool antigen.

Methods: This study was conducted in ٢٠٢٤ on ١٠٠ patients refering to Dr. Nemati Laboratory in Urmia. After blood sampling and serum isolation, IgG and IgM antibody titers were measured by ELISA method. On the other hand, stool antigens were also tested using the Helicobacter pylori Rapid Kit.

Results: Results showed that ٥٨٪ of IgG positive and ٦٥٪ of H.pylori Ag stool positive were studied. Other results showed that ٣٠٪ of patients were both IgG positive and H.pylori Ag stool positive. No association was found between H. pylori Ag stool and IgG with IgM. which means that IgM antibody was negative in all patients. That is, H.pylori Ag stool is the best and most accurate method for Helicobacter pylori screening.

Conclusion: Simple methods based on the search for antibodies and antigens with high sensitivity and specificity are available. The advantage of ELISA in addition to its high sensitivity and specificity also determines the antibody class. IgG has a higher diagnostic value and prognosis and represents a chronic stage of the disease.IgM is not very useful in the diagnosis of Helicobacter pylori and can be said to be an insensitive indicator of acute infection. On the other hand, for detection of Helicobacter pylori antigen in stool rapids can also be very useful due to its high accuracy and low test time.

Keywords: Helicobacter Pylori, Antibodies titer, ELISA

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Prevalence of screening colonoscopy among the first-degree relatives of patients with colorectal cancer and related factors (Research Paper)

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Introduction: First-degree relatives (FDRs) of colorectal cancer (CRC) patients possess a higher risk of developing CRC. Colonoscopy is among the most effective screening methods for preventing CRC. This study aimed to assess screening rates among FDRs of CRC patients and determine obstacles to screening in this population.

Methods: This cross-sectional study was conducted in Isfahan, Iran. A total of ١٦٠ asymptomatic FDRs were identified and considered eligible for inclusion in the analysis.

Results: The mean age of FDRs was ٥٠ years, and ٦٥,٦٪ were at high risk for CRC. Only ٣٢,٤٪ underwent screening according to guidelines, and all of them were classified as high-risk. Index patients (IP) aged under ٥٠ and receiving a recommendation for screening were identified as two main factors associated with guideline-based CRC screening. Among FDRs who did not undergo colonoscopy, ٦٤,٤٪ lacked knowledge about the procedure, and ٥٦,٣٪ were unaware of the risk of CRC.

Conclusion: Urgent implementation of effective interventions and improved education for both healthcare providers and patients on risk-based CRC screening for first-degree relatives is crucial. Further descriptive investigations are needed to identify barriers to CRC screening in this population.

Keywords: colorectal cancer, first degree relative, colonoscopy screening

Prevalence of Social Phobia in Infertile Couples in Zanjan City (Research Paper)

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Introduction: Couples who have been infertile for a long time may be questioned about their infertility status by relatives, friends and acquaintances. This issue may be uncomfortable for many infertile couples and may lead to social phobia. Social phobia is a severe fear of being in social situations. The purpose of this study was to investigate the prevalence of social phobia in infertile couples in Zanjan city.

Methods: This is a descriptive cross-sectional study that was conducted in Zanjan city in the second half of ۲۰۲۳. During this study, ۱۹۶ infertile couples referring to obstetrics and gynecology centers in Zanjan city were examined by interview and social phobia inventory (SPIN). Descriptive statistical analysis methods as well as chi-square tests and Cramer's V correlation coefficient were used and the data were analyzed by SPSS ۲۱ software (p<۰,۰۵).

Results: ۲۵,۸۸٪ of the couples met the diagnostic criteria of social phobia and were suffering from this disorder. These couples have stated that they have felt embarrassed, ashamed and anxious in interacting with relatives, friends and acquaintances in many cases and have avoided attending social situations in many cases.

Conclusion: The results showed that the prevalence of social phobia in infertile couples is very high. It is suggested that considering the consequences of social phobia for physical, mental health and individual and social activities, the awareness of society members about how to deal with infertile couples should be increased in different ways and the mental health of infertile couples should be given more attention.

Keywords: Infertility, Mental Disorders, Mental Health, Phobia, Social Phobia

Primary Bilateral Macronodular Adrenal Hyperplasia: A Rare Cause of Cushing's Syndrome – A Review of the Literature (Review)

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Introduction: Primary bilateral macronodular adrenal hyperplasia (PBMAH) is a rare cause of ACTH-independent Cushing syndrome (CS), accounting for <٢٪ of CS cases. Diagnosing PBMAH can be difficult and challenging for clinicians.

Methods: We conducted a comprehensive review of recent case reports on PBMAH available on Google Scholar and PubMed databases.

Results: The clinical manifestations of PBMAH can progress gradually for years, resulting in a lack of comprehensive epidemiological data and underdiagnosed cases. Characteristically, nodules in PBMAH exceed ١٠mm. The underlying mechanisms include aberrant receptor expression, local ACTH production, and genetic mutations, notably in ARMC٥. While cortisol levels in PBMAH are usually mildly elevated, many patients remain asymptomatic, although some may develop overt CS. Diagnosis poses challenges due to its rarity and the absence of specific symptoms, necessitating a combination of clinical criteria, imaging, and potentially genetic testing. Surgical intervention is the mainstay of treatment for those with overt CS, with unilateral adrenalectomy emerging as a favorable option due to lower associated morbidity compared to bilateral adrenlaectomy. However, the optimal treatment strategy continues to be the subject of ongoing debate

Conclusion: PBMAH should be considered in the approach to patients with CS manifestations. The diagnosis and treatment of this condition can be challenging, and further studies on the best possible treatment of PBMAH are recommended.

Keywords: Adrenal tumor; Cushing's syndrome; Primary bilateral macronodular adrenal hyperplasia; Adrenalectomy

Prime editing: A review on application of a novel gene editing approach in treatment of cancer

(Review)

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Introduction: Cancer is the second leading cause of death, with high rates of prevalence and mortality all over the world. It is characterized by unregulated cell proliferation resulting from oncogenes and tumor suppressor gene alterations. There are many traditional and novel strategies for the treatment of cancer. However, many side effects and recurrence after treatment have been reported due to the non-specific functions. Recently, a novel approach has been developed to treat various cancers by editing point mutations, insertions, and deletions on specific oncogenes and tumor suppressor genes by applying designed universal pegRNAs. There are five Prime Editors (PE) that can edit variants of these genes to raise levels of efficiency. This CRISPR-based genome editing technique has reduced off-target activity, so this generation is close to treating cancer without any side effects and chance of recurrence.

Methods: This review highlights the application of Prime Editing. It compares it with other gene editing techniques in the treatment of a variety of cancers, such as breast cancer, pancreatic cancer, human colorectal carcinoma, and liver cancer.

Results: It also targets mutations in several oncogenes and tumor suppressor genes, including KRAS, TP٥٣, CTNNB١, EMX١, HEK site٣, HEK site٥, PDCD١, and FANCF genes.

Conclusion: Therefore, this technique can be considered and developed as an efficient approach based on personalized medicine in treating different types of cancer.

Keywords: Prime editing; Cancer treatment; Mismatch repair; Universal pegRNAs; Nick-single-guide RNA(sgRNA);

Probiotic Bacteria: A Promising Approach for Enhancing Wound Healing and Combating Biofilm Infections (Review)

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Introduction: Wound healing is a complex biological process that can be significantly hindered by the presence of biofilm-forming bacteria, leading to chronic infections and delayed recovery. Probiotic bacteria, known for their beneficial effects on human health, have emerged as a promising therapeutic strategy for enhancing wound healing and combating biofilm infections.

Methods: This review article explores the mechanisms by which probiotics can modulate the wound healing process, including their roles in promoting angiogenesis, collagen synthesis, and immune response modulation. We discuss the ability of specific probiotic strains to inhibit biofilm formation through competitive exclusion, production of antimicrobial substances, and modulation of host immune responses.

Results: Recent clinical studies demonstrate the efficacy of probiotics in improving wound healing outcomes and reducing infection rates in various patient populations. The findings indicate that probiotics can serve as adjunctive therapies in wound care, addressing challenges such as strain selection, delivery methods, and regulatory considerations.

Conclusion: This review aims to provide a comprehensive overview of the current state of research on probiotic bacteria in wound healing and biofilm infection management, emphasizing their potential to revolutionize treatment approaches in biomedicine. Given the numerous benefits of probiotics, further research is essential to better understand their mechanisms of action and optimize their use in wound and infection treatment.

Keywords: Probiotic Bacteria, Wound Healing, Biofilm Infections, Antimicrobial Properties, Therapeutic Strateg

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Probiotics as a Viable Substitute for Antibiotics in Combatting Infectious Diseases: A Molecular Perspective (Research Paper)

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Introduction: With the escalating threat of antibiotic resistance, there is an urgent need for alternative therapeutic strategies to combat infectious diseases. Probiotics, live microorganisms with beneficial health effects, have emerged as a promising alternative to antibiotics. This study aims to investigate the efficacy of probiotics in modulating mRNA expression of immune-related genes and combating infectious diseases, providing novel insights into their therapeutic potential.

Methods: A randomized controlled trial was conducted involving ١٥٠ participants diagnosed with recurrent urinary tract infections (UTIs). Participants were divided into two groups: the probiotic group (n=٧٥) received a daily probiotic supplement containing Lactobacillus acidophilus and Bifidobacterium bifidum for ١٢ weeks, while the control group (n=٧٥) received standard antibiotic treatment. Urine samples were collected at baseline and post-intervention to quantify mRNA expression levels of immune-related genes, including interleukin-٦ (IL-٦) and tumor necrosis factor-alpha (TNF-α), using quantitative real-time PCR.

Results: The demographic characteristics of both groups were comparable at baseline. Participants in the probiotic group showed a significant reduction in UTI recurrence rates compared to the control group ($p<٠,٠٥$). Moreover, mRNA expression levels of IL-٦ and TNF-α were significantly downregulated in the probiotic group following the intervention (IL-٦: mean mRNA copies from ١٢٠٠ to ٦٠٠, $p<٠,٠٠١$; TNF-α: mean mRNA copies from ١٠٠٠ to ٤٠٠, $p<٠,٠٠١$), whereas no significant changes were observed in the control group.

Conclusion: This study provides evidence for the efficacy of probiotics in modulating mRNA expression of immune-related genes and reducing UTI recurrence rates. By targeting inflammatory pathways, probiotics offer a promising therapeutic approach for combating infectious diseases while mitigating the risk of antibiotic resistance. These findings support the incorporation of probiotics into clinical practice as a viable substitute for antibiotics in the management of infectious diseases.

Keywords: Probiotics_ Antibiotics_ Infectious diseases_ Gene expression

Probiotics as Therapeutic Agents in Parkinson's Disease (Review)

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Introduction: Parkinson's disease (PD) is the second most common neurodegenerative disease worldwide that affects ۳,۷٪ of the population over ٦٥ years of age; it is a progressive degeneration of dopaminergic neurons that are present in the substantia nigra pars compacta (SNPC) with a deficiency of dopamine, that can lead to altered motor movement. Based on recent evidence, due to the strong correlation between the gut-brain axis and PD, there is a positive relation between the consumption of probiotics with the improvement of Parkinson's disease symptoms through different pathways and mechanisms.

Methods: Studies published from the beginning to ۲۰۲۳ analyzing the effect of probiotics on PD were searched by searching Google Scholar, Pubmed, and Web of Science. Among the screened articles, related articles were reviewed.

Results: Probiotics play a beneficial role in the pathways that lead to the degeneration of dopaminergic neurons and ultimately the exacerbation of PD symptoms; For example, in the PARK-۲ gene mutation, which leads to the lack of expression of the E۳ ubiquitin ligase enzyme gene and the accumulation of alpha-synuclein, Saccharomyces boulardi and Lactococcus lactis probiotics, play a role in increasing the expression of this enzyme. As another example, SCFAs play a role in inhibiting DDT and ROTENONE pesticides, which cause the degeneration of dopaminergic neurons. In addition, considering that the only way to improve the symptoms (Especially movement disorders) in this disease is to increase the levels of dopamine, SCFAs have shown their beneficial effect here by inhibiting the enzymes that break down dopamine (MAO-B and COMT). It has been found that the use of probiotics increases the production of anti-inflammatory factors and decreases the gene expression of inflammatory factors, as well as reducing the accumulation of ROS and as a result, neuroinflammation, which is one of the main reasons for PD, is prevented. Our review shows that probiotics can be used to improve constipation and motor symptoms for patients with Parkinson's constipation, possibly by reducing the inflammatory response and improving gut-brain axis neuron function. Probiotics can directly stimulate electrical signals in the ENS and dorsal motor nucleus of the vagus (DMV) by transmitting signals through the vagus nerves to affect the center of the brain, thus reducing the accumulation of α-syn and reducing motor deficits in PD patients. According to research, ghrelin levels (which play a role in maintaining and protecting the normal function of nigrostriatal dopamine) is reduced in PD patients, and with Prevotella, ghrelin concentrations return to normal.

Conclusion: According to the results obtained from the present studies (considering the gut-brain axis), the consumption of probiotic supplements in a specified type and dose can have positive

effects on the symptoms of Parkinson's disease (especially constipation). More studies can help to understand and prove the mechanisms of the effects of probiotics on Parkinson's disease.

Keywords: Parkinson's disease, Probiotics, Dopamine, Motor symptoms, constipation, SCFAs

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Production of biological pesticide based on Laurus nobilis essential oil and its killing and repellent effect on wax aphid on rapeseed plant in simulated climate conditions of Khuzestan (Review)

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Introduction: Entre los insectos, los pulgones son una de las plagas importantes de los cultivos agrícolas y, debido a su resistencia a muchos venenos químicos, se han utilizado fuertes estrategias de control contra ellos. El uso indiscriminado de pesticidas puede contaminar el suelo y matar otros organismos no objetivo. Por este motivo se recomienda el uso de pesticidas orgánicos. La plaga más importante de la colza es el pulgón de la cera. El pulgón ceroso que se alimenta del xilema de la colza causa daños a la planta y una disminución del rendimiento agrícola. Nuestro objetivo de esta investigación es encontrar un tipo de aceite esencial ambiental que no solo tenga éxito en eliminar los pulgones de la cera, sino que, a diferencia de los pesticidas químicos, no dañe el suelo ni los cultivos.

Methods: In this research, after matching the age of wax aphid, the effect of Laurus nobilis essential oil on wax aphid was evaluated in the form of a completely randomized design with ٥ different concentrations of essential oil along with a control in ٣ replicates and each replication carried ١٠ .The number of aphids with rapeseed leaf disc, once in the simulated climatic conditions of Khuzestan and once in the simulated climatic conditions of Tehran province, separately, within the incubator after a period of ٢٤ hours and a period of ١٦ hours of light and ٨ hours of darkness was evaluated.

Results: The LC٥٠ value was recorded as ١٧,٧٨ microliters per liter of air in the climatic conditions of Khuzestan and ٣٧,٦٢ microliters per liter of air in the climatic conditions of Tehran province, which indicates that the essential oil of the leaves of the Laurus nobilis plant has an effect on killing and repelling wax aphids.

Conclusion: As the concentration of essential oil increases, the number of aphids killed increases, and due to the fact that the relative heat in Khuzestan is higher than the national average, and the essential oil evaporates more in the heat and creates more harmful respiratory vapors for the wax aphid, the effectiveness and efficiency of the biological pesticide under investigation is higher than the average. There is more country.It seems that this essential oil has a good pesticidal ability.

Keywords: Wax aphid, biological pesticide, Laurus nobilis essential oil, rapeseed

Proliferating Cell Nuclear Antigen (PCNA) Expression in Nasal Polyps: A Systematic Review and Meta-analysis (Review)

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Introduction: Nasal polyps (NP) are benign growths occurring in the nasal cavity and paranasal sinuses, often linked with chronic rhinosinusitis (CRS), specifically termed chronic rhinosinusitis with nasal polyps (CRSwNP). Proliferating cell nuclear antigen (PCNA) serves as a marker for abnormal cell proliferation, which can be valuable for evaluating nasopharyngeal lesions and upper airway cancers. This study investigates the expression of PCNA in NP tissue.

Methods: This study was conducted under the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. A thorough search using relevant keywords was performed on the electronic database to identify studies examining the PCNA expression in NP. A meta-analysis was performed using the metamean and metaprop functions in R software (version ٤,٤,٠) to analyze pooled data on PCNA expression. Quality assessments were based on the Joanna Briggs Institute (JBI) checklist.

Results: The analysis included ten articles. Findings indicated that PCNA expression in NP was significantly higher than in normal nasal mucosa (NNM) but lower than in inverted papilloma (IP). The mean percentage of PCNA expression in NP was ١٥,٧٣٪ (٩٥٪-CI [٢,٨٧-٢٨,٥٨]), with substantial heterogeneity (I^2=٩٧٪, p<٠,٠١). Using a cutoff of >٥٪ staining, ٦٤٪ of NP samples were found to be PCNA-positive (٩٥٪-CI [٤٢٪-٨١٪]), exhibiting high heterogeneity (I^2=٧٦٪, p<٠,٠١).

Conclusion: The study concludes that NP tissue exhibits a relatively high expression of the PCNA oncoprotein based on immunohistochemistry (IHC) staining. Despite over half of the NP samples testing positive for PCNA, the average expression level remains lower than that observed in IP tissue.

Keywords: Nasal polyp; NP; Nasal polyposis ; Proliferating Cell Nuclear Antigen; PCNA

Promising Roles of MicroRNA in Cncer Therapy (Review)

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Introduction: Cancer is one of the most common diseases affecting millions of people worldwide every year, representing the second leading cause of mortality after cardiovascular disease. MicroRNAs (miRNAs) are a group of small single-stranded RNA molecules involved in regulating the expression of many genes preserved in evolution. In humans, a miRNA molecule is most often ٢٢ nucleotides long. The use of miRNA in diagnostics has significantly expanded due to the discovery of their presence in other body fluids, such as urine, blood, bronchial lavage, synovial fluid, milk, saliva and cerebrospinal fluid. miRNAs play important roles in tumorigenesis and function as tumorigenic or tumor suppressors by regulating the levels of oncogenes or antioncogenes.

Methods: In the current study, keywords including Cancer, MicroRNA, and Treatment were reviewed from the list of Mesh and other credible websites including PubMed, Science Direct, and Google Scholar, and the data was organized. The searches comprised all published papers from ٢٠١٣ to ٢٠٢٣. All of the full text was considered, and the papers manifested as only abstract were excluded. The full papers selected focused on the specific roles of miRNAs in cancer therapy only. A total of ٥٠ papers were selected and studied in this review.

Results: Articles showed in colorectal cancer, the miRNA synthetic let-٧ contributed to an increase in apoptosis of cancer cells. Also, Simultaneous overexpression of the let-٧ and miR-٣٤a molecules inhibit the progression of lung cancer. Numerous studies concluded that miR-٣٤ family plays a critical role in the suppression of tumor development. In some study, ectopic expression of miR-٢١٧ significantly reduced tumor growth in a pancreatic ductal adenocarcinoma xenograft model. Some articles showed the therapeutic potential of exosome miRNAs on immune escape in neuroblastoma. These studies concluded that natural killer cell-derived exosomes or nanoparticles can be used to deliver and restore miR-١٨٦ levels and, thus, reduce tumor size, restoring natural killer-mediated cytotoxicity. Studies showed that miR-٢٠٠ family inhibits migration and invasion of breast cancer cells by degrading mRNA of multiple proteins including moesin (cytoskeleton-associated protein), extracellular matrix protein fibronectin ١, actin-regulatory proteins-formin homology ٢ domain containing ١ and protein phosphatase, Mg٢+ /Mn ٢+ dependent, ١F which inhibit migration and invasion through regulation of stress fiber formation. Numerous studies approved that miR-٣٥b, miR-١٤٥, miR-٢٠٥, mir-٢٠٠ family inhibit cancers by regulating oncogenes and/or genes that control cell differentiation or apoptosis. Their targets are oncogenes in cell differentiation, cancer invasion, apoptosis, proliferation, and metastasis.

Conclusion: Numerous miRNAs are currently in clinical trials as biomarkers for cancer classification and progression and as prognostic tools. Moreover, in a variety of studies miRNAs are suggested as promising diagnostic markers for the early detection of distinct cancer type. Monitoring the changes in the expression profiles of chosen miRNAs could help in early identification of cancer cells and serve as a prediction factor of the disease or treatment.

Keywords: Cancer, MicroRNA, Treatment

Properties of honey in the prevention and treatment of cancer (Review) (Review)

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Introduction: Honey is a sweet and natural substance produced by honeybees from the nectar of flowers or the secretions of living plant parts. This natural product consists of various carbohydrates, proteins, organic acids, amino acids, enzymes, essential minerals, and different phenolic compounds. It has been consumed by humans for a long time and is recognized as a valuable nutrient and medicinal substance. In addition to its significant role in traditional medicine, there has been a renewed interest in the medicinal properties of bee products, as they are believed to exhibit a wide range of biological activities, including antibacterial, antifungal, antiviral, antiarrhythmic, antidiabetic, liver protection, wound healing, antitumor, and anti-inflammatory effects. Regarding natural compounds derived from plants or Phyto-chemicals that have been considered dietary supplements in traditional medicine for centuries, these compounds and plant products may be used as complementary treatments against cancers to reduce the size of metastatic tumors. Cancer is recognized as a global health concern with a dynamic increase in incidence and is a major cause of mortality worldwide. It encompasses a group of diseases characterized by the abnormal growth of malignant cells with the potential to invade and metastasize to other parts of the body, with nearly ١٩-٢٠ million people diagnosed with cancer worldwide each year, resulting in the loss of approximately ١٠ million. Currently, conventional cancer treatments include surgery, chemotherapy, radiotherapy, immunotherapy, and targeted therapy, which are associated with side effects, recurrence risks, and drug resistance. Due to these adverse factors, the use of plant-derived products, whether alone or in combination with anticancer agents, generally has fewer adverse effects on healthy cells and tissues. These products are now being investigated as complementary treatments to minimize side effects and are known to modulate chemotherapy resistance, autophagy, proliferation, and apoptosis.

Methods: The anticancer activity of honey has been studied using several cancer cell lines and tissues, demonstrating its ability to reduce tumorigenesis in various cancers, including breast, prostate, colorectal, cervical, endometrial, and kidney cancers. In one study, acacia honey inhibited the growth of the human breast cancer cell line MCF-٧ in a dose- and time-dependent manner. In an experimental model of breast cancer in mice, honey exhibited anti-metastatic activity, potentially due to flavonoids like chrysin and quercetin present in honey. Quercetin has been shown to inhibit cell cycle progression in the M phase and halt progression in the G٢ phase, inducing apoptosis in MCF-٧ cells through the P٣٨MAPK pathway. In another study, honey was able to treat human liver

cancer cells (HepG٢) by reducing nitric oxide levels and the number of viable HepG٢ cells. The apoptotic effects of certain raw honeys on colorectal cancer cell lines (HCT ١٥ and HT ٢٩) were also investigated, confirming previously reported anti-proliferative effects of honey. Additionally, in a colon cancer model in mice, pre-treatment with honey before tumor cell inoculation showed anti-metastatic effects. Thyme honey has demonstrated anti-proliferative effects in breast cancer (MCF-٧), prostate cancer (PC٣), and endometrial cancer cell lines, reducing cell viability by up to ١٠٪. Another study indicated that honey significantly inhibited the proliferation of human bladder cancer cell lines, including RT٤, T٢٤, and ٢٥٣J, as well as a mouse bladder cancer cell line (MBT-٢).

Results: Overall, evidence from cellular and animal studies suggests that honey may serve as a complementary treatment to mitigate chemotherapy side effects and improve the quality of life and treatment outcomes for cancer patients. Honey is affordable, easily accessible, and has fewer side effects. However, the composition and properties of honey, along with its anticancer effects, can vary depending on the nectar source, bee species, climate, geographical region, processing methods, and packaging and storage conditions.

Conclusion: Standardized studies are needed to evaluate its clinical applications, as current findings indicate that honey could function as a complementary treatment to enhance the quality of life and therapeutic outcomes for cancer patients, but stronger clinical trials are essential to confirm these benefits.

Keywords: ١.Honey ٢.Cancer ٣.Phenolic and flavonoid compounds ٤.Bioactive compounds

Propolis nanoemulsion effect on multidrug resistant strains of Pseudomonas aeruginosa (MDR) biofilm (Research Paper)

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Introduction: Pseudomonas aeruginosa is a common cause of nosocomial infections and exhibits innate resistance to a wide range of antibiotics. In recent years, the current trend has been towards the identification of natural products in disinfection. Nanoparticles are able to penetrate bacteria and bacterial biofilms, so they can be a potential agent for controlling the growth of bacterial infections. In this study, our goal is to determine the antibacterial efficacy of synthesized the Propolis nanoemulsion and its combination with ciprofloxacin to obtain a synergistic effect against MDR strains of P. aeruginosa biofilm.

Methods: Propolis nanoemulsion (PN) was prepared by the ultrasonication method. Scanning electron microscopy and dynamic light scattering were used to measure the size and morphology of the produced nanoparticles. The PN was evaluated in vitro against ten MDR P. aeruginosa strains by disk diffusion and broth micro-dilution method. The checkerboard testing method was used to evaluate synergism among PN combined with ciprofloxacin against MDR P. aeruginosa strains.

Results: The Fe-SEM image reveals that the PN morphology is nearly spherical. PN, with average size ۲۱۹,۳ nm, was effective against MDR P. aeruginosa biofilm with MIC value of ۳,۲- ۱۵ mg/ml. However, ciprofloxacin showed strong antibacterial activity even at low concentrations. According to the checkerboard results, MDR P. aeruginosa had additive effect with FIC of >۰,۵ to ≤۱ for combining PN with CP. But, an isolate of MDR P. aeruginosa showed a synergistic antibacterial effect for combining PN (۰,۸ mg/ml) with CP (۰,۰۷ mg/ml).

Conclusion: PN was able to inhibit MDR P. aeruginosa that could be due to the reduced particle size, better nanoparticle penetration and the synergistic impact of main components in propolis. More research is needed to investigate the synergistic mechanism of PN in combination with antibiotics.

Keywords: Antibacterial, MDR P. aeruginosa, Nanoparticles

Protein and peptide based vaccines (mRNA) (Review)

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Introduction: For effective vaccination, mRNA formulation, delivery method and mRNA carrier composition play an important role. mRNA vaccines have been delivered in various formats: encapsulation by carriers, delivery, such as lipid nanoparticles, polymers, peptides, free mRNA in solution and outside the body through dendritic cells. Appropriate delivery materials and formulation methods often increase the efficacy of the vaccine. It is also influenced by choosing a suitable route of administration. Simultaneous delivery of multiple mRNAs has the same effect it is possible to increase and in some cases the immunity against different types of an infectious pathogen or in general increase several pathogens. mRNA vaccine technology has evolved over the past ٢٠ years from the first proof of concept to the first licensed vaccine against emerging pandemics such as ٢-CoV-SARS evolved is. Also, mRNA vaccines in the past years have been a revolution in the fight against the epidemic - COVID There have been ١٩. This versatile technology has become the prevention of infectious diseases and the treatment of cancer are in the vaccination process, mRNA formulation and delivery strategies, effective expression and delivery of anti facilitates genes and immune system stimulation.

Methods: To date, in vitro mRNA transcription technology has matured and become the most popular method of use RNA polymerase T٣, TV or SP٦ and linear DNA (linearized plasmid DNA or synthetic DNA) by PCR (for mRNA synthesis). Some basic structural elements of mature mRNA in There is a eukaryocyte that is necessary for the mRNA to remain functional. Modification of mRNA sequence the basis of its complete structure can optimize the efficiency of mRNA vaccine. Nevertheless, the original product in vitro transcribed mRNA is a mixture of target mRNA, non-target RNA, nucleotides, oligodeoxynucleotides and proteins. For purification of mRNA, sedimentation techniques and extraction to remove common impurities and chromatographic techniques in general for separation the target mRNA is used in this system from other mRNA impurities. UTRs are the non-coding parts of the mRNA sequence in the upstream domains (UTR'٥) and downstream of the mRNA coding region (٣' UTR). As reported, UTRs are associated with the processes of mRNA replication and translation and can greatly degrade mRNA and alter translation efficiency through interaction with RNA-binding proteins. in an effort to increase mRNA stability and translation efficiency, ensuring UTR optimization is essential.

Results: A preliminary study has shown that injecting naked mRNA in vivo can induce an immunotherapeutic response stimulate in mice. Currently, mRNA administration strategies generally

include the following injections cutaneous, intradermal injection, intranodular injection, intramuscular injection, intravenous injection, injection inside the tumor, etc., are the necessary methods to stimulate antigen presentation and initiation immune responses help. In ٢٠١٣, Phua et al. Discovered that delivery efficiency subcutaneous injection of naked mRNA in mice is even more effective than mRNA nanoparticle delivery methods. Van Lint et al suggested that intratumoral injection of tumor-associated mRNA a response it creates appropriate immunity and believed that it could be a promising vaccination strategy bare mainly for the near future. Today, direct injection of mRNA to treat or prevent infectious diseases are used. Nevertheless, even if the injection of naked mRNA can respond to create immunity, the working effect of this method of delivery is relatively weak and naked mRNA often after injection it breaks down quickly in the body. Direct injection of naked mRNA for use in human patients it is very simple and basic and is often used as a way to administer modified mRNA vaccines used with other delivery systems to achieve better vaccine effects.

Conclusion: Types of products based on messenger ribonucleic acid (mRNA) as a therapeutic strategy promising in immunotherapy and also known as a vaccine for infectious and viral diseases are There are tremendous advantages associated with mRNA vaccines, including high efficacy, relative intensity and low acquisition costs enable these vaccines to have minimal side effects clinical trials against infectious diseases and various cancers become common. Advances recent technological advances have alleviated some of the issues that have hindered mRNA vaccine development. Hope with the progress of science and conducting more experiments, we have witnessed the effectiveness of this achievement in the society and the production of products be mostly derived from mRNA.

Keywords: mRNA, Peptide, Protein, Virus, Cancer, VLP

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Protein Homeostasis and Aging (Review)

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Introduction: All cells rely on specific processes to control protein homeostasis in order to preserve a steady and useful proteome. As dysfunction in protein homeostasis, or proteostasis, is a universal hallmark of both the aging process and cancer. The cellular quality control is maintained by proteolytic systems and molecular chaperones, which guarantee the constant synthesis of intracellular proteins. The pool of all sorts of proteins found inside cells and in their plasma membrane is known as the cellular proteome, and it is strictly regulated to ensure that each protein is synthesized, folded, and sub compartmentalized as intended.changes in different components of the protein quality control systems have been shown to underlie the basis of some human diseases, which are generally known as protein conformational disorders, and which include pathologies such as neurodegenerative diseases, metabolic disorders, myopathies, liver diseases and systemic disorders type amyloidosis. The term "proteotoxicity" is currently used to describe the toxic effects of altered proteins in cells. Protein unfolding, abnormal cleavage or undesirable post translational modifications can all promote protein self-assembling into toxic oligomeric structures oraggregation into cytosolic inclusions, often bringing along other proteins. Lifespan extension is nearly always linked to resistance to environmental stress, such as oxidative, thermal, and osmotic stress, and the processes managing protein homeostasis are essential for cellular adaptation to stress. Various internal and external stresses that persist throughout life can disrupt protein homeostasis in organisms. oxidative damage to proteins plays a crucial role in accelerating aging.

Methods: Protein homeostasis and the major gate-keepers Chaperones are necessary for covering hydrophobic regions and preventing unwanted non-specific protein binding during these processes. Chaperonins, a subset of cellular chaperones, are more active because they provide a little chamber or microenvironment that helps proteins fold or refold away from the intracellular milieu that promotes aggregation. The "gate keepers" or primary effectors in protein quality control are therefore chaperones and intracellular proteolytic mechanisms. Molecular Chaperones in protein quality control When exposed to high temperatures and other stressors, stress factors known as molecular chaperones or heat shock proteins (HSP) are quickly produced. Chaperones can be divided into five main types based on their molecular weight: The small heat shock proteins (sHSP) and HSP١٠٠, HSP٩٠, HSP٧٠, and HSP٦٠ Cytosolic chaperones This group of chaperones regulates cytosol folding and unfolding events, primarily involving proteins from polysomes or other compartments, to prevent luminal cloggin. The ubiquitin/proteasome system and lysosomes, the two main proteolytic systems in this compartment, are intimately related to the role of cytosolic chaperones in quality control.

Results: Organelle-specific chaperones The ER chaperones that are in charge of maintaining protein homeostasis have the best characterised roles as organelle chaperones in quality control. The ER's

protein homeostasis-maintaining organelle chaperones have the best documented roles in quality control. Molecular chaperones in longevity and aging Increasing chaperone induction has been shown in numerous studies to extend the lifespan of both unicellular and multicellular organisms. Flies and worms carrying extra copies of an hsp-V· family member or sHSPs have been shown to be long-lived The inability of HSF to bind the heat shock element on the chaperone gene promoter has been identified as the cause of the failure of chaperone transcription to upregulate with ageing, at least in the case of hspV· . . Proteolytic systems This system consists of The ubiquitin/proteasome system which is is one of the main proteolytic systems that participate in protein quality control.

Conclusion: Protein quality control is essential for proper cellular function and in the orchestration of an efficient cellular response to stress. Growing evidence supports that functional decline of the different components of the proteostasis network is one of the essential factors that contribute to cellular and organism aging. Protein quality control is essential for proper cellular function and in the orchestration of an efficient cellular response to stress. Growing evidence supports that functional decline of the different components of the proteostasis network is one of the essential factors that contribute to cellular and organism aging. How aging affects this cross-talk and whether functional asynchronism could be behind defective quality control in old organisms remain to be elucidated

Keywords: aging, chaperones,, Protein Homeostasis, cancer

Pseudomonas aeruginosa: an overview (Review)

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Introduction: Pseudomonas aeruginosa is a Gram-negative, rod-shaped bacterium, that causes severe infections in human beings. Regarding to its inherent antibiotic resistance and capacity for biofilm formation, infections caused by this pathogen can present significant therapeutic challenges. This organism can adapt to a wide range of environments and is a prevalent cause of hospital-acquired infections, mainly affecting critically ill patients, such as those in intensive care units. Its potential to cause infections, particularly in immunocompromised people and those with chronic respiratory conditions such as cystic fibrosis, emphasizes its clinical relevance.

Methods: The identification and characterization of P. aeruginosa infections rely on a variety of analytical approaches. These encompass traditional microbiological methods, including culture techniques, biochemical assays, as well as cutting-edge biosensors that provide rapid and portable detection. Molecular techniques, such as PCR, are commonly used to identify specific genetic markers, while antigen detection methods like ELISA assist in pathogen identification through immune responses. Furthermore, analytical techniques for detecting quorum sensing molecules and virulence factors offer valuable insights into biofilm formation and pathogenic regulation. Together, these methods facilitate a thorough diagnosis and deeper understanding of P. aeruginosa infections.

Results: The review of the literature reveals that P. aeruginosa employs multiple virulence factors to establish and sustain infections. The pathogenicity of P. aeruginosa is multifactorial, involving the combination of virulence factors, biofilm formation, and antibiotic resistance. One of the most critical features of P. aeruginosa is its ability to form biofilms, which are dense bacterial communities surrounded by an extracellular polymeric substance (EPS), enhancing bacterial survival in hostile environments. Furthermore, P. aeruginosa has a remarkable ability to develop antibiotic resistance. The clinical implications of P. aeruginosa infections are significant, especially in hospital settings, where it is a major cause of ventilator-associated pneumonia, urinary tract infections, and surgical wound infections.

Conclusion: P. aeruginosa remains a formidable pathogen in clinical settings due to its adaptability, virulence, and multidrug resistance. Its capacity to form biofilms, complicates treatment, especially in chronic or hospital-acquired infections. Understanding the molecular mechanisms of its pathogenicity is crucial for developing new therapeutic strategies. Despite significant advancements in uncovering these mechanisms, effective treatment remains a challenge. In addition to these molecular mechanisms, recent studies have also shed the light on immune responses and bacterial defense mechanisms in biofilm-related infections. These insights pave the way for therapeutic innovations, such as modulating immune activity to reduce tissue damage, enhancing the interaction between antibiotics and the immune system, and disrupting biofilm structures. Continued

exploration of these strategies, alongside better diagnostic techniques, would be essential for mitigating P. aeruginosa-related infections and reducing the patient's infections.

Keywords: Pseudomonas aeruginosa, antibiotic resistance

Psychoneuroimmunology: a Brief overview of literature (Review)

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Introduction: Around ٢٠٠ AD, Galen observed that breast cancer was more prevalent among melancholic women. Since the mid-١٩٧٠s, an interdisciplinary field known as Psychoneuroimmunology (PNI) has arisen. PNI investigates the interplay and communications among the brain, behaviour, immune, and endocrine systems. Neurons are able to release and respond to pro-inflammatory cytokines, while immune cells can release and receive to neurotransmitters. This explains how the nervous and endocrine systems are connected in the same pathway and share signals to create an integrated behavior. Although many aspects of PNI interactions are complex and require further investigation, fundamentally PNI describes the relationship between psychological and physiological health. Mental disorders influence biological health and physiological diseases are associated with appearance of specific behaviors like irritability. This overview aims to provide a clear and brief description of PNI knowledge to help healthcare workers develop effective treatment protocols.

Methods: After providing keywords from MESH vocabulary thesaurus, preparation an overview study started from search in Pubmed, Google scholar and Elsevier databases. A total of ١١٣٥ studies was found which reduces to ١٨٣ after limit time in recent studies ٢٠١٨-٢٠٢٤. According to title and abstracts ١٤ eligible studies included this overview.

Results: As a psychological condition, stress can significantly impact the immune system. When a mammal experiences stress, the HPA axis starts to secrete of glucocorticoids, which bind to receptors on immune cells like monocytes and macrophages. This event is initially able to decrease pro-inflammatory cytokines, but prolonged stress can lead to glucocorticoid resistance and sustained inflammation. Psychological stress can also change gene expression by increasing levels of adrenaline, noradrenaline, and cortisol. Over time, high levels of serum cortisol known as hypercortisolemia, can reduce the lymphatic tissue of the spleen and thymus so that the body's immunity becomes poor. stress can suppress immunity, increase inflammation and contribute to disease symptoms. A significant portion of nervous system growth and development depends on elements like iron. Stress and psychological pressure can decrease absorption and homeostasis of iron also leading to iron deficiency which can disrupt nervous system function. Stress-induced iron deficiency during pregnancy leads to impaired fetal neurodevelopment that affects memory and maternal-child bonding. Additionally, early-life stress can cause physiological changes in the structure of the hippocampus, synapses and cerebral cortex that reduce learning abilities. Patients with depression are often at higher risk for diseases such as rheumatoid arthritis, cardiovascular and autoimmune diseases. Baseline diagnosis of depression is often associated with elevated levels of pro-inflammatory cytokines and C-reactive protein (CRP) which shows increased inflammation can contribute depression. Combining antidepressant treatments with common treatments for

rheumatoid arthritis patients can sometimes result in improved therapeutic effectiveness. inflammation is one of the factors that affects psychological health status; sometimes cause of inflammation is recognized as cause of psychiatric disorders. Evidence suggests that aspirin as an anti-inflammatory drug modify some depressive-like behaviors. Environmental conditions like isolation and social rejection associated with the expression of genes related to inflammation markers. Conversely, social support decreases inflammation factors such as CRP, interleukin-٦ (IL-٦), and tumor necrosis factor-alpha (TNF-α). Oxytocin released following social support directly affects immune cells, reduces inflammation and promotes wound healing.

Conclusion: Physiological and psychological health condition are closely interconnected. Environmental situations such as social support and stress reduction can enhance biological outcomes of treatments. it is recommended to consider psychological, emotional and mental health of patients in treatment protocols to achieve better biological results.

Keywords: Psychoneuroimmunology, Psychophysiology, Psychoimmunology, affect, health

Psychoneuroimmunology: a Brief overview of recent literature (Review)

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Introduction: Around ٢٠٠ AD, Galen noted a higher prevalence of breast cancer in melancholic women. Since the mid-١٩٧٠s, an interdisciplinary field known as Psychoneuroimmunology (PNI) has emerged. PNI investigates the intricate interactions between the brain, behavior, immune, and endocrine systems. Neurons can release and respond to pro-inflammatory cytokines, while immune cells can release and receive neurotransmitters. This highlights the interconnectedness of the nervous and endocrine systems, which share signals to produce integrated behaviors. While many aspects of PNI interactions remain complex and unexplored, PNI essentially describes the relationship between psychological and physiological health. Mental illness can influence biological health, and physiological diseases can be accompanied by specific behaviors like irritability. This overview aims to provide a clear and concise introduction to PNI knowledge, assisting healthcare workers in developing effective treatment protocols.

Methods: After providing keywords from MESH vocabulary thesaurus, preparation an overview study started from search in Pubmed, Google scholar and Elsevier databases. A total of ١١٣٥ studies was found which reduces to ١٨٣ after limit time in recent studies ٢٠١٨-٢٠٢٤. According to title and abstracts ١٤ eligible studies included this overview.

Results: As a psychological condition, stress can significantly impact the immune system. When a mammal experiences stress, the HPA axis starts to secrete of glucocorticoids, which bind to receptors on immune cells like monocytes and macrophages. This initially decreases pro-inflammatory cytokines, but prolonged stress can lead to glucocorticoid resistance and sustained inflammation. Psychological stress can also change gene expression by increasing levels of adrenaline, noradrenaline, and cortisol. Over time, high levels of serum cortisol, known as hypercortisolemia, can reduce the lymphatic tissue of the spleen and thymus so that the body's immunity becomes poor. In essence, stress can suppress immunity, increase inflammation, and contribute to disease symptoms. A significant portion of nervous system growth and development depends on elements like iron. Stress and psychological pressure can decrease iron absorption and homeostasis in the body, leading to iron deficiency, which can disrupt nervous system function. In pregnant women, iron deficiency following stress can impair the child's neurological development, affecting memory and maternal bonding and interaction. Additionally, early-life stress can cause physiological changes in the structure of the hippocampus, synapses, and cerebral cortex, leading to reduced learning abilities. Patients with depression are often at higher risk for diseases such as rheumatoid arthritis, cardiovascular disease, and autoimmune diseases. A baseline diagnosis of depression is often associated with elevated levels of pro-inflammatory cytokines and C-reactive protein (CRP), which can contribute to disease by increasing inflammation. Combining antidepressant treatments with common treatments for rheumatoid arthritis patients can

sometimes result in improved therapeutic effectiveness. The role of inflammation in causing disease is undeniable, and the underlying cause of inflammation is often recognized as a contributing factor to psychiatric diseases. Evidence suggests that aspirin, an anti-inflammatory drug, can modify some depressive-like behaviors. Environmental factors like isolation and social rejection can be associated with the expression of genes related to inflammation markers. Conversely, social support can lead to decreased inflammation factors such as CRP, interleukin-٦ (IL-٦), and tumor necrosis factor-alpha (TNF-α). Oxytocin, released following social support, directly affects immune cells, reduces inflammation, and promotes wound healing.

Conclusion: As demonstrated by the principles of Psychoneuroimmunology (PNI), physiological and psychological health are interconnected. Environmental factors like social support and stress management can significantly influence the biological outcomes of treatments. Therefore, it is essential to consider the psychological, emotional, and mental health of patients to achieve more effective disease management.

Keywords: Psychoneuroimmunology, Psychophysiology, Psychoimmunology, affect, health

purification and concentration anti-FZDV antibody for the treatment breast cancer (Research Paper)

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Introduction: Several factors and biomarkers are been used in diagnosis and treatment of breast cancer. Signaling pathways are suitable targets for the development of cancer treatments. One of signaling pathway is Wnt, Secreted Wnt ligands play a major role in the development and progression of many cancers by modulating signaling through cell-surface Frizzled receptors (FZDs). Ten FZDs are encoded in mammalian genomes, and among these, FZDV has been highlighted in recent years because of its particular contributions to tumor development. FZDV plays an essential role in carcinogenesis by regulating tumor proliferation and metastasis, maintenance of cancer stem cells, and chemo resistance. The aim of the present research is to purify the anti-FZDV antibody produced by the clone so that it can be used to treat breast cancer by targeting the FZDV receptors and it leads to increasing patients survival.

Methods: In previous research at the Motamed Breast Research Institute, an anti-FZDV antibody has been designed and produced. The antibody produced from the mentioned clones has been purified in the present research. The purification method of antibodies included the process of multiple chromatography techniques. Then Due to the presence of His-Tag fusion proteins, in designing the gene sequence for cloning, the desired protein was purified using NTA-Ni affinity chromatography columns. The column outputs were electrophoresed to check the presence of the target protein by SDS PAGE method. After staining the SDS gel and identifying the band, and Amidon column was used to concentrate the desired antibody.

Results: The bands related to anti-FZDV antibody were extracted and purified in SDS PAGE gel with a molecular weight of ۲۲ kD as a single band.

Conclusion: The dysregulation of Wnt-β-catenin signaling in cancer and other diseases has generated strong interest in developing therapeutic inhibitors of this pathway. This study has tried to purify and concentrate the designed anti-FZDV antibody from the produced clones. It is suggested that this antibody be tested on breast cancer cell lines to investigate its effect on the expression of other proteins of the target signaling pathway, including estrogen receptor (ER) and progesterone receptor (PR)

Keywords: anti-FZDV antibody, purification, concentration, breast cancer

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Quantitative analysis of biochemical characteristics and anti-cancer properties in MCF-٧ breast cancer cell line: a comparative study between Ziziphus jujube honey and commercial honey

(Research Paper)

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Introduction: There is increasing evidence that honey has anti-inflammatory, antioxidant, and anti-cancer effects. This study aims to assess and contrast the cytotoxic, anti-metastatic, and apoptotic effects of Ziziphus jujube honey and commercial honey on MCFV cells.

Methods: Two honey samples, Ziziphus jujube (JH) and commercial honey (CH), were categorized into high and low groups based on their phenolic content, antioxidant capacity, and diastase activity (PAD score). The viability and migration ability of MCF-V cells treated with JH and CH were evaluated. Also, quantitative polymerase chain reaction (Q-PCR) was performed to assess the effect of the two honey samples on the expression of Bax, p٥٣, p٢١ and Bcl-٢ genes.

Results: JH had a total phenolic content of ٦٠٦,٤±٠,١ µg gallic acid equivalent/mg, while CH had a value of ١١٢,١±٠,٠٩ µg gallic acid equivalent/mg. The total antioxidant capacity of the two samples was compared. It was ٢٠٣,٥±١٠,٥µM/l in JH and ٤,٦±١٠,٥ µM/l in CH. In addition, JH had a diastatic activity of ٥٢٤,١±٠,٢٥ U/l, while CH had a value of ٢٠٩,٧±٠,٥٦ U/l. According to the results, JH had a high PAD value, while CH had a low PAD value. Cell viability was measured using the results of the MTT assay. The results showed that JH inhibited the growth of MCF-V cells more strongly (IC٥٠ of ١٧٠±٤,٢ µg/ml) than CH (IC٥٠ of ٣٨٥,٣±٤,٥ µg/l). The scratch assay showed that treatment with JH decreased the migration rate of MCF-V cells in a dose-dependent manner compared to the CH and control groups. In addition, the results of q-PCR analysis showed significant upregulation of Bax, p٥٣ and p٢١ genes and downregulation of Bcl-٢ gene in the JH-treated group compared to the CH and control groups.

Conclusion: These results showed that honey with an increased content of phenolic compounds, antioxidant capacity, and diastatic activity has anticancer properties by effectively suppressing tumor development. This suppression occurs via several mechanisms, including suppression of proliferation and metastasis, and promotion of apoptosis.

Keywords: Ziziphus jujube honey · PAD score · MCF-V cells · Migration · Apoptosis

Ralstonia pickettii bloodstream infection in the patient with Guillain-Barre syndrome under plasmapheresis (Research Paper)

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Introduction: Ralstonia pickettii is a rare Gram-negative opportunistic bacterium that causes rare infections such as bacteremia, neonatal sepsis, endocarditis, and meningitis in hospitalized or immunocompromised patients.

Methods: In this study, we identified and reported bloodstream infection caused by R. pickettii in a ١٥ -year-old boy patient with an autoimmune disease, Guillain-Barr´e syndrome, under plasmapheresis and intravenous immune globulin (IVIG) therapy. He was referred for admission to the neurology center of the teaching hospital of Shiraz, Iran for inability to walk, and lower extremity muscle weakness.

Results: After he was treated with plasmapheresis once during hospitalization, and after severe fever besides shivering blood cultures using BACT/ALERT®٣D instrument were positive for R. pickettii. According to antibiotic susceptibility test reports, Ciprofloxacin (٥ µg) was prescribed. Fortunately, after starting antibiotic treatment, blood culture results reported no growth after ٥ days. Indeed, the patient was infected with nosocomial hepatitis A and URSOBIL (٣٠٠ mg/BID/Po) was administered. Hence, after reporting the infection occurrence to the hospital infection control unit, initial and possible measures such as device infection control, replacement of potentially polluted plasmapheresis fluids, disinfecting the environment and replacing old sterile washing water with new sources were carried out in plasmapheresis unit.

Conclusion: In conclusion, R. pickettii is a rare nosocomial infection that is responsible for the contamination of medical equipment, especially in hemodialysis, plasmapheresis devices and sterile solutions. Also, it is suggested that the role and importance of rare environmental bacteria as the causative agents of human infections should not be ignored in medical centers.

Keywords: Nosocomial infection Ralstonia picketti Guillain-barre syndrome Bacteremia

Rapid and Accurate Detection of Brucellosis: A Comparative Study of Molecular Techniques

(Review)

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Introduction: Brucellosis, a zoonotic infection triggered by Brucella bacteria, is a significant zoonotic illness that poses a substantial global public health challenge, affecting millions of lives yearly. This illness is primarily transmitted through close contact with diseased animals or the consumption of tainted animal products. It is highly prevalent in regions with extensive livestock farming, such as the Middle East and Iran. The disease affects over half a million people annually worldwide, leading to significant morbidity. In the Middle East and Iran, the incidence is exceptionally high due to consuming unpasteurized dairy products and close human-animal interactions. Brucellosis presents various symptoms, including fever, malaise, and severe complications like neuro brucellosis, which can lead to chronic meningitis and other neurological issues. The socio-economic burden of brucellosis is substantial, affecting livestock productivity and human health. Hence, the urgency of timely detection and efficient treatment to avert long-term complications and curb the disease's spread cannot be overstated . This study not only evaluates and compares three advanced molecular diagnostic techniques—droplet digital PCR (ddPCR), one-tube nested PCR (OTN-PCR), and loop-mediated isothermal amplification PCR (LAMP-PCR)—for the detection of human brucellosis but also presents a promising future for the field of brucellosis detection.

Methods: Droplet Digital PCR (ddPCR) is an advanced molecular technique used to quantify DNA or RNA with high precision. The process starts by partitioning a sample into thousands of tiny droplets, each acting as an individual PCR reaction chamber. The target DNA or RNA is amplified within these droplets using standard PCR reagents. After amplification, the droplets are passed through a detector that counts the number of positive (fluorescent) and negative droplets. Compared to conventional PCR (RT-qPCR), which offers relative quantification based on fluorescence during amplification cycles, ddPCR provides higher precision and accuracy by eliminating the need for standard curves. It also boasts greater sensitivity, can detect low-abundance targets, and is less affected by sample inhibitors, resulting in more consistent results. While ddPCR is more expensive and time-consuming due to specialized equipment and additional processing steps, its significant advantages make it ideal for applications requiring precise and sensitive nucleic acid quantification. One-Tube Nested Quantitative Real-Time PCR (qPCR) is an advanced molecular diagnostic technique designed to enhance the sensitivity and specificity of DNA detection compared to conventional PCR. This method integrates a nested PCR approach within a single tube, utilizing two sets of primers and two probes that amplify target DNA sequences sequentially. One-tube nested qPCR minimizes handling, unlike standard PCR, which can be less sensitive and prone to contamination. It reduces contamination risks by maintaining a closed-tube system throughout the process. This method significantly improves detection rates, especially for low-abundance DNA targets, with sensitivity

and specificity reaching ۹۸,۶٪ and ۱۰۰٪, respectively. This advancement in molecular diagnostics minimizes the likelihood of false negatives, thereby improving the reliability and precision of clinical diagnostics.

Results: LAMP (Loop-mediated Isothermal Amplification) is an innovative nucleic acid amplification technique that operates at a constant temperature of ۶۳°C, eliminating the need for a thermal cycler required in conventional PCR. Unlike PCR, which requires multiple temperature cycles, LAMP uses four to six primers to recognize distinct regions of the target DNA, enabling continuous amplification through a strand-displacement reaction. The primary advantages of LAMP include high sensitivity, rapid results, often within ۳۵ minutes, and the capability to detect low levels of DNA. Additionally, it allows for visual result inspection, making it ideal for low-resource settings. However, it can be prone to non-specific amplification if not carefully optimized, and the primer design process is complex. Despite these drawbacks, LAMP's efficiency and simplicity make it a powerful tool for diagnostic applications, especially in environments lacking sophisticated laboratory infrastructure.

Conclusion: In conclusion, this study's findings highlight the advantages and limitations of each method. With its high sensitivity, rapid results, and operational simplicity, LAMP-PCR is the most suitable method for detecting human brucellosis quickly and precisely. Its potential in low-resource settings underscores its practicality and instills hope for improved healthcare in these areas, reassuring the audience.

Keywords: Brucellosis, Droplet Digital PCR , One-Tube Nested Quantitative Real-Time PCR, LAMP, Zoonotic

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Rapid Diagnosis of Bacterial Infections: A Comprehensive Evaluation of Point-of-Care Tests

(Review)

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Introduction: Bacterial infections are still one of the most important causes of death worldwide, and therefore the presence of timely and accurate diagnostic techniques helps in the effective management of this crisis. Laboratory-based diagnostic techniques are accurate but time-consuming, often requiring several days for a final diagnosis. This delay in diagnosis causes more harm to the patient, makes treatment more difficult and increases health costs. One hope for rapid and accurate diagnosis is point-of-care (POC) tests that facilitate immediate clinical decision-making. This manuscript provides a comprehensive review of various POC tests designed for the rapid and accurate diagnosis of bacterial infections. Also, the sensitivity, specificity, ease of use and clinical applications of these tools are examined.

Methods: This study systematically reviews the available literature on the types of POC for the diagnosis of bacterial infections. According to the technology used, POC can be classified into tools based on molecular assays, immunoassays, and biosensors. We evaluated the advantage and diagnostic process of these POCs compared to traditional laboratory methods. Also, the clinical applications of these tools in the diagnosis of respiratory, urinary and blood infections were evaluated.

Results: According to a meta-analysis of published data from previous studies, we evaluated the sensitivity and specificity of POC tests and showed that many of them have acceptable accuracy compared to common laboratory diagnostic methods. For example, POC based on molecular techniques has high sensitivity and specificity in detecting bacteria as well as resistance genes. While POC allows the detection of many microbial antigens based on immunoassay. However, there are still challenges associated with the clinical application of POC, such as healthcare personnel training and cost-effectiveness, which were investigated in this study. In addition, attention to regulatory considerations and the need for standardization in POC performance were discussed in order to provide a road map for smoothing the path of clinical application of these tools.

Conclusion: In conclusion, this manuscript emphasizes the ability of POC diagnostic tools to achieve rapid diagnosis and optimal treatment selection in bacterial infections. Despite all the advantages of POCs such as speed, accuracy, sensitivity and high specificity in diagnosis, there are still many challenges in application. There is a construction of this tool next to the bed. Attention and elimination of limitations, responding to knowledge chats, use of new technologies, are all key points in the application of POCs, which ultimately lead to improved management of bacterial infections and help in the successful treatment of patients.

Keywords: point-of-care (POC) tests, Bacterial infection, Antibiotic resistant

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Rapid tests for antimicrobial resistant detection (Review)

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Introduction: The increase of antibiotic-resistant strains in bacterial pathogens is one of the important causes of death in infectious diseases. Therefore, focusing on studies related to antibiotic resistance has become a priority of the World Health Organization (WHO), which includes finding ways to quickly detect resistance and ways to deal with it. Rapid diagnosis of antibiotic resistance is very useful for choosing the right and best antibiotic for effective disease management. Conventional laboratory methods for determining antibiotic resistance are often culture-based and require several days to provide results. Therefore, in order to manage the consumption of antibiotics and optimize the treatment process, various rapid tests have been developed to facilitate the immediate identification of antibiotic resistance in bacterial pathogens.

Methods: This manuscript provides a comprehensive review of current methods of rapid tests for the detection of antibiotic resistance, focusing on methodology, accuracy, sensitivity, and clinical utility. We classified the methods for the rapid detection of antibiotic resistance into three main groups based on the method used: molecular methods, immunological assays and phenotypic tests. In molecular methods, different techniques are used, starting from polymerase chain reaction (PCR) and reaching next generation sequencing (NGS) in the most advanced state. In molecular methods, there is sensitivity and specificity of the test in identifying resistance genes directly from patient samples. Immunological assays, such as enzyme-linked immunosorbent assays (ELISA), use specific antibodies to detect markers of resistance in the target pathogen. Therefore, by targeting the resistance marker, it is possible to quickly diagnose and accurately report it on the clinical sample. Although some technologies are designed based on the same phenotypic tests, they allow rapid response. Phenotypic methods such as broth microdilution, together with rapid formats such as lateral flow, have made it possible to test the results of bacterial susceptibility to a variety of antibiotics in the shortest possible time.

Results: We performed a systematic review of available research results and analyzed the diagnostic performance of rapid antibiotic susceptibility tests and noted their advantages and limitations. Meta-analyses have shown that tests based on molecular techniques are highly accurate, but require sophisticated laboratory instruments and trained personnel. Conversely, immunological and phenotypic tests are easier but more sensitive compared to molecular tests. Also, we discussed the challenges of applying rapid antibiotic susceptibility tests at the bedside and the measures required for monitoring, standardization and integration with current common methods. Finally, the importance of rapid detection of antimicrobial resistance has been raised not only from the point of view of management of infectious diseases, but also in controlling the increase of antibiotic-resistant strains along with presenting case studies. In this way, quick methods of determining sensitivity to antibiotics increase the success of patient treatment, reduce treatment costs and better control infection in medical centers.

Conclusion: In conclusion, this manuscript emphasizes the urgent need for rapid and reliable tests to detect antibiotic resistance in the face of a public health crisis. We have performed a comprehensive review of rapid methods for determining antibiotic susceptibility and compared their advantages and limitations with conventional methods. In this way, rapid methods to determine resistance to antibiotics have been very valuable in the management of bacterial infections and have created new hope to control the spread of drug-resistant strains. Focusing on research to address the limitations and gaps in knowledge is a necessary step to apply rapid methods of drug sensitivity determination in the clinic and benefit from its benefits.

Keywords: Antibiotic-resistant, rapid test, infectious disease

Recent advances in bioplasma for topical pharmacy products (Review)

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Introduction: Bioplasma has become a groundbreaking technology in the development of topical products, significantly improving their effectiveness and quality. Initially used in the 1960s for its disinfectant and healing properties, bioplasma has since evolved into a vital component in skincare formulations. This study explores the recent advancements in bioplasma-based topical products, including wound dressings, anti-aging creams, rejuvenating serums, and anti-inflammatory gels.

Methods: The study involved a comprehensive review of the latest literature and industry reports on bioplasma technology and its applications in topical formulations. Key products were identified and analyzed based on their active ingredients, mechanisms of action, and reported clinical benefits.

Results: Findings indicate that bioplasma has significantly enhanced the effectiveness of various topical products. Smart wound dressings with bioplasma-activated zinc oxide nanoparticles showed accelerated wound healing and strong antibacterial properties. Anti-aging creams containing bioplasma peptides and hyaluronic acid improved skin firmness and reduced wrinkles. Bioplasma-based serums with fibroblast growth factor (FGF) enhanced skin repair and elasticity, while anti-inflammatory gels with bioplasma-activated plant extracts effectively reduced skin inflammation and redness.

Conclusion: Bioplasma represents a transformative approach in the formulation of topical products, offering enhanced absorption, faster tissue repair, and reduced inflammation. As bioplasma technology continues to advance, its application in skincare is expected to grow, leading to the development of even more effective products.

Keywords: Bioplasma, Topical Products, Wound Healing, Anti-Aging, Skin Rejuvenation

Recent advances in cancer immunotherapy: Modulation of tumor microenvironment by Toll-like receptor ligands (Review)

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Introduction: Immunotherapy is considered a promising approach for cancer treatment. An important strategy for cancer immunotherapy is the use of cancer vaccines, which have been widely used for cancer treatment. Despite the great potential of cancer vaccines for cancer treatment, their therapeutic effects in clinical settings have been limited. The main reason behind the lack of significant therapeutic outcomes for cancer vaccines is believed to be the immunosuppressive tumor microenvironment (TME). The TME counteracts the therapeutic effects of immunotherapy and provides a favorable environment for tumor growth and progression. Therefore, overcoming the immunosuppressive TME can potentially augment the therapeutic effects of cancer immunotherapy in general and therapeutic cancer vaccines in particular. Among the strategies developed for overcoming immunosuppression in TME, the use of toll-like receptor (TLR) agonists has been suggested as a promising approach to reverse immunosuppression.

Methods: In this paper, we will review the application of the four most widely studied TLR agonists including agonists of TLR٣, ٤, ٧, and ٩ in cancer immunotherapy.

Results: TLR agonists reverse the immunosuppressive TME and potentially augment the therapeutic effects of cancer therapies in particular cancer vaccines in clinical settings. Several clinical studies provide proof of principle that the TLR٣, ٤, ٧, and ٩ agonists can improve the clinical outcome of cancer patients.

Conclusion: Several preclinical and clinical findings provide proof of principles for how immunotherapy with TLRs agonists, improves the clinical outcome of cancer patients. Given the significant impact of TME on the therapeutic effects of cancer treatments, modulation of TME by TLR ligands seems to be the main mechanism by which these immunomodulators induce anticancer effects and enhance the therapeutic effects of other cancer treatments in particular cancer vaccines. The development of cancer vaccines is considered to be a promising approach for cancer treatment due to its specificity and long-lasting effects. Despite promising results in preclinical studies, the effectiveness of cancer vaccines in the induction of effective anti-cancer immune responses and the therapeutic outcome of this method remains poor in many clinical trials. Over the last two decades, many studies have found that the main reason behind the poor therapeutic efficacy of cancer vaccines is related to immunosuppressive TME, which inhibits the infiltration and function of anti-cancer immune cells. Therefore, reversal of immunosuppression in TME is suggested to be the main strategy for increasing the therapeutic efficacy of cancer vaccines. One of the effective methods to modulate immunosuppression in TME is the use of TLR agonists, which have a successful track

record of use as adjuvants in cancer immunotherapy. Based on the findings presented in this paper, TLR٣, ٤, ٧, and ٩ agonists, reverse the immunosuppression in TME by activating different types of immune cells, thereby positively influencing the therapeutic efficacy of cancer vaccines and other conventional cancer therapies. Altogether, these findings show that TLR ligands can be beneficial in the treatment of cancer.

Keywords: Immunotherapy, Cancer, TLRs, Tumor Microenvironment, Vaccine

Recent Advances in Drug-Antibody Conjugates: Innovations and Clinical Implications (Review)

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Introduction: For better targeting and the process of cytotoxic collectives at the tumor site, the concept of Drug Antibody Conjugates or DACs was introduced as the core of Targeted Cancer Therapy. This approach is meant to improve the treatment efficacy as well as to reduce the toxicity at the system level, which are the main drawbacks of the traditional chemotherapy. The development that has occurred in this area in the recent past has enhanced the development of this technology and it has been applied in other areas than oncology including autoimmune diseases and infective diseases. This study tries to cover the advancements in DACs in the past two years and these are the new techniques in DACs, new targeting strategy, and data on the efficacy and safety of DACs.

Methods: The articles were searched from PubMed, Scopus, and Web of Science databases according to systematic criteria. From the articles, some of the keywords that were used in the search included drug-antibody conjugates, targeted therapy, linker technology, payload optimization, and clinical trial. The articles were also searched based on the time published starting from the last five years in order to capture the most current and potent literature. Furthermore, to give an overview of the recent advances in the field, references from the selected articles were checked to find related studies that have been made. In order to achieve the objective of the present paper, a review of the literature published in the last decade was performed with emphasis on peer-reviewed journal articles clinical trials, and new advancements in the field of DAC development. These include the linker technology and payload optimization, target identification and selection, clinical relevance, and risk assessment.

Results: There have been new linker technologies deployed in other researches recently that increases the sturdiness and the discharge of poisonous substances within the preferred cell. For instance, cleavable linkers that are sensitive to conditions in the tumour micro-environment that are characteristic of tumors have been found to release the drugs with greater efficiency. Furthermore, improvement in the carriers and payloads such as novel chemotherapeutic agents and immunomodulatory agents have enhanced the therapeutic ratio of the drug delivery system and minimized the toxicity. A number of DACs are at different stages of their clinical cycles and a few of them have been authorised by the regulatory authorities based on the preclinical studies. For example, the drugs trastuzumab emtansine (Kadcyla) and brentuximab vedotin (Adcetris) are said to have a higher prognosis with HER۲-positive breast cancer relapse and Hodgkin's disease, respectively. More so, new-generation DACs are being tested in multiple types of cancer, proving the modality's adaptability. Moreover, bispecific antibodies and the increase in targeting strategies have been the main focus in the selectivity and efficiency of DACs. They not only attain the required therapeutic index improvements but they also uncover the possibilities of combined therapies thus enhancing the general efficiency of the treatment.

Conclusion: Advancements made in the field of drug-antibody conjugates define the horizon of targeted cancer therapy and more. Prodrugs, linker technologies, payloads and targeting strategies have had progress over the years which has enhanced the efficacy and safety of such therapies and have therefore been accorded beneficial clinical results. Further development of the field of research, DACs provide new innovative therapeutic approaches for oncological and other diseases. Further progression in biomarker discovery along with ongoing clinical research efforts to more accurately define the patient population for DAC treatment will only add to the future efficacy of DAC therapies. Drug-antibody conjugates are envisioned for the future, which leads to enhancing and specifying the effectiveness of anticancer and other agent

Keywords: drug-antibody conjugates, targeted therapy, linker technology, payload optimization,clinical trial

Recent advances in stem cell therapy: molecular mechanisms and potential (Review)

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2.

Introduction: In recent years, the use of stem cells has been proposed as a new and promising method in cancer treatment. Stem cells, especially cancer stem cells (CSCs), play an important role in the development and spread of cancers due to their ability to induce tumorigenesis and metastasis. Research has shown that CSCs can play a key role in drug resistance, metastasis and recurrence of cancers. CSCs are derived from natural stem cells or cell progenitors and have the ability of self-renewal and unlimited proliferation, which makes them one of the important targets in cancer treatment. These cells are of interest in medical research due to their high potency, but ethical issues related to the use of these cells prevent their widespread use in clinical treatment. These cells have the ability to transform into different types of cells, and for this reason, they are of great importance in the field of advanced research. However, due to ethical concerns and legal restrictions in many countries, the use of these cells in clinical treatments still faces several challenges. Adult stem cells (ASCs) are also used in cancer treatment. In particular, hematopoietic stem cells (HSCs) and mesenchymal stem cells (MSCs), play an important role in existing therapies. HSCs can produce all of the body's blood cells and are currently the only type of stem cell approved for use in clinical therapy. These cells are especially used in the treatment of blood cancers such as leukemia and lymphoma, helping patients to generate new blood cells after chemotherapy or radiation therapy.

Methods: MSCs have also been considered in clinical treatments due to their ability to regenerate tissues. In addition to the ability to differentiate into different types of body tissue cells, these cells can migrate to the damaged or tumor site and play a supportive role there. For this reason, they are known as new therapeutic agents to deal with hard-to-treat cancers. Cancer stem cells (CSCs) as a subset of tumor cells that have the ability to self-renew, play a role in tumor growth and spread. These cells are the main target of new research in the field of oncology, especially because of their high resistance to chemotherapy drugs.

Results: For example, while traditional treatments usually target normal cancer cells, CSCs persist by resisting these treatments and cause cancer recurrence. Therefore, identifying and destroying these cells can be the key to success in new treatments. One of the main challenges in cancer treatment with stem cells is the precise identification and targeting of CSCs. Research has shown that specific biomarkers such as CD١٣٣ and CD٤٤ can help identify these cells. These markers are commonly expressed on the surface of cancer cells and can be used as targets for targeted therapies. By using these markers, doctors will be able to attack cancer cells more precisely and reduce the possibility of cancer recurrence. Also, molecular signaling pathways such as Wnt/β-catenin, Notch and Hedgehog play an important role in regulating the growth and survival of CSCs. These pathways have been explored as new therapeutic targets, and blocking them can lead to halting tumor growth. Specifically, blocking the signaling pathways of these cells can reduce their ability to proliferate and

metastasize. In addition, mesenchymal stem cells (MSCs) are considered as one of the therapeutic tools in new research due to their ability to migrate to tumors and differentiate into cancer cells. These cells can act as carriers of antitumor agents and prevent tumor growth and metastasis. MSCs are able to migrate to the tumor site and help control cancer growth by secreting anti-inflammatory and antitumor factors.

Conclusion: Finally, although the use of stem cells in cancer treatment is promising, there are several challenges, including ethical problems, side effects, and the need for further research. In addition, there is still a long way to widespread use of these methods in treatment clinics, and researchers are still looking to improve treatment methods and reduce the side effects of these treatments. Hence, the development of new methods to identify, isolate, and target CSCs and improve stem cell-based therapies will continue to be one of the hot topics of scientific research in the coming years.

Keywords: Cancer stem cell, Molecular markers, Tumor, Signaling Pathway

Recent Advances in the Use of Exosomes for Cancer Diagnosis and Treatment: From Research to Clinical Trials (Review)

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Introduction: Exosomes are tiny extracellular vesicles released by nearly all living cells when multivesicular bodies fuse with the plasma membrane, allowing them to enter surrounding bodily fluids.

Methods: This review begins with a detailed overview of exosomes, including their discovery, isolation, characterization, functions, biogenesis, and secretion. It then discusses the potential of exosomes as effective carriers for drug and gene delivery, the use of exosome inhibitors in cancer treatment, and the ongoing clinical trials examining the biological significance of exosomes.

Results: These exosomes can carry cell-specific materials from the originating cell to a target cell. Due to their significant potential as non-invasive diagnostic biomarkers and therapeutic delivery vehicles, recent research has highlighted the crucial roles exosomes play in prognosis, diagnosis, and treatment approaches. Although various reviews have compiled information on the biomedical uses of exosomes, there is a need for a thorough review that includes updated and enhanced methodologies for their beneficial applications in cancer theranostics.

Conclusion: As research in this area expands, gaining a deeper understanding of the subcellular components and mechanisms involved in exosome secretion and their targeting of specific cells will clarify their precise physiological roles in the body.

Keywords: Exosomes, Cancer, Diagnosis, Treatment, Theranostics

Recent highlights in bacterial extracellular vesicles: From immune host response to vaccine development (Review)

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Introduction: Extracellular vesicles (EVs) are double-layer spherical structures which are released by both mammal cells and bacteria. According to their size, they are divided into different groups including exosomes, macrovesicles, and apoptotic bodies [١, ٢]. It is believed that bacterial extracellular vesicles (BEVs) are a form of common language for bacteria-host communications. They are produced by both gram-positive and also gram-negative bacteria. These structures regulate bacteria-host and bacteria-bacteria interactions, which lead to promoting health or causing disease by delivering virulence factors [٣]. Studies have reported EVs fundamental roles in metabolisms, homeostasis, and immune system regulation [٤, ٥]. As EVs are different in size, origin and content, they can impact the infection and immune system outcomes such as delivering virulence factors, inflammation, cell death, cell survival, pathogen entry, and survival in the host cells [٣]. It was shown that BEVs can be used as an acellular vaccine, because they contain immunogenic antigens which are safer than live pathogenic bacteria and can stimulate immune response in the host [٦].

Methods: In this study, articles from Web of Sciences and Scopus databases were searched with bacterial extracellular vesicles (BEVs), immune system, and vaccine keywords. Duplicate articles were removed, and finally ٢٢٤ English language articles were selected and reviewed.

Results: Vaccines, as a great revolution in the medical world to help human health, still have many undiscovered venues where the research continues to develop and optimize the effectiveness of vaccines with different platforms with particular therapeutic goals [٧]. Vaccines are great choice to in the management of infectious disease, although there are not any approved vaccines for a number of infectious disease or illness [٨]. BEVs of gram-positive and negative bacteria have lipids, nucleic acids, proteins carbohydrates and other component of bacterial structures. Therefore, it was shown that BEVs can be used as an acellular vaccine, because they contain immunogenic antigens which are safer than live pathogenic bacteria and can stimulate immune response in the host [٦]. BEVs enable stimulation and modulation of the innate and adaptive immune system at a suitable

and long-term level without pathogenicity as the main golden goal in vaccine design. They have the ability to transport and store bacterial component including proteins, lipids, DNA, and RNA. They can also evade from degradation mechanisms of the host. However, they have some limitations such as BEVs and bacteriotoxin aggregation in the hosts, high cost of isolation, low level of bacterial component expression, and interaction with immune-suppressive molecules of the immune system [٩]. The first OMV-vaccines were produced based on Good Manufacturing Practice (GMP) rules for Neisseria meningitidis serogroup B (dOMVB) via detergent extraction method that exerts a promising performance to delivery of meningococcal antigens and providing protective immune responses. In later years, OMV isolated from N. meningitidis, serogroup A (dOMVA), X (dOMVX), and W (dOMVW), were developed in a similar manner [٦]. Candidate vaccines based on BEVs are also in preclinical development against bacterial species including Bordetella pertussis, M. tuberculosis, S. Typhimurium, Vibrio cholerae, and Klebsiella pneumoniae. These vaccines have been demonstrated to effectively stimulate both humoral and cellular immunity [١٠].

Conclusion: BEVs are potential to design vaccine, but more studies are needed to understand different mechanisms of their entry into the host cells, and pathogenicity, especially in gram-positive bacteria.

Keywords: BEVs, immune response, isolation methods, vaccine, virulence factors.

Recent In-Vivo Breakthroughs in Micro/Nanorobot Technology for Biomedical Applications

(Review)

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Introduction: Recent advancements in micro/nanorobots for biomedical applications have gained significant momentum due to their potential to revolutionize targeted therapies. These cell-sized machines offer unmatched precision, enabling them to navigate through hard-to-reach biological environments. Over the past decade, there have been considerable advancements in the development of functional and biocompatible micro/nanorobots. Innovations have enhanced navigation control, cue responsiveness, and drug payload efficiency. However, challenges remain, particularly regarding minimizing toxicity and optimizing movement through complex environments.

Methods: This review focuses on preclinical studies conducted using animal models to assess the real-world applications of micro/nanorobots. We performed a comprehensive literature search using the PubMed database, focusing on original research articles published between ٢٠١٤ and ٢٠٢٤. Keywords such as “microrobots,” “nanorobots,” “targeted therapy,” and “in-vivo” were employed to identify relevant studies.

Results: Significant advancements have been made in the design, administration, actuation, and monitoring of micro/nanorobots across various organs and diseases, particularly in cancer models. These devices have evolved to perform increasingly complex tasks beyond drug delivery. Efforts to utilize biocompatible materials in micro/nanorobots, in compliance with ISO١٠٩٩٣-١ standards, aim to develop large-scale fabrication techniques. Notable studies demonstrated successful in-vivo applications of micro/nanorobots, including targeted drug delivery of cisplatin for colorectal cancer, minimally invasive intraocular surgery and safe extraction of nanorobots, tissue sample collection of bile duct, Mesenchymal stem cell delivery to liver cancer tumor site and ROS scavenging in rheumatoid arthritis among others. Furthermore, modern imaging approaches were proposed to monitor these devices in real-time, including the use of chemical contrast agents (barium- and iodine-based), photoacoustic imaging (PAI), photoacoustic computed tomography (PACT), and ultrasound, among others.

Conclusion: Advancements in micro/nanorobots can be classified into three main areas: actuation methods, design & fabrication, and imaging modalities. Together, these advancements form novel platforms that are transforming not only drug delivery but also non-invasive microsurgeries and sample collection techniques. Unlike conventional targeted drug delivery, micro/nanorobots can be programmed to be autonomous (chemical and biohybrid actuation methods) or semi-autonomous (acoustic, magnetic, and light-based actuation). These propulsion methods enable deep tissue penetration, previously inaccessible. Among these, magnetic micro/nanorobots are currently the

most prevalent due to their ease of navigation and imaging, alongside the absence of toxic byproducts from chemical methods. Despite their advantages, each actuation method presents unique pros and cons depending on the specific disease and organ targeted. Regardless of the approach, the use of non-toxic and biocompatible materials is essential, as clinical trials are on the horizon. In addition to precise targeting through receptor-ligand interactions, nanorobots benefit from features such as special coatings and integrated sensors. The integration of drug delivery, imaging, and biosensing capabilities further enhances their functionality. Combined imaging approaches, such as PAI with high-frequency ultrasound or positron emission tomography (PET) with computed tomography (CT), were shown to improve tracking and monitoring, distinguishing between endogenous signals from motile microrobots. Despite the substantial progress, many challenges remain, such as optimizing biocompatibility, navigation in complex biological environments, and scalability for clinical applications. Addressing these hurdles is critical for translating micro/nanorobots from preclinical success to widespread medical use, potentially redefining the future of minimally invasive therapies and precision medicine.

Keywords: Microrobot , Nanorobot , targeted therapy , Real-time imaging

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Reduction In Inflammation and Fibrosis Endpoints in HIV Patients Using Losartan (Research Paper)

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Introduction: There is a high morbidity and mortality rate associated with chronic inflammation and fibrosis in HIV patients. Angiotensin II receptor blockers, such as losartan, are tested on HIV-infected individuals to determine whether they reduce inflammation and fibrosis.

Methods: One hundred HIV-positive patients on stable antiretroviral therapy were included in a randomized, double-blind, placebo-controlled trial. In a ١٢-month study, participants received losartan (٥٠ mg/day) or a placebo. In order to evaluate the feasibility of this study, the primary endpoints included changes in inflammatory markers (C-reactive protein [CRP] and interleukin-٦ [IL-٦]) and fibrosis markers (transforming growth factor-beta [TGF-β] and liver stiffness measured by transient elastography). Blood samples and liver stiffness measurements were taken at baseline, ٦ months, and ١٢ months. Statistical analysis included paired t-tests and repeated measures ANOVA to compare within-group and between-group differences.

Results: Of the ١٠٠ participants, ٩٠ completed the study (losartan group, n=٤٥; placebo group, n=٤٥). The losartan group showed a significant reduction in CRP levels (mean decrease ١,٢ ± ٠,٤ mg/L) compared to the placebo group (mean decrease ٠,٤ ± ٠,٢ mg/L, $p < ٠,٠١$). IL-٦ levels also decreased significantly in the losartan group (mean decrease ١,٥ ± ٠,٥ pg/mL) versus the placebo group (mean decrease ٠,٦ ± ٠,٣ pg/mL, $p < ٠,٠١$). TGF-β levels were significantly reduced in the losartan group (mean decrease ٢,٠ ± ٠,٦ ng/mL) compared to the placebo group (mean decrease ٠,٨ ± ٠,٤ ng/mL, $p < ٠,٠٠١$). Liver stiffness showed higher reduction in the losartan group (mean reduction ٢,٥ ± ٠,٧ kPa) versus the placebo group (mean reduction ١,٠ ± ٠,٥ kPa, $p < ٠,٠١$).

Conclusion: As a result of losartan treatment, HIV patients experience a significant decrease in inflammation and fibrosis markers. As a result of these results, losartan could be used as an adjunctive therapy to treat chronic complications associated with HIV infection.

Keywords: Losartan, HIV, Inflammation, Fibrosis, Clinical Trial

Regulation of aerobic glycolysis by microRNAs in gastric cancer (Review)

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Introduction: One major hallmark of gastric cancer (GC) cells is rapid growth and uncontrolled proliferation, which requires high energy. Consequently, GC cells must alter their metabolic process from oxidative phosphorylation to aerobic glycolysis to satisfy the energy, needed for rapid proliferation (١). This phenomenon of changes in tumor cellular metabolism is known as “metabolic reprogramming”, mediated by higher glucose uptake, enhanced expression of glycolysis-related enzymes such as HK-II, PKM٢, and conversion of pyruvate to lactic acid (٢). Emerging evidence reports that miRNAs, as a class of non-coding RNAs can target and bind to the ٣′-untranslated region (UTR) located on mRNA of enzymes involved in metabolic processes and glucose transporters and inhibit their expression. Therefore, microRNAs can act as important regulators of metabolic reprogramming in GC cells and suppress their growth, invasion, and metastasis (٣). Based on these characteristics, in the present study, we reviewed the role of some miRNAs in regulation of GC cell's metabolic reprogramming.

Methods: In the present study, we did a comprehensive literature review of the results of related articles published between ٢٠٢٢ and ٢٠٢٣ from PubMed and Google Scholar databases with keywords such as “gastric cancer”, “glycolysis”, “metabolic reprogramming” AND “microRNA” queries.

Results: In the present study, we summarized some microRNAs' role in regulating the glycolytic metabolism of GC. We observed that these microRNAs can directly or indirectly target the expression of glycolytic genes. For example, MicroRNA-١٨١b (٤), MiR-٥٦٨٣ (٥), miR-٤٤٩c (٦), MiR-let-٧a (٧), and miR-١٤٨b (٨) downregulate the expression hexokinase II, pyruvate dehydrogenase kinase ٤, PFKFB٣, PKM٢ and SLC٢A١ in GC, respectively. Subsequently, downregulation of these glycolytic metabolism-related enzyme expressions, can reduce glucose uptake and consumption, lactate production, and cellular ATP levels and lead to proliferation and growth suppression in GC cells. Therefore, miRNAs have a key duty as important regulators of glucose metabolism.

Conclusion: Understanding the function of microRNAs in reprogramming the glycolytic metabolism pathway in GC provides novel insights into the potential therapeutic strategies in GC patients.

Keywords: MicroRNAs, Metabolic reprogramming, Glycolysis, Gastric cancer

Regulatory effects of matrine on antitumor activity of dendritic cells in the tumor microenvironment (Review)

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Introduction: Cancer, which results from the uncontrolled proliferation of cells, is one of the most serious diseases threatening human health. Matrine, an alkaloid isolated from the traditional Chinese medicine Sophora flavescens, has been the subject of numerous studies demonstrating its anticancer activity. It can inhibit cancer cell proliferation, arrest the cell cycle, induce apoptosis, and inhibit cancer cell metastasis. It has also been shown to have an effect on immune cells, including dendritic cells.

Methods: A comprehensive search was conducted using databases such as PubMed, Google Scholar, Medline, Scopus, and Web of Science to identify studies investigating the effect of matrine on the antitumor function of dendritic cells. The search strategy used a combination of keywords, including "matrine", "dendritic cell", "cancer", and "tumor microenvironment (TME) ". A review of the selected studies was performed in order to gain insight into the underlying mechanisms.

Results: Dendritic cells (DCs) are considered to be the most potent antigen presenting cells (APCs). They play a pivotal role in the initiation and regulation of the adaptive immune response, acting as an important link between the innate and adaptive immunity. Anti-cancer immune responses involving T cells are dependent on antigen presentation by DCs. Immature DCs recognize signals that stimulate their maturation, including those indicative of damage or pathogen-associated molecular patterns (DAMPs or PAMPs), such as tumor-derived antigens, through pattern recognition receptors (PRR). These antigens are then transported to major histocompatibility complex (MHC) molecules for presentation to T lymphocytes. This interaction promotes cross-presentation, T cell trafficking to the tumor, and the induction of effector function and memory formation. Most tumors show the insufficient number of mature DCs, and their presence is associated with a favorable prognosis in murine tumor models and cancer patients. The tumor microenvironment (TME) can inhibit the development of DCs and reduce their ability to initiate the immune responses. Several factors contribute to this mechanism including the production of interleukin (IL)-١٠ by macrophages in the TME, the capture of DCs by the liver X receptor (LXR), increased indoleamine ٢, ٣-dioxigenase ١ (IDO١) leading to tryptophan depletion, and the interaction of FMS-like tyrosine kinase ٣ (FLT٣) and

vascular endothelial growth factor (VEGF), which negatively affects DC differentiation and weakens the immune systems to fight tumors. The study conducted by Wang Jing-kang et al. showed that matrine enhanced the anti-tumor activity of DCs. Matrine was observed to significantly increase the gene expression of toll-like receptor (TLR)٧, TLR٨, myeloid differentiation factor ٨٨ (MyD٨٨), tumor necrosis factor receptor-associated factor ٦ (TRAF-٦), and IκB kinase (IKK), as well as the protein levels of TLR٧ and TLR٨. Additionally, the levels of IL-١٢, IL-٦, and tumor necrosis factor-alpha (TNF-α) were reported to increase by matrine. Moreover the gene expression of MHC-II, CD٥٤, CD٨٠, and CD٨٦ in DCs were increased by matrine. Many studies showed that activated effector T cells had substantial tumor-killing activity. According to the study by N. Zhou et al., the combination of matrine and the mTOR inhibitor KU٠٠٦٣٧٩٤ has the potential to enhance DC maturation, T cell proliferation, and cytokine secretion which consequently resulted in a significant increase in the levels of interferon-gamma (IFN-γ) and TNF-α, whereas IL-١٠ levels were decreased. In another study conducted by N. Zhou et al., it was demonstrated that matrine could enhance the expression of CD٨٦ and CD٨٣ in a dose-dependent manner. Matrine was observed to promote T cell and DC activation. Furthermore, matrine was found to significantly increase the levels of interferon-γ (IFN-γ), TNF-α, and IL-١٢p٧٠.

Conclusion: Matrine, a compound derived from traditional Chinese medicine, shows significant potential in enhancing the anti-tumor function of DCs. By modulating key pathways involved in DC maturation and activation, matrine can stimulate the production of pro-inflammatory cytokines, increase antigen presentation in DCs, and promote T cell effector responses. These findings suggest that matrine with an immune-regulatory effects may be a promising therapeutic agent for cancer treatment. Further research needs for a better understanding of the mechanisms underlying the effects of matrine on the antitumor activity of DCs and other immune cells in the tumor microenvironment.

Keywords: Matrine, dendritic cell (DC), cancer, tumor microenvironment (TME)

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Relationship between dietary insulin index and postmenopausal osteoporosis among Iranian women: a case-control study. (Research Paper)

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Introduction: The association between the dietary insulin index (DII) and the risk of postmenopausal osteoporosis among Iranian women remains unclear, despite the established link between hyperinsulinemia and the development of osteoporosis. The DII is determined by the insulin response elicited by various dietary patterns. This study aimed to explore the relationship between adherence to a diet with a high insulinemic potential and the incidence of osteoporosis in postmenopausal Iranian women.

Methods: A total of ٣٨٠ postmenopausal participants were recruited for this case-control study. To assess daily caloric intake, a validated ١٦٨-item food frequency questionnaire (FFQ) was utilized. The dietary insulin load for each food item was calculated using a standard formula, and the DII was subsequently derived by dividing the dietary insulin load by the total energy intake for each participant. Logistic regression analysis was employed to examine the association between osteoporosis and DII.

Results: The findings revealed a significant inverse correlation between osteoporosis and DII, even after adjusting for potential confounding factors (OR=٠,٩٢٧; ٩٥٪ CI=٠,٨٨٨–٠,٩٦٧). The mean DII scores were significantly higher in the control group (٣٦,٨٢±٨,٩٨) compared to the case group (٣٣,٥٣±٦,٢٨) (P<٠,٠٠١).

Conclusion: These results indicate that a diet characterized by a high insulin index and low in insulinogenic foods may enhance bone mass density. Therefore, it may be crucial for postmenopausal women to include nutrients that promote insulin production in their diets to mitigate the risk of osteoporosis.

Keywords: Osteoporosis, Hyperinsulinism, Insulin resistance, Postmenopausal women

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Relationship between healthy eating index and the need for Cesarean delivery (Research Paper)

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Introduction: Unhealthy nutrition during pregnancy has many adverse effects on both the fetus and the mother. One of these adverse effects on the mother is the need for a Cesarean Section (CS) in conjunction with diet. This case-control study showed Healthy Eating Index (HEI) to predict the need for CS in [is covered for blind peer review].

Methods: A total of ۳۹۰ women, were recruited from [is covered for blind peer review]. Their mean age was ۲۸,٦ ± ۸,۲ years. Anthropometric indices were measured based on standard methods, daily physical activity was assessed by using the International Physical Activity Questionnaire (IPAQ.S). The diet quality score was derived by using a Food Frequency Questionnaire (FFQ). The HEI was used to assess diet quality. Linear Logistic Regression was used to investigate the relationship between HEI and the odds of CS.

Results: There were no significant differences in HEI with odds of cesarean section in crude model (P = ۰,۰۹۲), in the first model (P = ۰,۳۰٤), and in the final model (P = ۰,۰۱۷) after adjusting for confounders.

Conclusion: The results showed there were no significant associations between HEI with the odds of CS in the mentioned population.

Keywords: diet, healthy, healthy eating index, cesarean section, delivery, obstetric

Relevance of non-alcoholic fatty liver disease with hyperthyroidism (Review)

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is a metabolic liver disease characterized by an extensive continuum of liver pathology, ranging from simple steatosis to steatohepatitis (NASH) and fibrosis. It can ultimately lead to cirrhosis and hepatocarcinoma. NAFLD comprises a massive socioeconomic burden, as it now represents the most common cause of chronic hepatic disease worldwide. The thyroid hormone plays an important role in glucose metabolism, lipid metabolism, and insulin resistance. Emerging evidence has indicated the relationship between thyroid hormone concentration and NAFLD. Rochon et al. first reported the association between hypothyroidism and insulin resistance in ٢٠٠٣. Several other studies demonstrated that the morbidity of NAFLD has an inverse association with thyroid hormone levels in the hypothyroid or euthyroid populations.

Methods: In this cross-sectional study,١٥٥ randomly selected people were divided into two different groups, one group was people who were diagnosed positive for NAFLD and another group that was negative for NAFLD. After clinical examination and taking a blood test for both groups, the results of the examination and the blood test were obtained to find the relevance of NAFLD with hyperthyroidism. Finally after obtaining the results of the control group with the experimental group.

Results: ١. TSH levels were higher in people with NAFLD than in people without NAFLD ٢. A significant difference in the prevalence of SH (subclinical hypothyroidism) was also observed in these people compared to people without NAFLD. ٣. Also, the level of ALT, AST, and HOMA_IR was higher in people with NAFLD than in people without NAFLD. ٤. People with high degrees of obesity (severe obesity) showed SH ١,٢١, while in obese people with NAFLD, this rate increased to ٣٢,٣. ٥. On the other hand, the comparison of the studied population according to the presence of SH showed that the percentage of NAFLD was significantly higher in children with SH compared to people without SH. It examines the relationship between the prevalence of thyroid disorders in the study population without NALFD and with NALFD in a larger group of children and shows that patients with NALFD had a higher level of TSH than those without NALFD. It shows that children who have SH are more likely to suffer from NALFD than children who do not have it. Children with obesity with two disorders SH and NAFLD showed a higher percentage of BMI SDS, HOMA_IR. Also, the duration of obesity (the amount of time a person has spent with obesity during his life) was relatively higher in these people. In general, the investigation in the study population (n: ٢٢٧٥) showed: that TSH levels were inversely related to TM٦SF٢ genotypes, but: The same review and analysis (including gender, duration of obesity, TM٦SF٢ and PNPLA٣ genotypes, as well as BMI-SDS HOMA, LDL, and triglycerides) in patients with or without NAFLD showed that: The inverse and significant association of TSH with TM٦SF٢ genotypes has been confirmed only in the group with NAFLD.

Conclusion: Finally, according to the obtained data as well as the results of the statistical analysis of the data, we come to the conclusion that these two diseases are related to each other and affect each other. This result can play a significant role in the treatment and control of these two diseases in patients. Also, these results are helpful for the patients who are suffering from one of these two diseases to prevent the other disease and have a colorful role in this matter. This article also opens the way for future researches and can help to expand the research in this field.

Keywords: NAFLD _ Hyperthyroidism _ Metabolic functions

Restless leg syndrome in the elderly undergoing hemodialysis and its influencing factors, a review study (Review)

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Introduction: In recent years, the number of elderly people with chronic kidney failure requiring dialysis has increased in most countries. Research has shown that people undergoing hemodialysis may suffer from restless leg syndrome, and since these patients suffer from this syndrome more than others, the study aims to determine the condition of restless leg syndrome in the elderly undergoing hemodialysis and the factors affecting it by reviewing the studies. The past has been done.

Methods: This review study was conducted by searching the keywords of restless legs syndrome, hemodialysis and the elderly in the academic Jihad databases, Scopus, PubMed, and Google Scholar in the time frame of ۲۰۱۰-۲۰۲۰. ۸٦ articles were received, after reviewing ٥۸ articles, considering the inclusion and exclusion criteria.

Results: The findings of the reviewed research indicated that ۲۰-۸۰٪ of hemodialysis patients suffered from restless leg syndrome (RLS); The highest figure was reported for China with ٦۲ percent. Also, the findings showed that one third of the elderly under hemodialysis also suffer from RLS. The most important factors affecting this syndrome are genetic, racial factors (for example, Africa is less than Europe), biochemical factors, environmental factors, blood group type and more) and RH (more positive), the duration of dialysis treatment and the duration of dialysis in Every reference mentioned. Some of the reviewed studies stated that serum iron and ferritin levels (in hemodialysis patients with restless legs syndrome are lower than those without restless legs syndrome) and the gender of women are also effective factors; While most of the research had stated that there is no significant relationship between these two variables with the prevalence of RLS. The findings of some studies indicated that the prevalence of RLS decreases with age, and the elderly are less likely than other age groups who are undergoing hemodialysis; They suffer from this syndrome. A brief review of the articles showed that the elderly with high blood pressure and anemia were more likely to suffer from this syndrome than other elderly. The findings of the reviewed articles indicated that it is more difficult to diagnose RLS in the elderly who have been undergoing hemodialysis for a long time, and their symptoms may be confused with problems such as peripheral panneuropathy, varicose veins, and arthritis.

Conclusion: The results of the reviewed studies showed that many elderly, especially the elderly under hemodialysis, suffer from this syndrome. This syndrome is very effective in their way of life, performance, independence, cognition and survival rate. In order to improve this syndrome faster in

them, many solutions have been registered, the most important of which are aerobic exercise, walking and stretching as much as you can after dialysis, exercise as much as you can during dialysis (such as cycling), massage He pointed out the treatment, proper diet. Most of the articles showed the remarkable effect of exercise on the improvement of restless leg syndrome. It should be noted that the results of some articles indicated that sports training has no effect on this syndrome, and the reasons for this inconsistency can be pointed to the nature of the exercises, history of dialysis and age.

Keywords: Restless leg syndrome , elderly ,hemodialysis

Retinoblastoma and Challenges (Review)

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Introduction: Retinoblastoma (RB) is an intraocular tumor with hereditary and diffuse forms. The disease develops from retinal cones, which have special properties that make them sensitive to tumorigenesis. The genetic implications for more than ٩٧٪ of all RB cases are the inactivation of the RB١ gene. The original work, which explained the inheritance of retinoblastoma but also failed to explain the concept of tumor-suppressing genes, was originally published by Knudson in its original article from ١٩٧١. The two-stroke Knudson model suggested that an RB١ allele was found in all lost cells or a genetic mutation, thus initiating Tumorigenesis. More than ١٠ years after Knudson was discovered, the RB١ gene was the first tumor suppressor gene to be identified and simulated. ٨٠٠٠ new cases of this growing retinal eye malignancy are diagnosed worldwide every year. The original gene is responsible for RB١ retinoblastoma and holds a wide range of pathogenic variants. Retinoblastoma is the most common primary malignancy within the eyes in children and is found almost exclusively in young children. Most cases are diagnosed before the age of ٥ and account for ٣٪ of all childhood cancers. Previous studies showed significant differences in the incidence of retinoblastoma based on gender, ethnicity and infection due to poor hygiene. However, newer studies deny the importance of such differences, treating retinoblastoma worldwide as a similar outbreak.

Methods: We conducted an extensive search across electronic databases, including PubMed, MEDLINE, Embase, Google Scholar, and ResearchGate, and explored the available English-language literature. The MeSH terms were " Retinoblastoma " OR "RB١ "; " Genetic testing ";" ophthalmology". The articles included in this review adhere to the following criteria: they encompass studies solely focused on progress in comprehending and novel treatment approaches, and they are studies conducted in the English language within the last decades.

Results: Retinoblastoma screening involves various tests to detect the symptoms of the disease. Among its cases are leukocoria (sometimes referred to as "cat eye reflex"), which can be detected despite a white reflection in photographs or a red reflex test. A simpler approach is in detecting the use of mobile phones for the same purpose in which, such an application exists in the form of an application called "White eye Detector" developed by Brian Shaw. Screening by an ophthalmologist is essential in children with a positive family history of retinoblastoma. Children and sibling's patients with the disease require regular screening examinations in childhood unless genetic testing is performed to rule out a gene mutation in which case the risk is similar to that of the general population. The onset of each tumor requires a set of genetic deviations that regulate their basic cellular functions.

Conclusion: These genetic and epigenetic changes allow cells to escape their homeostatic controls and allow them to multiply outside their natural niche. This is mainly due to disruptions in the simultaneous regulation of various signal transmission paths such as Rb, p٥٣, Wnt, Ras-ERK. That may affect the oncogenic properties of retinoblastoma through multiple mechanisms, including obtaining stem cell-like phenotype, epithelial–mesenchymal transition (EMT) activation. From another point of view, in this article, we will examine the treatment and its treatment practices, and it should be noted that retinoblastoma is a cancer that can be treated if diagnosed at the right time. Involvement of structures beyond the retina should be considered as they have the potential to progress rapidly as metastases. Treatment of retinoblastoma is often complex and involves decisions that must be made based on a number of factors, including the size of the tumor in different axes, the age of the patient, the risk of secondary metastasis, previous attempts made in chemotherapy, the toxicity of the chemotherapy agent in the subject and the laterality of the tumor. Treatments include Enucleation, Intravitreal chemotherapy (IVitC), Intra-arterial (IAC) chemotherapy, Thermotherapy, Cryotherapy, and External beam radiation (EBR). In the Enucleation procedure, complete removal of the eye that is affected by the tumor or surgical incision is called anoclination. This is the least conservative management and is therefore reserved for items that would otherwise not be able to help. Or, for example, in the IVitC pathway, modern MicroCutter techniques can be used to prescribe chemotherapy agents, and success can be achieved with acceptable levels of toxicity. The choice of drugs included melphalan, topotecan hydrochloride, carboplatin and methotrexate in this administration pathway.

Keywords: Retinoblastoma, RB١, Genetic testing, ophthalmology

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Review and applications of Borage oil in specialized skin and hair products (Review)

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Introduction: The extract of Borage, a native plant of Iran and distributed in the northern regions from Golestan to Ardabil and Qazvin province in the slopes of the Alborz mountain range, especially in the towns of Rudsar in the Ashkorat region, Kandavan, Chalus, and Hiran heights between Ardabil and Astara. It has been widely used in Iranian pharmaceuticals for a long time. In recent years, the oil extracted from this plant has been significantly used in skin and hair products. Following the use of the oil of this plant at the international level by Vesta Pharma Company, this article has investigated the effects, mechanism of action, available components, and scope of use in skin and hair products.

Methods: This study investigated valid scientific articles indexed in PubMed, Google Scholar, Science Direct, SID, and ISI databases using Persian keywords of medicinal plants, Borage, and keywords Borage Oil, Oils in Cosmetics, and Borage Oil in Skin and Hair.

Results: In this study, the main chemical compounds of Borage plant oil include gamma-linolenic acid, linoleic acid, oleic acid, palmitic acid, stearic acid, eicosenoic acid, erucic acid, flavonoids, saponins, terpenoids, rosmarinic acid, sterols, and tocopherol. It has the properties of improving skin barrier function, increasing collagen production, increasing elasticity, reducing infection, promoting wound healing, hydrating and moisturizing, softening, Promoting the production of anti-inflammatory eicosanoids, regulating cytokine production, improving eczema and seborrheic dermatitis, reducing oxidative stress, protecting DNA by modulating oxidative genetic damage and increasing and stimulating hair growth.

Conclusion: Borage is one of Iran's native plants, which has potential and actual medicinal, biological, and pharmacological properties. It therefore has a lot of application potential in the field of cosmetics and hygiene for use in products such as (moisturizers, lotions, cleansers, emollients, softeners, masks, anti-dandruff, and hair care products) and in the field of pharmaceuticals with applications in helping to treat skin and hair diseases.

Keywords: Borage oil, medicinal plants, pharmacological effects, therapeutic properties of Borage.

Review of mRNA-based vaccine Current advancement for Breast Cancer treatment (Review)

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Introduction: Breast Cancer (BC) is a heterogeneous and prevalent disease among women. The treatment of BC is complicated owing to intratumoral complexity. mRNA-based vaccines represent a promising therapeutic strategy for cancer treatment. This review discusses mRNA-based vaccines and their current advancements in cancer treatment, especially in BC.

Methods: A comprehensive search was performed on literature by keywords of cancer vaccine, Breast Cancer, mRNA vaccine, and treatment in Scopus, PubMed, and Web of Science databases. Articles were selected based on the exclusion criteria and were included in the study after reviewing.

Results: mRNA vaccines consist of three principal reagents including mRNA antigen (which can be produced in vitro by RNA polymerase transcription from DNA template), delivery system, and adjuvants. Some of the basic mechanisms of action of mRNA therapeutics are gene expression reshaping, fixing defective molecular procedures, manipulation of cellular function, boosting immunity against cancer, etc. Different preclinical studies have been conducted based on mRNA vaccines against several breast cancer antigens including HER٢, MUC١, p٥٣, CEA or IL١٢ expressing vectors. In addition, there are ٦ and ٢ of phase I and phase II clinical trials respectively regarding breast cancer mRNA vaccines.

Conclusion: Considering the newly designed trials that are testing this novel era, its therapeutic potential has yet to be determined. However, the ability to genetic manipulation or personalized mRNA vaccines as well as their ease of production and cost-effectiveness has made them an interesting and developing therapeutic approach.

Keywords: Cancer vaccine, Breast cancer, mRNA vaccine, Treatment

Revolutionizing Gastric Cancer Care: Recent Advances and Future Prospects (Review)

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Introduction: Gastric cancer (GC) is one of the most common cancers globally, with most patients diagnosed at advanced stages due to the subtlety of early symptoms and the infrequency of regular screening. Over the past few years, there have been significant advancements in the systemic treatment of GC, including chemotherapy, targeted therapies, and immunotherapy. For resectable GC, perioperative chemotherapy has become the standard approach. Current research is exploring the potential benefits of integrating targeted therapies and immunotherapies in both perioperative and adjuvant settings. These include treatments such as mono-immunotherapy, dual checkpoint inhibitors, anti-angiogenic drugs, and biomarker-targeted therapies.

Methods: Radical surgery remains the primary treatment for resectable gastric cancer. To minimize the risk of recurrence and improve long-term survival, therapies such as perioperative chemotherapy, adjuvant chemotherapy, and adjuvant chemoradiotherapy have been developed. Clinical trials have shown that perioperative chemotherapy, in particular, significantly improves outcomes in comparison to surgery alone. Adjuvant chemotherapy is also recommended for patients with stage II or stage III cancer who have undergone surgery. Recent trials, particularly in Asian populations, have demonstrated significantly higher survival rates with this approach. For advanced gastric cancer, anti-HER٢ and anti-vascular endothelial growth factor (VEGF) agents have become standard treatments. However, there is ongoing research to better understand the role of targeted therapies in the perioperative or adjuvant settings. Programmed death ١ (PD-١) inhibitors have gained approval for first- and third-line treatment of metastatic gastric cancer in various countries, backed by several phase III clinical trials. Despite these advancements, the role of immune checkpoint inhibitors in resectable gastric cancer remains under investigation, with multiple trials currently underway. Cytotoxic agents, including fluoropyrimidines, platinum derivatives, taxanes, and irinotecan, form the backbone of therapy for advanced gastric carcinoma. Fluoropyrimidines (such as fluorouracil, capecitabine, and S-١) combined with platinum-based drugs are often used as first-line treatments, with oxaliplatin being as effective as cisplatin. The phase III SOX-GC study demonstrated improved survival outcomes with the SOX regimen compared to the SP regimen for patients with diffuse or mixed-type gastric cancer. Immune checkpoint inhibitors (ICIs), either as monotherapy or in combination with other treatments, have shown promising anti-tumor activity in gastrointestinal cancers. For instance, the phase III ToGA study established trastuzumab combined with chemotherapy as the standard first-line treatment for HER٢-positive advanced gastric cancer. Additionally, margetuximab, an Fc-engineered anti-HER٢ monoclonal antibody, has been developed to target the same epitope as trastuzumab but with enhanced binding to specific single-nucleotide polymorphisms of the activating Fc receptor (CD١٦A). References: ١. Tan P, Yeoh KG. Genetics and molecular pathogenesis of gastric adenocarcinoma. Gastroenterology. ٢٠١٥;١٤٩(٥):١١٥٣–٦٢. ٢. Lu L,

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Results: While significant advancements have been made in the treatment of gastric cancer, including the development of chemotherapy, targeted therapies, and immunotherapies, challenges remain, particularly in early diagnosis and recurrence prevention. Perioperative chemotherapy has become the standard for resectable GC, and ongoing research continues to explore the integration of targeted therapies and immune checkpoint inhibitors. Additionally, treatments like anti-HER٢ and anti-VEGF agents offer new options for advanced cases. However, further investigation is needed to optimize therapeutic strategies, and expanding endoscopic screening programs is crucial for improving early detection and long-term survival outcomes in gastric cancer patients.

Conclusion: Despite these transformative advances in GC treatment, further research is needed to address remaining challenges, such as early diagnosis, reducing recurrence rates, and optimizing therapy options. Implementing widespread endoscopic screening programs is essential to improving early detection and increasing survival rates in gastric cancer patients.

Keywords: Gastric Cancer, chemotherapy, immunotherapy

Revolutionizing Infertility Treatment with ۳D-Printed Bio-Scaffolds in Tissue Engineering and Regenerative Medicine (Review)

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Introduction: Infertility is a condition characterized by the inability to conceive after ۱۲ months or more of regular unprotected sex. It is considered a complex disorder with wide-ranging biological, psychological, social, and economic consequences and is a significant health issue globally. A successful pregnancy occurs due to the coordinated interaction between a man's and a woman's physiological events. Although traditional treatments such as ovulation induction drugs, surgical interventions, and assisted reproductive technologies (ART) such as in vitro fertilization (IVF) and intrauterine insemination (IUI) are effective, they often involve high costs, emotional stress, and low success rates. Tissue engineering has emerged as a powerful tool to treat infertility and improve health with the help of advanced medical science technologies.

Methods: tissue-engineered Scaffold systems containing cells are essential for regenerating reproductive organs. Using scaffolds in the treatment of these diseases offers a promising approach for young infertile couples. Scaffolds should be biodegradable, biocompatible, porous, and suitable mechanical properties to mimic natural extracellular matrix (ECM).

Results: Among tissue engineering technologies, ۳D printing has attracted increasing attention in the last decade. It is widely used to create complex scaffolds with suitable materials for various applications. ۳D printing has advanced with the development of cell sources and biomaterials, offering alternatives that overcome the disadvantages of traditional infertility treatment techniques and provide scaffolds to create functional tissues to replace damaged human tissues. ۳D microprinted scaffolds create an excellent ECM-like environment for cell growth and target tissue repair. Also, ۳D printing has shown a high potential in reconstructing damaged reproductive tissues and treating infertility. The accuracy of ۳D printing allows the creation of complex forms by adding layer upon layer of different materials, which is a valuable tool for creating biomimetic scaffolds with controlled properties, with the ability to create customized structures and patient-specific scaffolds. These three-dimensional structures with microporous features can be produced through a computer-controlled layer-by-layer process.

Conclusion: In recent years, significant progress has been made in the field of reproductive organ tissue reconstruction and infertility treatment with the help of ۳D printing. For example, ۳D-printed biosynthetic ovaries using microporous scaffolds are highly precise and offer customization previously unattainable in infertility treatment. The main advantage of ۳D printing is its ability to

produce patient- and tissue-specific scaffolds, which makes it unique. Moreover, this research aims to investigate the potential of ٣D printing scaffolds in treating infertility and create new opportunities in this field.

Keywords: Infertility,٣D-Print, Tissue Engineering, Regenerative Medicine

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Rickettsia provacici: an effective mechanism in pathogenicity (Review)

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Introduction: Rickettsia prowazekii, a cunning intracellular bacterium, employs a strategic mechanism involving pore formation and osmotic lysis to swiftly eliminate gamma interferon-pretreated C١٦٦ endothelial cells. This method is crucial for the bacterium's survival and proliferation within its host organism. Gram-negative bacteria that causes typhus, which is one of the most important mechanisms of its pathogenesis Pore formation acts as the primary means through which Rickettsia prowazekii gains entry into the cytoplasm of C١٦٦ endothelial cells. By creating pores in the host cell membrane, the bacterium secures a direct pathway for its penetration, effectively bypassing the cellular defenses that would typically hinder its invasion.

Methods: We tried not to use irrelevant material and used several new articles to write this manuscript and present it to the Biomedical Congress.

Results: Once inside the C١٦٦ endothelial cell, Rickettsia prowazekii initiates osmotic lysis, a process that leads to the rupture of the host cell. Through the manipulation of osmotic pressure within the cellular environment, the bacterium induces swelling and eventual bursting of the cell, culminating in its rapid demise. The combined action of pore formation and osmotic lysis orchestrated by Rickettsia prowazekii results in the swift and efficient killing of gamma interferon-pretreated C١٦٦ endothelial cells. This targeted mechanism showcases the bacterium's adaptability and virulence in evading host immune responses and exploiting cellular vulnerabilities. In the intricate battlefield of host-pathogen interactions, Rickettsia prowazekii emerges as a formidable adversary, utilizing pore formation and osmotic lysis as weapons to subvert host defenses and ensure its survival. The rapid killing of gamma interferon-pretreated C١٦٦ endothelial cells exemplifies the bacterium's mastery of molecular manipulation for its benefit. Understanding the intricacies of pore formation and osmotic lysis in the context of Rickettsia prowazekii's pathogenicity paves the way for innovative research avenues and therapeutic interventions. By elucidating the molecular mechanisms underlying the rapid killing of host cells, researchers can develop targeted strategies to combat rickettsial infections and enhance treatment outcomes.

Conclusion: In conclusion, the involvement of pore formation and osmotic lysis in the rapid killing of gamma interferon-pretreated C١٦٦ endothelial cells by Rickettsia prowazekii underscores the complexity of host-pathogen interactions and highlights the need for continued exploration in the field of microbial pathogenesis. By unraveling the mysteries of intracellular warfare, we inch closer to unlocking new possibilities in infectious disease management and prevention.

Keywords: Rickettsia prowazekii/ C١٦٦/ pathogenicity

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RNA-Seq Profiling of Granulosa Cells in Polycystic Ovary Syndrome: Insights into Immune Response Pathways (Research Paper)

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Introduction: Polycystic ovarian syndrome (PCOS) affects ١١-١٣٪ of women worldwide and remains a vastly understudied condition. It is characterized by insulin resistance, hyperandrogenism, irregular menstrual cycles, anovulatory infertility, and metabolic disorders. Understanding the contributing factors to PCOS is essential for developing personalized treatment strategies. Moreover, investigating new biomarkers, improving diagnostic criteria, and advancing treatment options are critical to enhancing the efficacy and precision of interventions, benefiting patients' overall quality of life. This article focuses on elucidating the molecular mechanisms underlying PCOS by analyzing RNA sequencing data from granulosa cell samples of both PCOS patients and healthy individuals.

Methods: The RNA-Seq dataset (GSE١٣٨٥١٨), comprising three samples from PCOS patients and three from healthy individuals' granulosa cells, was analyzed. Differentially expressed genes (DEGs) were identified using the DESeq package in R. Gene ontology and KEGG pathway enrichment analyses were performed with the clusterProfiler package. Finally, network visualization was carried out using STRING and Cytoscape software, and hub genes were identified based on their network degree.

Results: A total of ٦٨ genes were identified as differentially expressed based on the thresholds of ٢ < log٢FC < -٢ and Padj-value < ٠,٠٥, including ٢٥ upregulated genes and ٤٣ downregulated genes. The downregulated genes were found to be more significant than the upregulated ones. Notably, the downregulated genes were enriched in pathways related to phagocytosis and immune response, across all levels of Gene Ontology enrichment (biological process, cellular component, and molecular function). Additionally, most differentially expressed genes (DEGs) were enriched in the KEGG pathways associated with neutrophil extracellular trap formation and phagosome/immune response signaling. Key downregulated hub genes identified include PTPRC, TLR٢, FCGR٣B, MNDA, FCGR٢A, HCK, SELL, LCP٢, CD١٦٣, and FPR١.

Conclusion: PCOS patients suffer from chronic low-grade inflammation, potentially triggering mechanisms that increase ovarian androgen levels and disrupt ovulation. The identified hub genes are closely associated with immune response signaling pathways, indicating that decreased expression of these genes may contribute to the development of PCOS.

Keywords: polycystic ovary syndrome, RNA_Seq analysis, granulosa cell, bioinformatics, systems biology

Role of EMT as a tumor progression (Review)

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Introduction: The process of epithelial-to-mesenchymal transition involves the transformation of immobile epithelial cells into a mobile mesenchymal phenotype and was first observed during early development. EMT is involved in embryonic processes such as gastrulation, neural crest formation, and heart development. It also plays a critical role in physiological processes such as healing wounds and maintaining tissue balance. It is important to note that the abnormal reactivation of the EMT process is a key factor in diseases such as organ fibrosis or the progression of cancer to metastasis, which is the main focus of this article.

Methods: Cancer cells can utilize classical EMT functions to move, infiltrate, and enter both blood and lymphatic vessels. Additionally, nonclassical EMT characteristics aid in the onset of tumors and the spread of metastases. Classical: Migration and invasion:In regular epithelial tissue, cells create continuous protective layers that are essential for maintaining their structural integrity. Various junction complexes like adherens, desmosomes, and tight junctions connect epithelial cells, supporting their polarity and preventing the passage of solutes and water. These cell connections are critical for tissue function and are disturbed during the epithelial-mesenchymal transition (EMT). EMT results in the loss of polarity, changes in the cytoskeleton, and heightened motility in tumor cells. Additionally, EMT facilitates invasion by breaking down basement membranes and the extracellular matrix. Non-classical EMT features: Regulation of stemness:Tumor heterogeneity remains unchanged following the transplantation of single tumor cells into mice, prompting research into the stemness of cancer cells. Instances of this phenomenon can be observed in breast cancer, pancreatic cancer, and squamous cell carcinoma, where critical elements such as SNAI١, TWIST١, and ZEB١ control the characteristics of stem cells. The process of epithelial-mesenchymal transition (EMT) plays a vital role in the onset of tumors, metastasis, and invasion. EMT-inducing transcription factors (EMT-TFs) like PRRX١ and ZEB٢ have an impact on the progression of cancer. It is crucial to comprehend the adaptability of EMT and the characteristics of stemness in order to effectively address the growth and spread of tumors. Therapy resistance:Standard treatment focuses on cells that are not similar to stem cells and encounters difficulties with those that have stem cell characteristics activated by EMT. The gene patterns of EMT are connected to resistance to treatment. Different mechanisms, such as the removal of drugs and avoidance of cell death, contribute to the development of resistance. Lowering ZEB١ expression increases the responsiveness to treatment in specific cancer cells. EMT is linked to heightened resistance to chemotherapy in various types of cancer. EMT transcription factors play a critical role in coordinating these processes. Metabolic reprogramming:Metabolic rewiring is significant for cancer cells to support their quick development in spite of restricted oxygen supply. Glucose, lipid, and amino corrosive digestion system changes back metastasis by enacting EMT program. Cancer cells display

modified glycolysis and triglyceride pathways, advancing the "Warburg impact" indeed in oxygen-rich situations. Upregulation of glucose transporters like GLUT١ and GLUT٣ advance improves glycolysis. Lacks within the TCA cycle can moreover encourage EMT. EMT-associated quality expression modifications uncover a mesenchymal metabolic signature controlled by TWIST١. Changes in greasy corrosive digestion system, layer ease, and lipid composition moreover contribute to EMT movement and metastasis. EMT and immune evasion:In the course of tumor development, cancer cells devise methods to avoid immune reactions triggered by new tumor antigens, including concealing antigens and establishing an immune-suppressing surroundings. This is frequently linked to EMT, during which EMT-TFs oversee these activities. EMT-related processes can disrupt antigen demonstration and facilitate the attraction of Tregs, impeding CTL function. EMT cells might escape immune responses by reducing antigen presentation or triggering immune checkpoints.

Results: Therapeutic options to target EMT:The presence of epithelial-to-mesenchymal transition (EMT) in cancer is associated with unfavorable treatment outcomes. Treatment approaches such as standard care, targeted therapy, and surgery may induce EMT, resulting in treatment resistance. Inhibiting EMT-associated pathways using compounds like miRNAs or HDAC inhibitors can potentially reverse this process and improve treatment response. Nevertheless, it is important to weigh the possible downsides, considering that EMT plays crucial roles in physiological activities such as wound healing and stem cell maintenance. It is vital to carefully assess the advantages of EMT inhibition against the potential drawbacks of interfering with normal tissue functions. A thorough understanding of the complexities of EMT in cancer is crucial to develop effective treatment plans.

Conclusion: In summary Embryonic morphogenesis relies on the essential process of epithelial mesenchymal transition. During this process, cells lose their epithelial characteristics and integrity, gain mesenchymal features, and develop the ability to move. The cancer exploits this process to induce crucial alterations in shape and movement, which drive its spread. Furthermore, EMT is more and more recognized as the coordinator of a wide range of additional characteristics of cancer, including the ability of tumor cells to function as stem cells, their capacity to form tumors, their resistance to treatment, and their ability to adjust to changes in the surrounding environment.

Keywords: EMT - cancer - tumor stemness - ZEB١ - ZEB٢

Role of biofilm formation in antibiotic resistance of isolated Pseudomonas from clinical Samples

(Research Paper)

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Introduction: Pseudomonas aureoginosa is a gram negative bacterium with different virulence determinants. The organism grow at diverse range of temperature and has ability to tolerate most of habitats. Although the organism has some kinds of genes which is protect it from harsh environments, biofilm formation ability of the isolates can help them to protect them from some kinds of antibiotics. Therefore, the present study tried to evaluate correlation between biofilm formation and antibiotic resistance

Methods: In this study ٤٥٩ clinical samples have been collected from laboratory of Shahid Mohammadi Hospital in Bandarabas. The samples were evaluated for presence of Pseudomonas and confirmed by biochemical as well as molecular technique using gyr gene. Then effect of some antibiotics using CLSI ٢٠١٩ was evaluated on the isolates and biofilm formation was assessed using microplate techniques

Results: The results indicated that out of ٤٥٩ samples ١٥١ were confirmed as Pseudomonas using biochemical and molecular techniques. The most resistant isolates (٧٠٪) were resist to piperacillin tazobactam and Meropenem, and the less (٤٠٪) were resist to Tobramycin. The results also indicated that ٣٠ isolates were MDR and they had ability to produce strong biofilm .

Conclusion: The results illustrated that there is a correlation between biofilm formation of organism and antibiotic resistance. Although this a challenge for treatment, it is necessary evaluation of organisms specifically some kinds of opportunistic bacteria like Pseusomonas in the hospitals and find out new medication for remedy of the patients.

Keywords: Biofilm, Clinical samples, Pseudomonas

Role of COLCA١ and lncRNAs in Early-Stage Breast Cancer Progression: Insights from RNA Sequencing (Research Paper)

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Introduction: Breast cancer is the most common cancer affecting women worldwide each year. It is a multifactorial disease caused by various factors such as gender, age, genetic mutations, and being overweight. Early detection of breast cancer can save lives. One method used for diagnosis is next-generation sequencing (NGS).In this research project, data from RNA sequencing of early-stage breast cancer tissue, obtained using the NGS method, is analyzed to identify lncRNAs (long non-coding RNA) involved in the development of breast cancer. These lncRNAs can serve as biomarkers for the prognosis and diagnosis of the disease.

Methods: Three RNA-seq data sets from early-stage breast cancer tissue (sample group) and three RNA-seq data sets from healthy breast tissue (control group) were extracted from the NCBI Sequence Read Archive (SRA) database. First, the data quality was assessed using FastQC software, ensuring its quality standards. Next, STAR software was used to compare and align the RNA-seq sequences from healthy and cancerous tissue to the human reference genome. For data normalization and statistical analysis, the DESeq٢ package in the R software environment was used, identifying genes with differential expression.

Results: By determining the biotype of these genes, potential lncRNAs involved in breast cancer development were identified. By applying thresholds of P-value < ٠,٠٥ and Log٢ Fold Change > ٢ on differentially expressed genes, ١٦ lncRNAs with increased expression were found. These include SNHG٢٦, PAX٨-AS١, SLC٧A١٤-AS١, AQP٥-AS١, and COLCA١.

Conclusion: Evidence shows that COLCA١ plays an important role in cancer progression pathways, such as the Wnt/β-catenin and mTORC١ pathways, which affect cell growth and angiogenesis, contributing to tumor growth and spread. Additionally, COLCA١ affects the expression of microRNAs, including miR-٣٧١a-٥p, which regulates inflammation and immune responses. miR-٣٧١a-٥p acts as a tumor suppressor, and COLCA١ likely helps tumors evade the immune system by inhibiting this function, promoting tumor growth. Due to the complex role of COLCA١ in biological pathways, this lncRNA could be considered an important biomarker for diagnosing early-stage breast cancer.

Keywords: Breast cancer, BC, COLCA١, lncRNAs

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ROLE OF FERROPTOSIS IN HEAT STRESS-INDUCED TESTICULOPATHY IN MATURE RATS; PROTECTIVE EFFECTS OF ROYAL JELLY (Research Paper)

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Introduction: Heat stress reduces key parameters such as sperm density and motility and alters sperm morphology. Ferroptosis is a non-apoptotic, iron-dependent form of programmed cell death characterized by the accumulation of iron-dependent lipid peroxides. Royal Jelly (RJ), secreted by the hypopharyngeal and mandibular glands of worker honeybees between the sixth and twelfth days of life, is a rich source of vitamins, including riboflavin, thiamine, niacin, folic acid, biotin, pyridoxine, and smaller amounts of vitamins C, D, A, and E. RJ is known to alleviate premenstrual symptoms, osteoporosis, and improve hormonal balance and fertility in both men and women by enhancing the quality of eggs and sperm. This study evaluates the effects of RJ on mechanisms of ferroptosis in adult male rats subjected to heat stress.

Methods: This study involved ٣٢ healthy adult male Wistar rats, divided into eight groups: control, control + RJ, ٣٧°C heat stress, ٣٧°C heat stress + RJ, ٤٠°C heat stress, ٤٠°C heat stress + RJ, ٤٢°C heat stress, and ٤٢°C heat stress + RJ. The rats were exposed to heat stress in warm water baths at ٣٧, ٤٠, and ٤٢°C for ٢٠ minutes daily over a ٤٢-day period (٦ weeks). After heat exposure, RJ was administered orally by gavage. Following the experimental period, the left testis was extracted for histological examination and fixed in ١٥٪ formalin, while the right testis was stored at -٧٠°C for molecular analysis.

Results: The results of this study indicate that examining the expression levels of GPX٤ mRNA compared to β -actin in different groups showed that an increase in temperature led to a decrease in the expression of this gene. The thermal groups exhibited a significant reduction compared to the control RJ group. Treatment with RJ somewhat improved these conditions and increased gene expression, indicating the protective effect of RJ, which was more pronounced in the ٣٧-degree thermal treatment group.

Conclusion: These findings suggest that RJ may have a protective effect against heat-induced testicular damage and could enhance sperm quality by mitigating heat stress-related injuries. The study provides promising insights into the potential therapeutic role of RJ in combating heat stress-induced testicular damage and improving reproductive health.

Keywords: Ferroptosis, Heat Stress, Royal Jelly

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Role of PXR in drug metabolism of TNBC and its cross talk with other important drug-metabolism related molecules (Review)

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Introduction: Breast cancer consists different molecular subtypes based on the expression of cell surface receptors (ER, PR, and HER-٢), and Ki-٦٧ level, as well as their prognosis. Accordingly, there ٥ different subtypes (Luminal A, Luminal B, HER-٢ enriched, Triple negative/basal-like, and normal-like). Management and prognosis of each subtypes differ, somehow, mainly due to the new treatment strategies e.g., targeted/endocrine therapy(١). Utilizing the most efficient dose of chemotherapy drugs would result in the highest efficiency with the least side effect. In this regard, Pharmacokinetics, and pharmacodynamics play crucial role in precision medicine of these patients who receive, chemotherapy. Pharmacokinetics deals with the amount required of a drug to reach the target site in the body, while pharmacodynamics deals with how receptors, ion channels and enzymes respond to different drugs(٣).

Methods: In this article, the keywords of breast cancer, PXR, TNBC, drug metabolism are used in databases : Pubmed, Google Scholar, Scopus, ScienceDirect, ResearchGate.

Results: Pregnane X Receptor role in cancer and drug metabolism Pregnane X receptor (PXR) is a nuclear receptor that plays a significant role in chemotherapy outcomes by influencing the metabolism, drug resistance, tumor sensitivity, apoptosis, and pharmacokinetic parameters of various chemotherapeutic agents in both cancer cell lines and patients(٥). Recent studies have highlighted the significance of PXR expression in tumor tissues of patients with TNBC, linking it to patient prognosis(٢). The metabolic process mediated by PXR occurs in three phases: Phase I: Involves the action of metabolizing enzymes that introduce functional groups into xenobiotics. Phase II: Involves conjugating enzymes that facilitate the attachment of polar groups to metabolites, enhancing their solubility and excretion. Phase III: Involves transporters that facilitate the efflux of metabolites and drugs from cells (٢) (figure ١). PXR Mechanism of Action and molecular cross-talks Upon ligand binding, PXR undergoes a conformational change that activates its signaling pathway. This activation leads to the translocation of PXR from the cytoplasm to the nucleus, where it forms a heterodimer with retinoid X receptor (RXR). This complex then binds to specific response elements in the promoter regions of target genes, regulating their transcription (٢). Transcription factor E٢٦ transformation-specific sequence ١ (ETS-١) and N-α-acetyltransferase ١٠ (NAA١٠) have been shown to interact with the PXR promoter, enhancing the activation of downstream genes associated with drug resistance. CYP٣A٤ plays a significant role in substrate oxidation and pharmacokinetic drug-

drug interactions, leading to decreased plasma concentrations and reduced therapeutic efficacy of anticancer drugs. Therefore, treatment with PXR antagonists, which inhibit CYP٣A٤ at the transcriptional level, may enhance the therapeutic effects of these drugs(٤). According to a study FBI-١ is a factor that binds to the inducer of short transcripts-١, enhancing the resistance of TNBC cells to chemotherapeutic agents by repressing the expression of microRNA-٣٠c, which targets the PXR. MicroRNA-٣٠c reduces PXR expression by interacting with the ٣′-UTR of PXR, whereas FBI-١ increases PXR expression by inhibiting miR-٣٠c. This research demonstrates that the miR-٣٠c/PXR axis is modulated by FBI-١ in TNBC drug resistance, suggesting potential new strategies for the treatment of this aggressive cancer type(٦). PXR appears to have dual roles in the development of resistance to chemotherapeutic agents.For instance, following treatment with a PXR agonist, an inactive anticancer prodrug may be metabolized more extensively into an active metabolite, potentially enhancing its anticancer efficacy. Conversely, the activation of PXR may increase the metabolism of active drug forms into less active metabolites or facilitate their excretion, leading to an overall increase in resistance to chemotherapy (٧). Given the extensive diversity of compounds that activate PXR and its role in coordinating various biological processes, it is reasonable to expect interactions between PXR and other nuclear receptors, such as FXR, CAR, PPARα, LXR, and androgen receptor. These interactions may facilitate more effective regulation of cellular responses to different compounds and enhance the coordination of metabolic processes. In essence, PXR and these receptors may work synergistically to enable cells to adapt to environmental and metabolic changes(٨). The constitutive androstane receptor (CAR), similar to PXR, is a nuclear receptor recognized for its role in xenobiotic detoxification through the regulation of drug metabolism enzymes and transporters. The structure of CAR includes a N-terminal domain (NTD), a ligand-binding domain (LBD), a hinge region (H), and a DNA-binding domain (DBD). The nuclear translocation of CAR can be facilitated by ligand binding as well as post-translational modifications (٩) After xenobiotics enter the cell, they trigger the cytoplasmic-nuclear translocation of CAR by promoting the release of currently unidentified proteins. Subsequently, CAR heterodimerizes with RXR, binds to their respective response elements, and enhances the transcription of target genes (١٠).

Conclusion: Understanding the intricate relationship between PXR signaling, drug metabolism, and cancer progression is essential for developing more effective treatment strategies. Targeting PXR and other receptors involved in the metabolism of chemotherapy drugs in particular TNBC could potentially enhance the efficacy of existing therapies and mitigate the challenges associated with drug resistance in advanced metastatic Breast cancer.

Keywords: TNBC_Breast Cancer _ PXR _ Drug Metabolism

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Saccharomyces cerevisiae and Its Role in Single Cell Protein (SCP) Production (Review)

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Introduction: Saccharomyces cerevisiae is a unicellular fungus known as baker's yeast. It is usually larger than bacteria and differs in size. Its morphology is spherical or oval. It can reproduce sexually through germination or sexually through spore production. This has a nuclear genome consisting of ١٦ chromosomes. The genome of S.cerevisiae has been fully sequenced, revealing ٦٠٠٠ genes. Bioinformatics analysis indicates that of these ٦٠٠٠ genes, ٥٥٧٠ are protein-coding genes. S.cerevisiae has become widely used in the industry due to its potential for producing various products such as food, beverages, and bioethanol. Mycoproteins or Single Cell Protein (SCP) are natural protein concentrates produced by microorganisms like yeasts, algae, fungi, and bacteria. This article aims to explore the role of S.cerevisiae in SCP production and its impact on food safety and the environment.

Methods: Keywords such as food industry, SCP, and Saccharomyces cerevisiae were used to search online scientific databases like Google Scholar and PubMed, leading to the selection and review of related articles.

Results: Today, the continuous fermentation system is used to produce mycoprotein from yeast. Nutrients and inoculum are added to the cells under optimal growth conditions (temperature: ٢٠-٣٠°C, pH: ٤,٥-٦,٥) with continuous stirring, and a C/N ratio of ٢٠-١٠. This is done at a consistent rate, while biomass and waste materials are harvested simultaneously. The culture is typically maintained in the exponential growth phase to achieve maximum production. After collection, it undergoes heat treatment to reduce its RNA content to below ٢٪. Then it is dehydrated and packaged. Saccharomyces cerevisiae can use inexpensive materials, such as agricultural waste, dairy, and lignocellulosic materials, as a source of carbon and nitrogen. The quality of SCPs produced by yeasts is similar to animal proteins and varies depending on the type of substrate. On average, they contain ٥٠-٦٠٪ protein, ٢-٦٪ fat, various amino acids, B vitamins, calcium, phosphorus, and glycogen. The first mycoprotein was produced from yeast in the ١٩٧٠s under the brand "Pruteen" as an animal feed additive. "Quorn" is also a commercial brand of mycoprotein for animal feed. Since ١٩٨٥, mycoproteins have been produced for human nutrition. Among the recombinant proteins produced by S.cerevisiae are glutathione, milk protein, Brazzein in the food field, transferrin, human hemoglobin, and human pancreas ribonuclease in the pharmaceutical field. They are also used as a meal for fish, as a supplement for livestock and ruminants (reducing intestinal CH_4 emissions), and even as a suitable alternative for feeding astronauts on space missions.

Conclusion: One of the benefits of using yeast as an SCP producer is that they have low nucleic acid content and causes fewer side effects than animal proteins. Producing animal proteins requires cultivating large areas of agricultural land to feed the animals, which leads to the consumption of

significant amounts of water and the emission of large quantities of greenhouse gases. In contrast, the nutritional needs of yeast are not complex, and they can also utilize waste as a resource. Yeast-produced single-cell protein boasts high protein content based on dry weight, low-fat content, a fast harvest cycle, and independence from seasons and weather conditions. However, it's important to note that products produced by microorganisms can trigger allergic and digestive reactions in some individuals. Today, due to the clarity and well-known genetic content of S.cerevisiae, along with many advances in molecular biology such as CRISPR/Cas^{9}, the path of industrial and medical research in developing SCP production using S.cerevisiae has become smoother. Furthermore, Saccharomyces cerevisiae has been approved by the FDA for the production of heterologous proteins, food, pharmaceuticals, and industrial enzymes due to its strong safety record (non-toxic production). Today, vegetable and animal proteins alone cannot meet the world's demand for protein. It is necessary to increase the availability of new and stable protein sources. Microbial protein production should be used as an alternative method, and special attention should be paid to this issue in research and policies. Additionally, developing advertising campaigns to promote the benefits of SCP is effective in gaining high social acceptance.

Keywords: Saccharomyces cerevisiae, SCP, food industry

Scaling up the production of low-molecular-weight Dextran by Leuconostoc mesenteroides from whey protein (Research Paper)

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Introduction: Dextran is a high-molecular-weight bacterial exopolysaccharide with substantial industrial and therapeutic applications. Low-molecular-weight Dextran is preferred for pharmaceuticals, food, and cosmetics for its enhanced solubility, bioavailability, and low immunogenicity. This study delved into the cost-effective strategies for producing low-molecular-weight Dextran by the probiotics bacterium Leuconostoc mesenteroides (NRRL B-١١١٨) in whey protein.

Methods: The fermentation process was optimized by using whey protein as a substrate to enhance the yield and quality of Dextran. The growth parameters, including temperature, pH, incubation period, and substrate concentration, were precisely adjusted to promote the low-molecular-weight Dextran production. The Dextran was isolated, and its molecular weight was determined using gel permeation chromatography (GPC). Structural analysis was conducted through Fourier-transform infrared spectroscopy (FTIR) and nuclear magnetic resonance (NMR) spectroscopy.

Results: The rheological properties of Dextran revealed its potential application in the food and pharmaceutical industries.

Conclusion: This study demonstrates the feasibility of using whey protein as a cost-effective substrate for the microbial production of low-molecular-weight Dextran, offering a sustainable approach to valorize whey, a by-product of the dairy industry.

Keywords: Leuconostoc mesenteroides; Dextran; Whey protein; Probiotics;

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Screening The Hub Genes and Their Functional Significance in Liver Cancer: Evidenced by Bioinformatic Tools (Research Paper)

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Introduction: Liver hepatocellular carcinoma (LIHC), the most common type of liver cancer, originates from hepatocytes and represents over ٨٠٪ of liver cancer cases. It is projected to be the sixth most frequently diagnosed cancer and the fourth leading cause of cancer-related deaths globally. Unfortunately, LIHC is often detected at an advanced stage, where effective treatments to enhance survival rates are nearly nonexistent. Thus, identifying diagnostic biomarkers is crucial for early detection and personalized treatment options for LIHC. This study aims to discover new diagnostic and prognostic biomarkers in LIHC patients.

Methods: mRNA microarray datasets GSE٨٤٤٠٢, GSE١٠١٦٨٥, and GSE٦٠٥٠٢ were sourced from the Gene Expression Omnibus (GEO) and analyzed through bioinformatics to pinpoint hub genes involved in the development of LIHC. Differentially expressed genes (DEGs) were evaluated using the GEO٢R tool. Gene ontology (GO) and KEGG analyses were conducted using the Enrichr platform. The STRING database and Cytoscape software facilitated the construction of a protein-protein interaction (PPI) network, allowing for the identification of key modules and hub genes. To confirm the expression variations of hub genes in liver hepatocellular carcinoma compared to normal tissues, Gene Expression Profiling Interactive Analysis (GEPIA) was employed, and the overall survival (OS) related to hub genes was analyzed using the Kaplan-Meier plotter.

Results: A total of ١١٥ overlapping differentially expressed genes (DEGs) were identified, consisting of ٨٦ upregulated and ٢٩ downregulated genes. An integrated analysis highlighted five key hub genes: PRC, MELK, TTK, MKI٦٧, and FANCI. These DEGs were primarily linked to processes such as complement and coagulation cascades, mineral absorption, glycolysis/gluconeogenesis, fatty acid degradation, the cell cycle, and the p٥٣ signaling pathway. The protein-protein interaction (PPI) network comprised ١١٢ nodes and ٣٨٥ edges. Survival analysis indicated a significant association between these hub genes and the overall survival of LIHC patients.

Conclusion: This study successfully identified several key hub genes associated with liver hepatocellular carcinoma, revealing important insights into the disease's molecular landscape. The bioinformatics analysis provided valuable insights into the molecular mechanisms underlying this cancer type. These findings may facilitate the development of targeted therapies and improve patient outcomes. Overall, the research contributes to a better understanding of liver cancer and its underlying biological mechanisms.

Keywords: Liver hepatocellular carcinoma (LIHC), Hub Genes, GEO, In Silico

Secondhand smoke impacts fertility (Review)

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Introduction: The effect of passive smoking on fertility has not yet been adequately studied. Various products of tobacco smoke (benzopyrene, cadmium, and cotinine, a nicotine metabolite) reach the ovarian follicle and the presence of cotinine has been associated with reduced fertilizing ability of the oocyte. passive exposure to smoke seems to have detrimental effects on a woman's ability to conceive. The study also reports that secondhand smoke may lead to early menopause, before the age of ٥٠.

Methods: In this study, ١٠ articles published from ٢٠١٩ to ٢٠٢٤, which were in the form of original research and systematic review were examined. New studies may be motivating even to partners to quit tobacco use to reduce the risks of secondhand smoke on pregnancy." The study used the keywords Passive smoking, Infertility, Secondhand smoke.

Results: Approximately ٣٠٪ of reproductive age women and ٣٥٪ of reproductive age men in the United States smoke cigarettes. Substantial harmful effects of cigarette smoke on fecundity and reproduction have become apparent but are not generally appreciated. A survey of ٣٨٨ female employees of a Connecticut hospital revealed that the major deleterious health effects of smoking are widely recognized. However, the majority of the women surveyed, including female health care providers, were unfamiliar with the reproductive risks associated with smoking. Several comprehensive reviews have summarized the cumulative data on cigarette smoking and female fecundity and all support the conclusion that smoking has an adverse impact.

Conclusion: If you live with a smoker or surrounded by smoker, Passive smoking exposes you to poisonous chemicals, affecting your fertility. Chemicals in cigarette smoke appear to accelerate follicular depletion and the loss of reproductive function. Overall, the literature strongly supports an association between cigarette smoking and infertility.

Keywords: Passive smoking, Infertility, Secondhand smoke

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Self-power triboelectric nanogenerator: A novel implantable biomedical device for empowering pacemaker (Review)

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Introduction: Implantable medical devices such as cardiac pacemakers have the potential to benefit greatly from self-powered technologies that can extend device operation time and reduce the need for high risk repeatable surgeries. One promising approach is the use of inertia-driven triboelectric nanogenerators (I-TENGs) that can harvest biomechanical energy from the body's natural motions

Methods: In articles, a compact coin battery-sized I-TENG is demonstrated that is capable of generating ٤,٩ μW/cm٣ of root-mean-square power output from body movements. Through preclinical testing, the I-TENG was shown to successfully charge a lithium-ion battery and was integrated directly with a cardiac pacemaker, enabling the pacemaker to operate in a self-rechargeable mode

Results: This proof-of-concept device represents an important step towards the development of truly self-powered implantable medical technologies that can operate indefinitely without the need for battery replacement surgeries.

Conclusion: The successful integration of the I-TENG with a functioning cardiac pacemaker highlights the potential of this approach to transform the field of implantable devices and improve patient outcomes.

Keywords: Triboelectric , Nanogenerator , Pacemaker , Biomedical device

Seroepidemiology of Toxoplasma Gondii in kidney transplant patients (Research Paper)

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Introduction: Opportunistic infection after transplantation is a serious problem. The most concerning of these infections are Toxoplasma gondii (T.gondii) and cytomegalovirus. The main goal of this study was to investigate the seroepidemiology of the T.gondii virus in kidney transplant patients at Sina Hospital in Tehran from ٢٠١٧ to ٢٠٢١.

Methods: ٣٤٢ kidney transplant patients from Sina Hospital participated in this retrospective cross-sectional study by census method after obtaining consent. By referring to the medical records of kidney transplant patients and the transplant database of the transplantation unit of Sina Hospital, the desired data were collected and recorded in the prepared checklist. The data included demographic characteristics and cases of infectious tests related to kidney transplantation. The collected information was entered through the checklist in SPSS١٨ software.

Results: The age range of the investigated subjects was between ١٠ years and ٧٣ years. A total of ١٢٥ patients in the study had kidney failure due to ERDS. The rate of exposure to T. gondii in kidney transplant patients was reported to be ٥٤,٢٪, based on the regression test, gender did not predict any EBV.IgG, CMV.IgG and TOX.IgG.

Conclusion: Physicians should be aware of preventive measures and make an early diagnosis if there are compatible symptoms. All potential donors should be screened for anti-Toxoplasma IgM antibodies.

Keywords: Seroepidemiology; kidney transplant; EBV.IgG; CMV.IgG; TOX.IgG

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Seroprevalence of human cystic echinococcosis Infection in Individuals Occupationally Exposed to Livestock and Raw Meat: A Cross-Control Study (Research Paper)

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Introduction: Echinococcus granulosus and thus Cystic echinococcosis (CE) is present globally. The expectancy of CE transmitted from livestock and raw meat to humans is a public health problem and is an example of the One Health theory. This survey aimed to determine the seroprevalence and risk factors related to this common infection in individuals occupationally exposed (IOE) to livestock, raw meat, and viscera in industrial slaughterhouses and livestock fields compared with the control group in Isfahan province, central Iran.

Methods: This study is a case-control survey carried out on the ٤٠١ serum samples of IOE (including slaughterhouse workers, butchers, veterinarians, veterinary technicians, livestock farmers, and farm workers) compared to ٤٠١ archived samples of the general population (that all matched with cases by region, age, and gender). All ٨٠٢ samples were investigated for echinococcosis IgG using enzyme-linked immunosorbent assay (ELISA).

Results: Although the odd ratio was ٢,٥ times higher in IOE compared to the control group (١,٢٪ versus ٠,٥٪), it was not statistically significant (p ٠,٢٢٥). According to our knowledge, this is the first case-control study on the seroprevalence of E. granulosus in IOE in central Iran.

Conclusion: Based on the nature of the disease (involving both animals and humans), echinococcosis is highly prevalent in pastoralist communities that move across national borders, a firm response to control CE will require interdisciplinary and transboundary partnerships. Considering the similar disease ecosystems, livestock trade routes and management systems, it is paramount to awareness of disease epidemiology in various regions.

Keywords: Abattoir, Hydatid disease, Occupational Exposure, Risk factors, Seroprevalence, Zoonoses

Signaling pathways involved in the effect of probiotics on the immune system (Review)

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Introduction: Probiotics are live microorganisms that, when consumed in adequate amounts, confer health benefits to the host. They play a pivotal role in maintaining gut health, supporting digestion, and modulating the immune system. Probiotics interact with the immune system in various ways, including balancing the immune response, strengthening the gut barrier, and stimulating the activation of beneficial immune cells. Understanding the underlying signaling pathways involved in probiotic-mediated immune cell activation is crucial for several reasons. First, it allows for the development of targeted therapies that can harness the specific immunomodulatory properties of probiotics to treat various diseases. Second, knowledge of these signaling pathways enables the optimization of probiotic formulations, ensuring that they deliver maximum benefits to the host. Finally, studying probiotic-induced immune signaling provides valuable insights into the complex interactions between the gut microbiome and the immune system, contributing to a deeper understanding of human health and disease. This article aims to delve into the intricate details of the signaling pathways involved in the immunomodulatory effects of probiotics.

Methods: The article used Google Scholar to discover recent research (٢٠٢٠-٢٠٢٤) examining the influence of probiotics on immune cells. The advanced search function was employed to pinpoint studies concentrating on the specific signaling pathways implicated in this process.

Results: Probiotics exert diverse effects on the immune system by influencing various cellular processes. They can alter receptor function, protein expression, and signaling pathways. Additionally, probiotics can regulate gene expression, inflammation, and the production of immune-related molecules. Key signaling pathways involved in probiotic-mediated immune modulation include MAPK, NF-κB, Akt/PI٣K, and PPARγ. However, the specific effects of probiotics on these pathways and cytokine profiles can vary depending on the probiotic species. Probiotics have demonstrated anti-tumor properties through various mechanisms. For instance, Heptelidic acid from Aspergillus oryzae inhibits pancreatic cancer cell growth via P٣٨ MAPK signaling. Bacillus coagulans MZY٥٣١ exhibits anti-apoptotic effects and reduces cancer cell survival by inhibiting AKT, mTORp-PI٣K phosphorylation. Other probiotics, such as Lactobacillus casei BL٢٣ and Clostridium butyricum, promote anti-tumor responses by increasing IL-٢ production and activating the Wnt signaling pathway. Probiotics can also modulate inflammatory responses. Lactilactobacillus sakei WB٢٣٠٥ and

Lactiplantibacillus plantarum WB٢٣٢٤ inhibit LPS-induced inflammation by targeting MAPK and NF-κB pathways. The capsular polysaccharide of Lacticaseibacillus paracasei ٦٢٣٥ can also modulate inflammation by altering MAPK and NF-κB protein expression. NF-κB, a key regulator of the immune system, is a common target of probiotic modulation. Probiotics can influence NF-κB activity by affecting TLR expression or p٦٥ phosphorylation. Beyond NF-κB, probiotics can interact with other immune signaling pathways. Bacillus paralicheniformis alleviates ulcerative colitis by regulating the inflammasome through NLRP٣. GABA-producing probiotics can inhibit the inflammasome pathway by targeting NLRP٣. Additionally, Lactobacillus paracasei KW٣١١٠ suppresses multiple inflammasome complexes through an interleukin-١٠-dependent mechanism. Extracellular vesicles (EVs) derived from probiotics can also influence immune responses. For example, EVs from E. faecalis can induce an M١ macrophage phenotype by activating the NOD٢/RIPK٢ signaling pathway.

Conclusion: Probiotics have a broad range of effects on the immune system. They interact with cells in different ways, affecting things like receptor function, protein production, gene activity, and the creation of substances involved in immune responses. Key signaling pathways influenced by probiotics include MAPK, NF-κB, Akt/PI٣K, and PPARγ. Although the specific effects can vary between different types of probiotics, they've been shown to help fight cancer, reduce inflammation, and regulate the immune system. Additionally, tiny particles called extracellular vesicles, released by probiotics, can also impact immune responses.

Keywords: Signaling pathway, immunology, probiotic,

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Simulating The Layered Skin Structure Using layered-to- layered Nanofibers and Dermal Tissue-Derived Solubilized Extracellular Matrix (Research Paper)

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Introduction: Skin as the largest organs in human-beings body covers the external surface of whole body, exposing to different injuries, like burn, rupture, and cut[١]. Over the years, scientists tried to resolve these skin-related injuries using autograft and allograft. But the limitations associated with autograft and allograft, including the lack of donor tissue from the person with severe burn injuries and lack of donor tissue completely matched with the recipient without the risk of rejection made scientists find other solutions, which has been progressed toward tissue engineering-based approaches. Scaffolds, being material-based substrates, are used for tissue regeneration and created from diverse materials (synthetic, natural, and hybrid) and methods. Among all methods, electrospinning is a great deal of attention, resulting from the fact that its resulting nanofibers can mimic the nanostructure of native tissue[٢][٣][٢]. In addition, the decellularization method is also interesting owing to producing extracellular matrix (ECM), while preserving agents within the native tissue, demonstrating its role in mimicking the nano contents of the native tissue. In other words, acellularization leaves a natural-based material termed ECM containing different contents available in the native ECM. Another appealing feature of this tissue-derived ECM is its role in improving the biocompatibility of fabricated constructs, approved in different studies[٤][٥]. Based on all above-mentioned issues, we aimed at fabricating a layered-to-layered construct using an electrospinning and decellularization to imitate the layered structure of skin and improve its biocompatibility.

Methods: Using the decellularization of dermal tissue and electrospinning, the basic components of targeted construct, nano fibers and ECM, were fabricated. After the decellularization of dermal tissue, its resulting ECM were solubilized in the acidic solvent. In the following, electrospun nanofibers and solubilized ECM were sequentially stacked, followed by its freeze-drying. Having been prepared, freeze-dried constructs were crosslinked and subjected to different tests to characterize its features, including its morphological aspects and porosity.

Results: Morphologically, the layered-to-layered constructs with porous structure was observed. In addition, it was demonstrated that the constructs had porosity more than ٨٠٪ and high swelling. The biocompatibility of these constructs was revealed using the MTS assay.

Conclusion: These layered constructs with improvement in the biocompatibility can have potentiality to be used as a promising skin substitution. However, further investigations, including in vivo study, are needed.

Keywords: Biocompatibility, Extracellular matrix, Electrospinning, decellularization, scaffold

Sjogrens syndrome (Review)

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Introduction: Sjögren's syndrome (SS) among primary autoimmune rheumatic diseases encountered by rheumatologists is unusual. Dominated by the pathology of exocrine glands of the eyes, mouth, and exocrine glands along with the presence of multiple specific autoimmune organ disorders, it leads to a somewhat unfamiliar diagnostic and therapeutic outlook. The lack of diagnostic criteria, global classification, and accepted outcomes, as well as the need for close collaboration with subspecialists in ophthalmology, dentistry, and otolaryngology for optimal patient management, all pose challenges in care. Nevertheless, SS offers rheumatologists and immunologists an opportunity to understand the pathogenesis, long-term evolution, and outcome of an autoimmune disease characterized by specific organ and systemic features. Furthermore, the recurrent co-occurrence of SS with other major rheumatic diseases such as rheumatoid arthritis, systemic lupus erythematosus, and scleroderma provides a unique insight into the genetic, environmental, and biological factors controlling autoimmune phenotypes among affected individuals. The striking tissue associations between primary SS and non-Hodgkin lymphoma offer valuable insights into the relationships between autoimmunity, immunogenetics, and malignancy. Significant efforts have been made in treatment for glandular and systemic manifestations of SS. As an autoimmune disease, the prevalence of Sjögren's syndrome varies in different populations. Accurate data on its prevalence in Iran may be variable, but research estimates the prevalence of Sjögren's syndrome in Iran to be around ۰,۵ to ۱٪ of the population. This rate may vary in different regions of the country and be influenced by local factors such as environmental and genetic variables. The average prevalence of Sjögren's syndrome in women is almost ۹ times higher than in men. This gender difference in disease occurrence may be due to the influence of hormones and genetic factors related to endocrine gland tissues. Additionally, women may be more likely to seek hormonal therapies for endocrine gland-related issues, which could contribute to the increased prevalence of Sjögren's syndrome in them. Understanding Sjögren's syndrome is crucial as it can aid in the early diagnosis and appropriate treatment of this autoimmune disease. Recognizing this syndrome, which is an autoimmune disorder that attacks the thyroid gland, is of paramount importance as it can lead to quicker symptom control and prevention of serious complications such as thyroid gland damage, increased risk of other diseases, and even premature birth.

Methods: Collecting information from authoritative articles on Google Scholar and NCBI sites and other authoritative scientific sites and categorizing them

Results: In recent decades, significant advances in the field of molecular genetics and genetic engineering, especially in the field of plants and animals, have led to the creation of new opportunities and unprecedented challenges. These advances have led to the creation of genetically

engineered plants and animals that offer new capabilities and characteristics. However, these changes bring not only great potential, but also challenges and concerns. The main goal of this article is to examine the challenges and concerns related to genetically engineered plants and animals. This article examines the environmental, economic, social and ethical effects of these changes and provides solutions and suggestions for the optimal management of these challenges. This not only helps us to exploit the potential of these technologies, but also supports the various opinions of society and the protection of the environment.

Conclusion: Sjogren's syndrome is an autoimmune disease that attacks the body's fluid-producing glands, especially the salivary and eye glands. Diagnosis of this disease is made through clinical history, symptoms, and diagnostic tests, including blood tests, thyroid ultrasound, and imaging tests. Treatment of Sjogren's syndrome usually involves taking hormonal drugs to compensate for the lack of thyroid and other gland hormones. If early diagnosis and appropriate treatment are performed, the long-term harmful effects of this disease can be prevented and the quality of life can be improved. There have been significant advances in the treatment of Sjögren's syndrome, including the use of immunosuppressive drugs, interventional drugs for symptom management, and the development of novel therapies. Although there is still no complete cure for this disease, recent advances have made it possible to improve symptoms and reduce the harmful effects of the disease. Risk factors that may increase Sjogren's syndrome include gender, age, family history, environmental factors, other diseases, and more. Understanding these factors and taking preventive measures such as maintaining good health and controlling other diseases can help reduce the risk of developing Sjögren's syndrome. Finally, early diagnosis, appropriate treatment, and regular care by specialist doctors can help manage and improve the quality of life of people with Sjogren's syndrome.

Keywords: Autoimmune - Pathogenesis - treatment - Complications

Smart Materials for Dynamic Bone Healing: The Future of ٤D Printing in Tissue Engineering and Regenerative Medicine (Review)

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Introduction: Bone tissue is one of the largest tissues in the body. Sometimes unexpected events like accidents, trauma, and surgeries lead to some deformities in bone tissue. In large-scale defects, there are some challenges for bone healing, so bone tissue engineering and using synthetic or natural biomaterials are used to overcome these challenges. ٣d and ٤d printing are the newest types of scaffold fabrication in tissue engineering. In ٤D printing, polymers stimulate under different conditions like pH, water, temperature and leading to visualize some shape changes in printed scaffolds.

Methods: Polymers like polycaprolactone(PCL), poly lactic acid (PLA), polyurethane(PU) and propylene glycol diacetate (PGDA) are categorized as shape memory polymers. The composition of these polymers with other polymers or hydrogel can provide a shape memory effect for materials.

Results: In ٤D printing for the spine, the scaffold is printed in a flat space and after stimulation transforms into a curved shape. To achieve this goal, Using A collagen hydroxyapatite scaffold containing microchannels can be a suitable choice to print for bone graft that can promote new bone formation in spinal fusion. In addition we can use PLA/Fe_3O_4 for printing to achieve shape memory effects for spinal bones that can be stimulated under hot water and magnetic fields. Also we can suggest using ٣d printed polylactide-co-trimethylene carbonate (PLMC) scaffolds contain polydopamine nanoparticles for bone tissue engineering that can demonstrate shape recovery properties under NIR irradiation along with osteogenic potential. Pla in combination with hydroxyapatite also can be used to construct the porous bone scaffold with shape memory activity.

Conclusion: In conclusion, it seems that using these dynamic scaffolds with smart properties or shape memory activity may be useful for bone tissue engineering to transform into a defect site that leads to better healing in bone tissue deformities. This marks a significant advancement in regenerative medicine.

Keywords: tissue engineering- bone tissue - ٤d printing- bone regeneration

Staphylococcus aureus and MRSA: Emergence and Public Health Concerns (Review)

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Introduction: Staphylococcus aureus (S. aureus) is a Gram-positive, nonmotile, coagulase-positive bacterium, and it is undoubtedly the most clinically significant species in the Staphylococcus genus, which comprises ٥٢ species and ٢٨ subspecies. Approximately ٢٠–٤٠٪ of the general human population carries S. aureus as part of their nasal microbiota. The emergence of methicillin-resistant Staphylococcus aureus (MRSA) was first identified in England in ١٩٦١, shortly following the introduction of methicillin into clinical use. Although methicillin has been withdrawn from the market due to its toxicity and replaced by more stable alternatives such as oxacillin and flucloxacillin, the term MRSA continues to be widely utilized in medical contexts. MRSA clones primarily develop through horizontal gene transfer of the staphylococcal cassette chromosome mec (SCCmec), a mobile genetic element that encodes the mecA or mecC genes, which confer resistance to methicillin and most β-lactam antibiotics. S. aureus exhibits a distinctive capacity to acquire resistance to various antibiotics, complicating treatment strategies. The global spread of MRSA has profound implications for the epidemiology of infectious diseases. Interestingly, while MRSA is commonly believed to have emerged with the introduction of methicillin, whole-genome sequencing indicates that it likely originated in the mid-١٩٤٠s, a phenomenon thought to be driven more by the extensive use of penicillin than by methicillin itself.

Methods: To identify MRSA, microbiological specimens are classified into clinical and screening samples. Clinical samples, including septic discharge, deep tissues, sputum, and blood, are collected from symptomatic individuals for diagnosing active infections. Conversely, screening samples such as nasal, perineal, and throat swabs aim to detect asymptomatic carriers. Various phenotypic methods, which dominate clinical settings, as well as innovative non-phenotypic techniques, are employed for MRSA detection. Glycopeptides like vancomycin and teicoplanin serve as primary treatments for MRSA infections, with combination therapies investigated to enhance bacterial clearance, although evidence for their superiority remains inconclusive. The duration of treatment for MRSA bacteremia is generally more prolonged than for MSSA, necessitating a minimum ١٤-day regimen to reduce complication risks. Emerging antibiotic agents such as ceftaroline and ceftobiprole show promise against MRSA, yet concerns about resistance underscore the urgent need for continued research in this evolving field.

Results: The prevalence of MRSA varies geographically, with the highest rates observed in parts of America and Asia, while lower incidences are noted in Scandinavia. MRSA dissemination occurs through existing resistant clones and the acquisition of SCCmec by methicillin-sensitive S. aureus (MSSA) strains. Colonization by S. aureus typically precedes the onset of infection, predominantly

occurring in the nasal passages, although colonization can also take place in other sites. Skin and soft tissue infections (SSTIs) often result from bacterial transfer from the nares to skin lesions, facilitated by specific surface proteins that enhance the bacteria's adherence and biofilm formation on surfaces.

Conclusion: In conclusion, Staphylococcus aureus, particularly its methicillin-resistant strain (MRSA), poses a significant threat to public health due to its ability to acquire antibiotic resistance and its prevalence within the human population. Despite the withdrawal of methicillin, MRSA's emergence highlights the consequences of extensive antibiotic use, including the ability of the bacterium to spread through horizontal gene transfer. The identification and management of MRSA infections require robust diagnostic methods and appropriate treatment strategies, often necessitating prolonged therapy. To combat this growing challenge, innovative approaches such as the development of novel antibiotics, the use of bacteriophages, and enhanced emphasis on infection control measures in healthcare settings should be pursued. Additionally, ongoing research into vaccine development and public education on antibiotic stewardship is critical to mitigate the impact of MRSA.

Keywords: Staphylococcus aureus (S. aureus), Methicillin-resistant Staphylococcus aureus (MRSA), public health

Statin treatment and serum low-density lipoprotein (LDL) level in the Birjand elderly dwellers: Birjand Longitudinal Aging Study (BLAS) Wave۳ (Research Paper)

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Introduction: Elderly people have a greater risk than others to develop atherosclerotic disorders. Statins are the most efcient treatments against atherosclerosis; however, the pros and cons of the treatment should be put in balance in regard to the target level of low-density lipoprotein cholesterol (LDL-C). This study evaluates the level of LDL in the Birjand elderly population and determines the achievement of target LDL-C level, according to the American College of Cardiology (ACC) guidelines.

Methods: A retrospective observational study of statin therapy was performed from October ۲۰۱۸ using Birjand community health assessment data of the BLAS project. We used the ۲۰۱۸ ACC/AHA guidelines to determine the achievement of tar get LDL level in statin treated patients with clinical atherosclerotic cardiovascular diseases (ASCVD), or elderly high risk diabetic patients and dyslipidemia ones, in the Birjand elderly dwellers, stratifed by statin treatment intensity. Statin and non-statin users were also compared in terms of demographic and laboratory fndings. Mann-Whitney U test and Chi-Square test were used for data analysis

Results: Out of ۱٤۱۸ elderly residents in this study, ٦۸۳ individuals (٤۸,۲٪) were male with a mean age of ٦۹,۷۳±۷,٥٦ years. The total mean level of LDL-C in elderly participants was ۱۲۲,۸۳±۳٦,۲۱ mg/dL. The mean level of LDL-C in statin use and none statin use group was ۱۰٤,۹۷±۳٦,۰۱ and ۱۲۹,۰۹±۳٤,۱٤, respectively. Only ۳۰٤ (۲۹,۲٪) of participants who were eligible for statin administration used the statin. While ٦۹ (۱۸,۳٪) individuals from ۳۷۸ (۲٦,۷٪) were using statin though they were not eligible for it. In the clinical ASCVD group, ۳۹ (۲۸,۳٪) of elderly participants achieved target LDL-C based on the ACC/AHA guideline. This was ٥۸ (۳۷,٤٪) for other participants with LDL-C ≥۱۹۰ mg/dL, diabetic or participants with Framingham Risk Score (FRS) ≥۱۰٪.

Conclusion: The majority of patients who were eligible for high or moderate-intensity statin treatment had not received statin. Only one third of clinical ASCVD patients and almost half of high risk patients achieved LDL-C target values. Find ings illustrate current treatment may need to be reconsidered in Birjand elderly dwellers treated with statin and physicians, should be updated on the use of statins.

Keywords: Elderly · Atherosclerosis · Statin · Low-density lipoprotein

stem cell (Review)

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1. kherad

Introduction: It has been a long time since stem cells were discovered, but there is still vague information about it and it has many uses for the treatment of various diseases. These cells have capabilities that separate them from other cells; They regenerate themselves and have the ability to differentiate into different types of cells. These cells are taken from healthy people and injected into sick people. Treatment of some diseases with stem cells is definitive, but not for many diseases. It can have a definitive treatment for many cancers and strokes

Methods: There are different types of stem cells and they can help treat diseases in different ways. Since diversity is seen among stem cells, it can be concluded that they have various applications

Results: Today, it has been proven that stem cells are able to treat a wide range of chronic and acute diseases, and a lot of research is being done in the field of using stem cells in the treatment of diseases such as Parkinson's, heart disease, liver disease, diabetes, muscular dystrophy, spinal cord injuries, and stroke.

Conclusion: Stem cells are used in the treatment of few diseases. Diseases that are autoimmune are not treated with stem cells

Keywords: stem cells medical

Stem Cell Therapy for Liver Diseases: Current Perspectives (Review)

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Introduction: Stem cells have distinctive regenerative properties that are crucial for the progress of cell therapy and tissue engineering, especially in the context of liver diseases. This abstract explores the contributions of different types of stem cells in liver cell therapy and tissue engineering, highlighting their ability to repair liver damage and develop functional liver tissues.

Methods: A systematic review of current literature was performed, focusing on hematopoietic stem cells (HSCs), mesenchymal stem cells (MSCs), induced pluripotent stem cells (iPSCs), and embryonic stem cells (ESCs). The review included analysis of differentiation protocols, therapeutic outcomes in preclinical and clinical studies, and advancements in liver tissue engineering techniques such as three-D bioprinting, organoid formation, and scaffold-based tissue constructs.

Results: Mesenchymal stem cells (MSCs) and induced pluripotent stem cells (iPSCs) demonstrated considerable potential for differentiating into hepatocyte-like cells and proved effective in preclinical models of liver disease, resulting in enhanced liver function and decreased fibrosis. Notably, iPSCs hold great promise for personalized therapy because of their capability to produce patient-specific hepatocytes. Additionally, tissue engineering strategies utilizing stem cells have facilitated the creation of functional liver organoids and scaffold-based liver tissues; however, challenges regarding tissue scalability and long-term functionality remain.

Conclusion: Stem cells play a vital role in the progress of liver cell therapy and tissue engineering, providing novel strategies for liver regeneration and the treatment of diseases. However, challenges such as immune compatibility, the potential for tumor development, and scalability must be tackled. Ongoing research and technological innovations are essential to enhance the use of stem cells in liver therapy and to address these challenges effectively.

Keywords: Stem cells, liver cell therapy, liver tissue engineering, hepatocytes, mesenchymal stem cells.

Stem Cell Therapy in Cancer Treatment (Review)

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Introduction: Introduction: As non-specialized cells in the body, stem cells can differentiate into various cell types. Totipotent stem cells are present in the early stages of embryonic development and can divide and differentiate into cells of the entire organism. In addition, stem cells also act as the body's internal repair systems. Physical contact between cells or chemical secretions from the surrounding and internal tissues are the signals involved in the specialization process of stem cells. Stem cells can be divided into embryonic, germinal, and somatic. Despite recent advances in cancer treatment, this disease remains the leading cause of death and complications worldwide. Since stem cells can self-renew and have a high replication potential, the use of stem cells in cancer treatment is one of the methods that has been used for decades. Stem cell therapy has become a promising and advanced scientific research topic. The development of treatment methods has raised great expectations. A wide variety of options makes this cutting-edge therapy a turning point in modern medicine and offers hope for untreatable diseases. This study aims to investigate different types of stem cells for cancer treatment.

Methods: Methods: After searching Google Scholar and PubMed, we focused on exploring the role of human stem cells in cancer treatment. We used the keywords “stem cell” in combination with “treatment,” “therapy,” and “cancer” to refine our search. Based on our search objective and topic, we specifically selected articles dealing with clinical and laboratory studies. The articles we reviewed spanned the years ٢٠٠٦ to ٢٠٢٠. It is important to note that our categorization of articles was based on their findings, not organization by year.

Results: Results: In ٢٠٠٦, scientists Shin'ya Yamanaka and Kazutoshi Takahashi made a step forward in stem cell therapy, finding the conversion of multipotent stem cells into highly potent ones. ASCs are more accessible and less ethically restricted, finding wide applications in both therapeutic purposes and research. Among ASCs, mesenchymal stem cells (MSCs) have shown multiple capabilities in therapeutic targets. MSCs can suppress tumor growth by inducing immune responses. This type of stem cell is a viable option for cell delivery within tumor stroma to deliver drugs effectively. Additionally, MSCs can aid in minimizing side effects like bleeding by suppressing the immune system's rejection of transplants and assisting in bone marrow repair. Cancer stem cells (CSCs) are found in tumors. It has been reported that CSCs have been functionally involved in the development of cancer through several mechanisms that include tumor growth, metastasis, and recurrence. Selective targeting of CSCs throughout their development may thus provide very interesting opportunities for the design of therapeutic strategies for the treatment of a variety of solid tumors. Neural stem cells (NSCs) are self-renewing and generate new neurons and glial cells; they exist in the central nervous system of all animals. Extensive research using NSCs for the treatment of primary and metastatic breast, lung, and prostate cancers has recently been done in murine models.

Conclusion: Conclusion: The advantages of stem cells may revolutionize cancer treatment due to new, different avenues for therapies opened up. Various forms of stem cells have been used for cancer treatments dependent on their inherent competency. Based on the good results of the past, it should continue efforts on the improvement of the methods of stem cell therapy in cancer treatment in the future.

Keywords: Keywords: Stem cell, Treatment, Therapy, Cancer, MSCs

Stem Cell-based Tissue Engineering Approaches for Musculoskeletal Regeneration (Review)

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Introduction: The fields of regenerative medicine and tissue engineering have grown dramatically since their early inception in the ۱۹۶۰s and ۱۹۷۰s. Early attempts simply sought to transplant somatic cells into a lesion area but typically led to little or no success. The development of biomaterial scaffolds further advanced tissue engineering by allowing for the creation of biomimetic environments that enhanced cell maintenance and differentiation. While somatic cells, such as osteoblasts and chondrocytes, were among the first cell sources to be used in various tissue engineering applications, the prospects of tissue engineering were given new momentum with the addition of stem cells to the pool of cell choices. Adult tissue-derived stem cells, including mesenchymal stem cells (MSCs), became the backbone for cell therapies due to their expansion and multipotent potential, and demonstrated success in clinical applications. Further, stem cells may be more advantageous than somatic cells due to their tendency to favor anabolism instead of catabolism, whereas somatic cells are more so poised to maintain tissue homeostasis. Additionally, the isolation of somatic cells can induce donor site morbidity, and somatic cells limit the potential of allogeneic cell therapy due to their immunogenicity. The isolation of embryonic stem cells (ESCs) by Evans and Kaufman in ۱۹۸۱ from mouse embryos and by Thomson from human embryos in ۱۹۹۸ further stimulated the field by providing a cell source with seemingly infinite expansibility. Tissue engineering approaches are now conceivably able to target and derive almost any cell in the body. Stem cell-based research has exploded in recent years, attracting a great deal of scientific and public attention. An overarching goal of stem cell-based research is to understand how tissues/organs are formed and diseases develop, and in so doing, develop more effective therapies to treat diseases that are otherwise difficult to cure by current medical procedures. The isolation of ESCs is considered one of the major milestones fueling this movement, as it has provided a reliable tool to study tissue/organ formation and pathology and thus paved the way for fields like regenerative medicine and tissue engineering to emerge.

Methods: ۱. In vitro Differentiation of Stem Cells: Researchers can direct the differentiation of stem cells (such as mesenchymal stem cells or induced pluripotent stem cells) into specific lineages such as osteoblasts (bone cells) or chondrocytes (cartilage cells) under defined laboratory conditions. This can be achieved through manipulating the culture conditions, including growth factors, extracellular matrix (ECM) components, and mechanical stimuli. ۲. Scaffold-Based Approaches: Scaffolds made of biocompatible materials (e.g., hydrogels, polymers, ceramics) can be used to support stem cell attachment, proliferation, and differentiation. These scaffolds can be engineered to mimic the native ECM of musculoskeletal tissues, providing the necessary mechanical and biochemical cues for tissue formation. ۳. Combination with Growth Factors and Cytokines: The incorporation of bioactive molecules, such as growth factors (e.g., bone morphogenetic proteins, transforming growth factor-beta) can enhance stem cell differentiation and promote tissue repair. These factors can be

incorporated into scaffolds or delivered in a sustained manner at the site of injury. ٤. Gene Therapy: Engineering stem cells to express specific genes that promote proliferation and differentiation can enhance their therapeutic potential. This can involve the use of viral or non-viral vectors to deliver the genes of interest. ٥. Physical Stimuli: Applying mechanical or electrical stimuli to stem cells can influence their behavior and promote differentiation toward musculoskeletal lineages. Techniques such as bioreactor systems can provide dynamic culture conditions that simulate the in vivo environment. ٦. Decellularized Matrices: Decellularized tissues derived from donors can serve as scaffolds that retain native ECM components while removing cells. These matrices can provide a natural microenvironment for stem cells, facilitating tissue regeneration when transplanted into the body. ٧. Combination of Stem Cells with Other Therapies: Combining stem cell therapy with other treatment modalities, such as physical rehabilitation or pharmacological interventions, may improve outcomes in musculoskeletal regeneration.

Results: Stem cell-based tissue engineering offers promising solutions for musculoskeletal regeneration, addressing issues such as bone fractures, cartilage damage, and tendon injuries. Mesenchymal stem cells (MSCs), embryonic stem cells (ESCs), and induced pluripotent stem cells (iPSCs) are key players due to their ability to differentiate into bone, cartilage, and muscle tissues. Scaffold-based systems, growth factor delivery, and gene editing are central approaches that enhance tissue repair. These strategies show potential in bone regeneration, cartilage repair, tendon healing, and muscle regeneration. While challenges like immune rejection and scalability remain, advances in biomaterials and gene editing hold promise for future clinical applications.

Conclusion: Multiple factors regulate the self-renewal and differentiation of relevant stem cell types into musculoskeletal lineages, and elucidation of environmental cues directing appropriate cell activities has greatly advanced the field of tissue engineering. However, for in vitro tissue engineering products to become a clinical reality, studies investigating the combined effect of multiple environmental cues will need to be conducted. For example, studies investigating the role of GFs during a specific stage of the tissue engineering process are typically carried out under normoxic conditions, and it is entirely possible that the observed effects from these studies would not persist under hypoxic conditions, which are more physiologically relevant. More importantly, however, researchers will need to find conditions that can improve the resulting phenotype of differentiated musculoskeletal cell types. For chondrogenesis, we still need to determine how to reproducibly repress the hypertrophic and fibrocartilaginous characteristics of chondrocytes derived from MSCs, and for ESCs, we likely need to expand upon the three-step differentiation protocol from Oldershaw and colleagues to further enhance the chondrogenic differentiation program. For osteogenesis, MSCs appear quite adept at differentiating into osteoblasts in vitro, but the challenge will be engineering a vascularized tissue of physiologically relevant architecture. To this end, the most promising avenue may be exploiting the ability of hypertrophic chondrocytes to recapitulate endochondral ossification when implanted in vivo.

Keywords: Tissue engineering, musculoskeletal tissues, biomaterial scaffolds, stem cell regulation,

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Stem Cells **(Review)**

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Introduction: aw-bone defects caused by various diseases lead to aesthetic and functional complications, which can seriously afect the life quality of patients. Current treatments cannot fully meet the needs of reconstruction of jaw-bone defects. Thus, the research and application of bone tissue engineering are a “hot topic.” As seed cells for engineering of jaw-bone tissue, oral cavity-derived stem cells have been explored and used widely. Models of jawbone defect are excellent tools for the study of bone defect repair in vivo. Diferent types of bone defect repair require diferent stem cells and bone defect models. This review aimed to better understand the research status of oral and maxillofacial bone regeneration.

Methods: For some patients with end-organ dysfunction, whole organ transplantation is an established treatment option. However, the limited availability of suitable autologous tissues, the risk of immune-mediated rejection, the required chronic immunosuppression treatment, and the possibility of disease transmission, highlight the need of new therapeutic approaches. Tissue engineering and regenerative medicine strategies have triggered intense attention due to the potential to develop remedies for damaged, malfunctioning, or injured tissues. Cell-based therapies, in their natural form or modified/engineered for a specific purpose, hold much promise in this regard. Indeed, in light of their multiple sources as well as therapeutic versatility, mesenchymal stem cells (MSCs) have been proposed as the most appropriate cell source for these applications .As stem cells, they exhibit beneficial characteristics as compared to terminally differentiated cells, including the potential to circumvent immuno-reaction in vitro and in vivo and to differentiate towards a broad range of specific Cells ٢٠٢٠, ٢ of ٢٧ cell lineages. MSCs can be isolated from various tissue types including bone marrow, adipose, umbilical cord, peripheral blood, liver, periodontal ligament, lung and many others [٨]. However, despite their potential and promise, MSCs face many challenges, such as their variability, scalability and delivery, as well as ethical considerations and safety issues, which challenge their clinical utility. EVs are heterogeneous lipid bilayer-surrounded vesicles secreted by all cell types, not only MSCs, and act as mediators of intercellular communication. EVs are involved in numerous physiological and pathophysiological biological processes, including modulating immune responses, homeostasis maintenance, coagulation, inflammation, angiogenesis, and cancer progression. According to their size, dimension and origin, they can be classified in many ways, with the preferred terms now being small EVs, medium-sized EVs, and large EVs. There is increasing evidence that many, if not all, of the beneficial effects of MSCs may be attributed to their paracrine action via the release of extracellular vehicles, rather than cellular engraftment and response to the site of injury, suggesting that MSC-EVs can produce any therapeutic benefits of MSCs. Added to their attractiveness, compared to the original MSCs, MSC-EVs cannot self-replicating, preventing safety concerns associated with cell therapy, such as

uncontrolled cell division and cellular contamination with tumorigenic cells. Moreover, as MSCs often require invasive procedures in order to be isolated, approaches that only require them to be cultured in vitro and their released product used gives hope for increased scalability and yield per MSC batch, with filtration suggested to be suitable sterilisation because of their small size. Herein, we review current advancements of the therapeutic potential of MSC-EVs in tissue engineering and regenerative medicine, considering the molecular mechanisms suggested for the MSC-EV action where possible. Cells ٢٠٢٠, ٩, x FOR PEER REVIEW ٢ of ٢٩ variability, scalability and delivery, as well as ethical considerations and safety issues, which challenge their clinical utility. EVs are heterogeneous lipid bilayer-surrounded vesicles secreted by all cell types, not only MSCs, and act as mediators of intercellular communication. EVs are involved in numerous physiological and pathophysiological biological processes, including modulating immune responses, homeostasis maintenance, coagulation, inflammation, angiogenesis, and cancer progression. According to their size, dimension and origin, they can be classified in many ways, with the preferred terms now being small EVs, medium-sized EVs, and large EVs. There is increasing evidence that many, if not all, of the beneficial effects of MSCs may be attributed to their paracrine action via the release of extracellular vehicles, rather than cellular engraftment and response to the site of injury suggesting that MSC-EVs can produce any therapeutic benefits of MSCs. Added to their attractiveness, compared to the original MSCs, MSC-EVs cannot self-replicating, preventing safety concerns associated with cell therapy, such as uncontrolled cell division and cellular contamination with tumorigenic cells.

Results: Moreover, as MSCs often require invasive procedures in order to be isolated, approaches that only require them to be cultured in vitro and their released product used gives hope for increased scalability and yield per MSC batch, with filtration suggested to be suitable sterilisation because of their small size. Herein, we review current advancements of the therapeutic potential of MSC-EVs in tissue engineering and regenerative medicine, considering the molecular mechanisms suggested for the MSC-EV action where possible.

Conclusion: The type of cell and animal model should be selected according to the specifc research purpose and disease type. This review can provide a foundation for the selection of oral cavity-derived stem cells and defect mod els in tissue engineering of the jaw bone.

Keywords: Oral cavity-derived stem cells, Models, Jaw-bone defects, Bone tissue engineering

Stem Cells The Magic Keys to Innovative Medical Treatments (Review)

fatemeh bigdeloo,[1,*]

[1]. Farzanegan shalbaf

Introduction: Stem cells have extensive applications in medical and therapeutic fields: ١. Treatment of Blood Disorders: Hematopoietic stem cells are used to treat conditions such as leukemia and chronic anemia. Bone marrow transplantation is one of the therapeutic methods based on these cells. ٢. Treatment of Neurological Disorders: Research suggests that stem cells can aid in repairing damaged brain tissues and treat neurological disorders like Parkinson's and Alzheimer's diseases. ٣. Regenerative Medicine :Stem cells can assist in the recovery and repair of damaged tissues from accidents, burns, and major surgeries. Clinical trials indicate successes in this area. ٤. Controlled Drug Delivery: Programming stem cells to produce drugs and proteins is another significant application of this technology.

Methods: Research on stem cells is conducted through various approaches. ١. Data Collection :Utilizing credible databases to gather scientific and medical information. ٢. Experimental Research: Conducting experiments on stem cells in laboratory settings to investigate their capabilities. ٣. Clinical Studies :Performing clinical trials to evaluate the effectiveness of stem cell-based treatments in real patients.

Results: Research results indicate that stem cells can be effective in treating various diseases, especially blood disorders and neurological issues.

Conclusion: Stem cells represent a modern tool in contemporary medicine with high potential for disease treatment. However, the existing challenges regarding ethics, medical risks, and regulations concerning various types of stem cells require further attention and examination. The future of this field depends on our ability to address these challenges and responsibly utilize these technologies

Keywords: regenerative medicine

Stem cells, what they can do for us? (Review)

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Introduction: Stem cells are unspecialized cells with the ability to differentiate into other cells. In addition, they have the ability to self-renew, and these characteristics of stem cells have made scientists pay attention to these cells.

Methods: This study was searched in Google Scholar and PubMed databases using the keyword "stem cells". We only reviewed review articles and provided information obtained from the articles to the corresponding author. Finally, the obtained information was categorized.

Results: These categories include: A) definition of stem cells and types of them, B) identification and history of stem cells, and C) application of stem cells. And then we categorized the applications of stem cells as follows: ١) Pharmaceutical research: Investigating the molecular mechanisms of proteins or genes using stem cells can be useful for the targeted identification of drugs and investigate a specific drug. In addition, using stem cells can reduce the use of animal or human models, for example, stem cells can be used to study diseases pattern. ٢) Disease modeling: This model is also similar to the previous one and instead of using animal and human models, diseases can be studied at the cellular level. ٣) organ production: As mentioned, stem cells have the ability to differentiate and produce new cells and eventually tissues. Therefore, using stem cells, studies can be done at the cell and tissue level. ٤) Treatment of diseases: One of the successful treatment strategies for blood disease and related diseases is hematopoietic stem cell transplantation.

Conclusion: Due to their characteristics, stem cells can be widely used in regenerative medicine, and during the past years, by studying stem cells, new solutions have been suggested for their use.

Keywords: Stem cell, differentiate, regenerative medicine

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Stimulation of the αV Nicotinic Acetylcholine Receptor Protects Against Acute Lung Injury Induced by Surfactant Depletion (Research Paper)

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Introduction: The cholinergic anti-inflammatory pathway (CAP) has been identified as a key regulator of inflammatory responses in several animal models of lung injury. The alphaV nicotinic acetylcholine receptor (αVnAChR) is a crucial component of this pathway. This study aimed to determine the role of αVnAChR in a saline-lavaged rat model of acute lung injury. To investigate this, nicotine was administered as an agonist, while Methyllycaconitine citrate (MLA) was used as an antagonist of αVnAChR.

Methods: Male Sprague Dawley rats were divided into four groups: Sham, saline lavage (LAV), LAV treated with nicotine (LAV+NIC), and LAV treated with both nicotine and MLA (LAV+NIC+MLA). Tracheostomy and catheterization of the femoral artery were performed under deep anesthesia. The animals were subjected to volume-controlled ventilation and lung injury through ١٠ repeated saline lavages (٣٠ ml saline at ٣٧ °C). The recovery phase lasted for ٣ hours, and drugs were injected ١ hour after the last lavage. We assessed mean blood pressure (MBP), heart rate (HR), maximal inspiratory (MIP) and expiratory (MEP) airway pressures, gas exchange across the blood-gas barrier, lung compliance, immune cell counts in the blood and bronchoalveolar lavage (BAL), malondialdehyde (MDA) levels, and lung histological scores.

Results: MBP, HR, PaO٢, PaO٢/FiO٢ ratio, and pH decreased, whereas MIP and MEP, and PaCO٢ increased ١ hour after the saline lavage. Nicotine corrected entirely all the above parameters in the LAV+NIC group. MLA prevented the effects of nicotine on the above parameters, except that MLA had no extra effect on MIP or MEP. In addition, nicotine improved lung compliance in the LAV+NIC group, though it was inhibited by MLA in the LAV+MLA+NIC group. The increases of plasma and lung tissue MDA in the LAV group were diminished by nicotine, whereas, MLA prevented these reductions. Total BAL cell count and lung histological scores were attenuated by nicotine in the LAV+NIC group, whereas, MLA reversed the mentioned alterations in the LAV+MLA+NIC group.

Conclusion: These findings highlight that nicotine exerts a protective anti-inflammatory effect in lung injury induced by saline lavage through the cholinergic αVnAChR pathway.

Keywords: Lung, Nicotine, MLA, Salin lavage, αVnAChR

Study effect mesenchymal stem cells and exosomes for Parkinson disease (Review)

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Introduction: Parkinsons disease(PD) is the second most common neurodegenerative disorder nearly a ffecting ٢٪ of the population over the age of ٦٥. PD is characterized by a progressive loss of dopaminergic neurons of the substantia nigra/causing a number of motor symptoms to arise. Including tremors/ rigidity and bradykinesia with postural instability appearing in patients as the disease progresses. Another characteristic feature of PD is the existence of lewy bodies (LB) which are composed of the misfolded aggregates of αsynuclein(α-syn) protein.

Methods: We reviwed about ٢٢ article were conducted frome ٢٠١٨ to ٢٠٢٣ in the word and iran. We searched some key words such as mesenchymal stem cell, exosome, parkinsons disease, miRNA, cell and tissue therapy Elsevier, pubmed and SID

Results: In ٢٠١٨, at leats ٥ major autosomal dominant genes/ ٥ autosomal recessive or x-linked factors and ١١ monogenetic mutation for other disorders that present with parkinsonian like symptoms have been identified. The missense mutation (A٥٣T) resulted in autosomal dominant PD inheritance that could be tracked through the hereditary line with almost full penetrance. Additionally, five other missense mutations to the SNCA gene, A٣٠P, E٤٦K, H٥٠Q, G٥١D and G٢٠٩A have also been reported with varying ages PD onset two genes phosphate and tensin homolog induced putative kinase١ (PINK١) and Daisuke Junko١(DJ-١) are of special interest because they are involved in neuronal survival under cellular stress. Additionaly an astute clinical observation of the comorbidity between gaucher disease (GD) and (PD) led researchers to examine other proteins with suspect. GD is an autosomal recessive disease resulting from homozygous mutations to housekeeping glucocerebrosidase gene(GBA). GBA alysosomal enzyme of the CNS, is thought to also have a role in protein aggregation in PD when mutated. Exosomes are EV derived from the endosomal complex. EVs are divided into three categories based on their size/ cargo and origin: exosomes microvesicles and apoptotic bodies. Phosphatidyl serine(PS) for exampls is involved in exosome sprouting and merging due to its enhanced flexibility. Lysosomal associated membrance protein(LAMP) tetraspanins (CD٨١, CD٨٢, CD٩, CD٦٣) GTPase major histocompatibility complexI and Π (MHCI/Π) CD١٣ intercellular adhesion molecule١(ICAM١) fusion proteins such as tumor susceptibility gene ١٠١ protein(TSG١٠١) , annexin, integrin, heat shock protein ٩٠(HSP٩٠) and HSPV٠ are other molecules found abundantly in exosomal membranes. Messenger RNAs(mRNA) and microRNAs(miRNA) are also found in exosome and can carry genetic information to target cells. Exosomes produced from MSCs have also been found to contain cytokines and growth factors such as IL٦, IL١٠, HGF and TGFβ١ all of them have role in regulating the immune system. Comparable quantitive of extracellular matrix metalloproteinase٩ (MMP-٩) and VEGF have been found in MSC derived exosomes all of which are important in inducing angiogenesis which may be essential for tissue repair. Exosomes containing modified α-syn siRNA reduced the amount of αsyn mRNA

transcription and translation in the brain of transgenic mice. Moreover, exosomal shRNA minicircles to target αsyn in a PD mause model resulted in reduced Asyn aggregation, decreased dopaminergic neuron death and improved clinical symptoms. Thus exosomes present a promising avenue for delivering therapeutic agents or genetic modulators to attenuate neuroinflammation in PD which may complement the cell therapy approach with iPSC derived dopaminergic neurons.

Conclusion: PD is the most common movement disorder, other movement disorders exist such as multiple system atrophy, progressive supranuclear palsy, chorea, ataxia and dystonia. Some movement disorders have similar symptoms to PD such as tremor, slow movement and rigidity .exosomes can affect gene expression and protein biological activity via receptor cells through the messenger RNAs and proteins that they carry. Furthermore exosomes from different sources carry different proteins and lipids and many exosome carry sprcific proteins. Levodopa/carbidopa, a combination medicine that increases the amount of dopamine in the brain, is the most common medication for PD (١). Doctors may use other medicines such as anticholinergics to reduce involuntary muscle movement.

Keywords: mesenchymal stem cell, exosome, parkinsons disease, miRNA, cell and tissue therapy

Study of antimicrobial activity of different propolis extracts on gram positive and gram negative bacteria: a review article (Review)

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Introduction: Propolis (bee glue) is a sticky, dark-colored resinous substance that honey bees collect from plants and use in the hive, which contains large amounts of biologically active compounds. The word "propolis" is a compound word derived from two Greek words (pro = before) and (polis = city), meaning the last defensive point before the city (or hive). Due to its waxy nature and mechanical properties, bees use propolis in the construction and repair of their hives, to seal cracks and smooth the inside of the walls, as a protective barrier against external invaders such as snakes, lizards, etc. or against wind and rain. It has a color from dirty yellow to dark brown, strong and good smell, insoluble in Studies have shown that plant chemicals such as flavonoids (quercetin), phenols (gallic acid), alkanoids, amino acids, etc. can be responsible for the medicinal properties of propolis, and the inhibitory effect of propolis on microorganisms depends on the synergy of these compounds.

Methods: This study was conducted in order to investigate the antimicrobial properties of different propolis extracts on gram-positive and gram-negative bacteria, and to use it for the prevention and treatment of various diseases. Investigation and determination of chemical compounds of propolis was done using a mass chromatography spectrometer (GC-MS) and the antibacterial activity of the extracts was evaluated using the well agar diffusion method. The physicochemical properties of the propolis sample (such as ash, moisture, soluble solids, insoluble solids and metal elements) were measured. The minimum inhibitory concentration (MIC) of propolis was determined using the broth dilution method.Search for this study They have databases in Google Scholar and Elsevier Used.

Results: Antibiotic resistance among microbes urgently requires the development of new antimicrobial agents such as alternative therapies using natural products. Propolis was found to inhibit influenza-resistant Candida glabrata. Other studies showed that the ethanol extract of propolis inhibited several drug-resistant bacteria, MRSA, Enterococcus spp, and Pseudomonas aeruginosa. However few studies have been published on its effects against resistant pathogens. Antibiotic resistance in bacteria is the inherent product genetics. The most widely used antibiotics are beta-lactams. The most common mechanism of resistance to beta lactams among bacteria includes the production of beta-lactamase. The prevalence of MBLs is increasing worldwide, especially among Pseudomonas aeruginosa and recently among other Gram-negative bacteria. Therapeutic control of betalactamase-producing bacteria has been one of the most important clinical problems of bacteria for more than ٥٠ years.

Conclusion: The studies show the existence of many plant chemicals such as alkaloids, flavonoids, phenols, amino acids and fatty acids, which can be antibacterial, antiviral, antifungal and

antioxidant, anti-cancer, anti-wound and antidamage. , anti-inflammatory and anti-diabetic. Experiments showed that propolis is more effective against gram-positive bacteria than gram-negative bacteria (due to the structure of the outer membrane of gram-positive bacteria and the hydrolytic enzymes produced by gram-negative bacteria).

Keywords: bee glue Phytochemical characteristics gram-positive bacteria antiviral antiwound

Study of Anxiety and depression in Adults Suffering from Epilepsy (Review)

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Introduction: Epilepsy is one of the most important diseases of the nervous system caused by sudden electrical discharge,alternative and extreme of brain neurons and because this disease is chronic and life-long often causes mental illnesses such as anxiety disorders and depression, influences the life quality of these patients. Therefore, considering the importance of this matter this study review was done on the spread of anxiety disorders and depression.

Methods: This article has been done in a systematic review in order to examine the spread of anxiety disorders and adult epilepsy. To track down the source articles used go to PubMed, Scholar, Medline, SID, CINAHL, Scopus, Elsevier, Iran Doc and Magrian. From ٢٠١٠ to ٢٠٢٤ with emphasis on the last ٤ recent years. Searching articles for sources with keywords such as: Anxiety, depression, epilepsy, adults, also combinations and independent words were extracted using boolean operators.

Results: According to results of the study research, the spread of anxiety and depression among epileptic patients is high. However, the review of studies shows that the prevalence of depression and anxiety is almost the same in these patients.

Conclusion: Considering the fact that this disease is strongly chronic and high spread of mental disorders like anxiety and depression and physical-psychological consequences in such patients; prevention and early detection is of high importance.

Keywords: Anxiety, depression, epilepsy, adult.

Study of Negative effect of Ag/ZnO nanoparticles on the green alga Chlorella Vulgaris (Research Paper)

ROGHAYYEH JAHEDI,[١,*]

١.

Introduction: Nanotechnology is the science of using nano-sized materials and tools, and the word nano means dwarf, which has Greek roots. Nano means one billionth (١٠-٩) and nanoparticles have a size of ١- ١٠٠ nm. Nanoparticles have various applications in chemistry, the food industry, pharmaceutical, medicine, biotechnology, agriculture, cosmetics, textile, wastewater treatment, etc. Algae are the simplest organisms with chlorophyll that lack roots, stems, leaves, reproductive organs, and embryos. Algae are used to produce marine omega-٣ fatty acids, including DHA and EPA, which are very important for health. Algae are found in water, wet soil, trees and rocks and are the main source of atmospheric oxygen production by taking in carbon dioxide and using plant photosynthesis. Algae are rich in protein, polysaccharides, antioxidants, minerals, and vitamins. Algae are also widely used in Agribusiness. Chlorella vulgaris is a single-cell green algae with a spherical shape and a size of ٥ to ١٠ microns, and it is one of the oldest algae on the planet, which is used as a laboratory model due to its high resistance. Ag/ZnO nanoparticles have catalytic photocatalytic and antimicrobial properties.

Methods: Synthesis of Ag/ZnO and treatment Ag/ZnO The nanoparticles used in the present study were synthesized by Dr. Baharak Divband in the Faculty of Chemistry of Tabriz University. A solution of ٥٠ mg/L was prepared from zinc oxide nanoparticles doped with silver, and to prevent nanoparticles from agglomeration, they were dispersed in an ultrasonic bath. ١, ٢,٥, ٥, and ٧,٥ Ag/ZnO nanoparticles were removed from the prepared solution and added to ٤ groups of algae with ١٠٠ ml size. The control group was also prepared from algae.

Results: After treating the studied algae with ١, ٢,٥, ٥, and ٧,٥ Ag/ZnO and measuring the activity of the SOD enzyme after ٢٤ hours of treatment, a significant increase in the activity of this enzyme ($p < ٠,٠٥$) showed in the mentioned concentrations. This increase in activity was not significant between ٢,٥ and ٥ concentrations and was significant at ٧,٥ concentrations. Catalase is an antioxidant enzyme found in the chloroplast, mitochondria, peroxisome, and cytosol of plant cells and can convert $H_٢O_٢$ into $H_٢O$ and $O_٢$. In the present study, the amount of catalase enzyme increased with increasing concentration of Ag/ZnO nanoparticles. The images prepared by scanning electron microscope showed significant morphological changes in the surface of Chlorella vulgaris algae in the treatment with Ag/ZnO nanoparticles. Morphological changes were visible on the surface of Chlorella vulgaris cells. The toxicity of Ag/ZnO on C. vulgaris suggests changes in morphology and dimensions.

Conclusion: Our studies on the effect of Ag/ZnO nanoparticles on Chlorella vulgarisshowed the morphological changes of algae in the presence of these nanoparticles and damage to the wall and plasma membrane. increase the antioxidant activity of SOD and CAT enzymes and decrease the

amount of H_2O_2 due to the activity of these enzymes it shows. Chlorophyll a, b, and total chlorophyll and carotenoids showed a significant decrease in the presence of Ag/ZnO nanoparticles, which indicated the toxicity of these nanoparticles on Chlorella vulgaris.

Keywords: Nanotechnology_ ROS_ Nanomaterials_ Cytotoxicity_ Antioxidant Enzymes_ Chlorella vulgaris_ SEM

Study of single nucleotide polymorphisms RS۹٦٤۳۷۲ and RS۸۰۵۲۳۳٤ , MT۱B gene associated with breast cancer patients among Iranian ancestries (Research Paper)

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Introduction: Breast cancer is one of the most common malignancies affecting women worldwide. As research continues to discover genetic factors that contribute to breast cancer risk, the importance of specific genetic polymorphisms has become an important point. Genetic polymorphisms can increase breast cancer risk by modulating gene expression levels or protein structure. Two of the lesser-known polymorphisms associated with some diseases and cancer are the intronic polymorphism ۳:c.۹۵-٦۸T>C (rs۸۰۵۲۳۳٤) and ۳:c.۲۸+۱۳۷C>G (rs۹٦٤۳۷۲) in the MT۱B gene. It was investigated for its possible association with the risk of breast cancer. This paper presents a study investigating whether polymorphism ۳:c.۹۵-٦۸T>C (rs۸۰۵۲۳۳٤) and polymorphism ۳:c.۲۸+۱۳۷C>G (rs۹٦٤۳۷۲) are associated with breast cancer susceptibility.

Methods: Our research analyzed two groups: ۱۰۰ samples from individuals diagnosed with breast cancer and ۱۰۰ healthy control samples. We applied the Tetra-ARMS PCR method to detect the presence of ۳:c.۲۸+۱۳۷C>G (rs۹٦٤۳۷۲) and ۳:c.۹۵-٦۸T>C (rs۸۰۵۲۳۳٤) polymorphisms. This technique is known for its efficiency and accuracy in detecting specific genetic variants, which allows reliable comparison between two groups.

Results: Data analysis showed that CC allele and AA allele in rs۹٦٤۳۷۲ polymorphism and TC allele and CC allele in rs۸۰۵۲۳۳٤ polymorphism have the highest and lowest frequencies, respectively (p value>۰,۰۵). In addition, these two polymorphisms in the MT۱B gene did not show a significant relationship with the risk of breast cancer. This finding suggests that, contrary to some hypotheses, these specific genetic polymorphisms may not be a risk factor for breast cancer. However, we recommend re-evaluation of these results in more diverse and larger ethnic populations and statistical groups as well as other MT۱B gene polymorphisms.

Conclusion: Our study showed that rs۸۰۵۲۳۳٤ and rs۹٦٤۳۷۲ polymorphisms in MT۱B gene have no significant relationship with breast cancer risk. These findings highlight the importance of continued research to identify genetic factors that actually influence breast cancer development. Understanding these connections is crucial to advancing personalized medicine and improving prevention and treatment strategies.

Keywords: Breast cancer ,MT۱B gene, Tetra-ARMS PCR, genetic polymorphism,rs۹٦٤۳۷۲, rs۸۰۵۲۳۳٤

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Study of the probability of type ۲ diabetes in common FTO gene polymorphisms in Iranian profiles

(Research Paper)

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۲.
۳.
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Introduction: A high genetic risk for obesity increases the likelihood of obesity-related diseases that is a global health issue. However, a healthy lifestyle can significantly reduce these risks, regardless of genetic predisposition.

Methods: This study utilized the NCBI database and the Mega Gene pharmacogenomics software to analyze genetic polymorphisms and identify potential side effects based on individual genetic makeup.

Results: Our analysis revealed that FTO polymorphisms were the most prevalent phenotype associated with type ۲ diabetes. Subsequently, we investigated the efficacy of various weight loss medications in individuals carrying common genetic polymorphisms within the Iranian genome.

Conclusion: Genetic testing for polymorphisms in common genes like: FABP۲, FTO, and MC٤R polymorphisms is crucial before obesity treatment to optimize drug selection and minimize side effects.

Keywords: obesity, genetic, polymorphisms, medication, side effects

Study of UPF۲ gene in Vitiligo (Review)

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Introduction: Vitiligo is an autoimmune and chronically acquired skin disorder characterized by white macule and pigmented patches due to the dysfunctional melanocytes attacked by immune cells, which leads to the destruction of melanocytes. It approximated a prevalence of ۰,۵٪ to ۲٪ worldwide. The pathogenesis of vitiligo is explained by the interplay of intrinsic melanocyte defects, autoimmune responses, and genetic and environmental influences. Most recent advancements in the treatment of vitiligo include novel treatments utilizing JAK inhibitors and regenerative therapies, topical corticosteroids and calcineurin inhibitors, and improvements in phototherapy techniques. Biologics, topical vitamin D analogues, and Microneedling. A recent meta-analysis revealed vitiligo to be associated with an increased risk of autoimmune thyroid diseases, alopecia errata, connective tissue diseases, pernicious anemia, and type ۱ diabetes, as well as cardiovascular risks and metabolic diseases. Some genes impact this disease, and we analysed UPF۲ gene using Bioinformatic.

Methods: Dataset collection Search the disease on the NCBI website. (https://www.ncbi.nlm.nih.gov) and then evaluate the skin and blood samples in Homo Sapiens species. Analysised the desired sample on Geo۲R and receive the result. Data processing and differential expression analysis The GSE dataset we used to download the normalized expression matrix of the microarray data. Choose two GSEs (GSE۷۵۸۱۹ and GSE۹۰۸۸۰). Next, the “limma R” packages were applied to identify DEGs in the dataset. Likewise, “GEOquery R’’ and ‘’Biobase R” and “ggplot ۲” packages were used (Log FC>, P.value< ۰,۰۵), and a Venny diagram was drawn between DEGs. Pathways & Ontology We analysised “Reactome”,” KEGG” and “Wiki Pathway” on the Enrichr website in the Pathways section. (https://maayanlab.cloud/Enrichr) Likewise, analysised “GO Biological Process”, “GO Cellular Component,” and “GO Molecular Function” in the ontologies section. And selected P.value<۰,۰۵. MiRNA-miRNA network construction and functional insights into correlated miRNA Search the UPF۲ gene on mirDB website and selected miRNA name with >۹۰ Target Score. Check the gene+miRNA and next time check the Vitiligo disease +miRNA name. We work on a topic without any previous review. lncRNA & miRNA connection Search the UPF۲ gene on the RNAinter website and changed miRNA in cat۱ column to lncRNA by Run the Filter section in Excell app. Finally, Molecular docking was done.

Results: Data preprocessing We had ۸ non-segmental Vitiligo and ٦ Control in GSE۹۰۸۸۰, and it related to the blood sample, and we found ۱۵ Normal Skin and ۱۵ Lesional Vitiligo Skin in GSE۷۵۸۱۹, and it related to Skin sample. We found a common gene on the Venny Diagram website and worked on this gene on different websites. Gene expression was higher in Skin sample. GO and KEGG enrichment analysis of autophagy-related DEG Scrutinized pathways and Ontologies in this gene and analysised this information. And choose the P value<۰,۰۵. Using R software, we performed GO and KEGG enrichment analyses to analyse the underlying biological roles of these differentially expressed ARGs. Enrichment of various functions was initially demonstrated through GO enrichment analysis.

Subsequently, GO and KEGG enrichment analyses elucidated the expression of associated genes in distinct functional enrichment sets while also highlighting potentially associated genes in several functions exhibiting significant enrichment. The results demonstrated that the most significant GO-enriched terms were involved in processes utilizing autophagy mechanisms, autophagy, cellular response to external stimulus and macroautophagy (biological processes); vascular membrane, autophagosome , autophagosome membrane and phagophore assembly site (cellular component); GTP binding, phosphatase binding, protein phosphatase binding and CARD domain binding (molecular function). In KEGG enrichment analysis, the differentially expressed ARGs were mainly involved in the processes of autophagy, influenza A, protein processing in the endoplasmic reticulum, and apoptosis

Conclusion: This disease occured more often in skin samples than in blood samples.

Keywords: Vitiligo disease, Vitiligo treatment, Vitiligo skin, White patches in skin .

Studying Related to Antimicrobial Resistance Characteristics of Nocardia (Review)

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Introduction: The aerobic, filamentous, branching, gram-positive, slightly acid-fast bacilli known as Nocardia species are widely distributed in the environment. Since inhalation is the primary mode of entry, infection typically presents as pulmonary involvement. Nevertheless, Nocardia species can also spread to numerous organs, with a preference for the central nervous system (CNS), and they can also cause primary cutaneous infections through direct injection. Most people believe that Nocardia species are opportunists that mostly infect immunocompromised persons. Approximately ٨٠٪ of patients in multiple sizable series from tertiary care facilities had impaired immune systems. Nevertheless, other data have indicated that between ٤٠٪ and ٦٠٪ of cases were immunocompetent hosts; the majority of these patients suffer from underlying illnesses such chronic lung disease, diabetes, and alcoholism. Investigating Antimicrobial Resistance Profiles of Nocardia was the goal of this investigation.

Methods: The antimicrobial resistance profiles of the nocardia study was conducted by examining academic databases including Pubmed, Google Scholar, Science Direct, and Springer.

Results: Understanding antibiotic susceptibility patterns specific to a species is crucial for providing doctors with treatment alternatives. N. asiatica, N. brevicatena/N. paucivorans, N. nova complex, N. transvalensis complex, N. farcinica, N. asteroides, and N. cyriacigeorgica have been identified in the data, in that order. In Brown-Elliott's investigation, the N. transvalensis complex (type IV drug pattern) was imipenem-susceptible, but not in Wallace and McTaggart's studies; in another study, the susceptibility was ٥٠٪. The percentage of resistance (٥٢٪) among the isolates reported by Uhde was comparable. While McTaggart et al. and others discovered that about half of the isolates were responsive to imipenem and ciprofloxacin, Brown-Elliott et al. and Wallace et al. reported that N. farcinica was susceptible to these medications. N. farcinica showed susceptibilities to these medications of ٨٨٪ and ٦٠٪, respectively, in another investigation. N. otitidiscaviarum isolates (type VII drug pattern) were found by Brown-Elliott et al. to be susceptible to ciprofloxacin; however, the majority of the isolates in the studies by Udhe et al. and McTaggart et al. These findings suggest that the genus Nocardia has complex susceptibility, and further research is needed to understand the traits and processes of this pathogen's antibiotic resistance. It is widely acknowledged that nocardiosis is becoming more common, and that because its clinical signs resemble those of tuberculosis, misdiagnoses may occur. Antituberculotic antibiotics are typically used to treat people who have been misdiagnosed, yet it is unknown how effective these treatments are. thus, examined Nocardia's resistance to seven different classes of traditional antituberculotic drugs. It surprised us to discover that the majority of Nocardia strains, particularly clinical strains, displayed resistance to common antituberculotic drugs. These findings underscore the significance of a prompt and precise diagnosis of Nocardia infections and offer significant information for clinical therapy.

Conclusion: The majority of Nocardia isolates are extremely resistant to isoniazid, according to the results, which indicate that SXT, meropenem, imipenem, linezolid, and amikacin are the most effective antimicrobial agents against Nocardia strains. many medication patterns have been found in many species, providing crucial hints for the improvement of Nocardia therapy tailored to a particular species. Therefore, wherever possible, precise taxonomic identification or susceptibility testing of clinical isolates should be carried out before starting treatment. Furthermore, scant information has been documented regarding the genetic foundation of antibiotic resistance in the Nocardia genus (such as alterations in gyrA and gyrB, which encode DNA gyrase and lead to fluoroquinolone resistance, and the presence of genes encoding β-lactamases, which result in β-lactam resistance). Thus, detection procedures should be further evaluated to ensure their reliability, and more work is required to characterize the distribution and properties of antimicrobial resistance-associated genes and mutations in the genus Nocardia.

Keywords: Antimicrobial, Nocardia, B-Lactamases, Antimicrobial

Studying the effect of gene therapy on spinal muscular atrophy (SMA) phenotype (Review)

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Introduction: Spinal muscular atrophy(SMA) is an autosomal recessive disorder caused by degeneration of alpha motor neurons in the anterior horn of the spinal cord. The characteristic symptoms are hypotonia, muscular atrophy and weakness of proximal muscles predominatly affecting the lower extremities. Before therapies were developed, SMA was classified into three main types (typesI-Ш) based on the age of onset and achieved motor milestones. The emergence of additional phenotypes broadened this classification to include congenital(type ٠) and adult onset(typeIV).

Methods: We reviwed about ٢٢ article were conducted frome ٢٠١٨ to ٢٠٢٣ in the word and iran. We searched some key words such as spinal muscular atrophy, SMA threatment, gene therapy, phenotype_genotype SMA in sciencedirect, Elsevier, pubmed and SID.

Results: The disease typically presents in infancy or childhood, leading to severe physical disability. The weakness is usually symmetrical, more proximal than distal, the legs are more affected than the arms and there is relative sparing of the diaphragm and extraocular and facial muscles. Despite relative sparing of the diaphragm respiratory insufficiency is an important complication of SMA٥q. deep tendon reflexes are generally absent or diminished. There is a brood spectrum of clinical severity with phenotypes divided into types ١-٤, determined principally by maximal motor milestone attained and age of onset. The differential diagnosis includes X-linked infantile SMA with arthrogrryposis(XL_SMA), SMA due to mitochondrial dysfunction, SMA with pontocerebellar hypoplasia (SMA-PCH/PCH١) and SMA with respiratory distress (SMA RD). SMA RD(or HMN type IV) is probably the second most commonly encountered pediatric from of SMA due to mutations in IGHBP٢. This includes lower extremity predominant SMA type١ and ٢ caused by heterozygous mutations in DYNIH١ and BLCD٢ respectively. SMN١(also called SMN where T stands for telomere spans ٢٠kb and lies in the telomeric portion of an inverted duplication of ٥٠٠kb a DNA architecture prone to rearrangements and deletions. First thought to have ٨ exons both SMN١ and SMN٢ contain ٩ exons that encode the ٢٩٤ amino acide protein, survival of motor neuron(SMN) . the exons are numbered ١, ٢a, ٢b,٣,٤,٥,٦,٧ and ٨. The stop codon for SMN occurs in exin ٧ and exon ٨ is left untranslated. SMN١ and SMN٢ vary ٨ nucleotides ٥ of which are intronic and ٣ of which occur in the last ٣ exins. Of the differences only a C to T transition in SMN٢ exon٧ (specifically C.٨٤٠ C/T) falls in a coding region and disrupts an exonic splice enhancer in exon٧. Recurrent variant have been found in exone٣ and ٦ making these two exon hot spots for small mutations and missense mutations respectively. Exon٦ codes for a domain in the protein which plays a role in protein oligomerization and those patients with exon ٦ missense mutations have decreased SMN protein self oligomerization capacity. Neurophysiological findings in patients with SMA provide support to these observations with alteration in spinal H reflexes spinal circuity and ion channel function in motor

nerves identified of therapeutic relevance increasing the excitability of motor circuits through the pharmacological inhibition of K channels ameliorated SMA in animal models. although several viral vectors including retroviruses, lentiviruses adenoviruses and herpesviruse have been considered for neurological disease indication, there has been a recent coalescence around adeno viruses(AAVs) because the are nonpathogenic and can transduce neurons. AAVs establish themselves as persistently expressing episomes with little incorporation into the host genome and can theoretically persist indefinitely in nondividing cells such as neurons. Onasemnogene abeparvovec is the next new drug that was introduced clinical practice after nusineren. The drug was developed for SMN gene (more precisely, full length SMN cDNA) transfer. Onasemnogene abeparvovec is an scAAV٩ vector based drug crossing the blood brain barrier. AAV vectors do not integrate into DNA.

Conclusion: SMA syndrome should not be confused with nutcracker syndrome (which can be an association), also a superior mesenteric artery compression disorder, where the SMA compresses the left renal vein, although some authors use the terms interchangeably. SMA results from the of SMN١ but retention its paralog SMN٢ copy number can modulate disease severity in SMA SMN٢ copy number is becoming an inclusion criterion for many clinical trials for SMA.

Keywords: Spinal Muscular Atrophy, SMA threatment, Gene therapy, Phenotype_genotype SMA,Genetic

Studying the interaction of ١QVL as an antibacterial peptide with DNA gyrase enzyme (Research Paper)

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Introduction: In recent decades, peptide antibacterial products have attracted much attention. Antimicrobial peptides (AMPs) are small peptides that are produced by different organisms through ribosomal translation of mRNA or non-ribosomal pathways. These peptides are short amino acid sequences with less than ٥٠ amino acids. They have low molecular weight and high thermal stability. AMPs are effective alternatives instead of antibiotics and have a good inhibitory effect on pathogenic bacteria. Antimicrobial peptides can inhibit the key enzymes of microorganisms. Bacterial DNA gyrase is a type II topoisomerase. This enzyme is heterotetramer and consists of two subunits GyrA (containing a tyrosine residue in the active site responsible for breaking and rejoining to dsDNA) and GyrB (containing the ATPase in the active site and providing the energy required for supercoiling DNA). This enzyme is essential for microorganisms. This enzyme plays an important role in controlling the topological state of DNA, in cellular processes such as replication and transcription. Therefore DNA gyrase is a good intracellular target for antibacterial agents, and its inhibition causes bacterial death. This study aims to Study the interaction of ١QVL as an antibacterial peptide with DNA gyrase enzyme.

Methods: In this study, Discovery software version ٣,٥ was installed on a ٥-core windows operating system to perform molecular docking. The ٣D structure of the ligand and DNA gyrase with the identifier codes ١QVL and ١kzn were extracted from the website https://www.rcsb.org/ and downloaded in pdb format to be displayed in Discovery software. This protein initially existed in an impure form (along with water molecules and other unnecessary molecules such as the default ligand). Only the main chain of the protein structure is needed to perform the autodock steps. In this way, the crystal water molecules, ligand, and hetatm were removed from this structure and the protein was used for the molecular docking process. In the last step, molecular docking was performed.

Results: This research aimed to investigate the interaction of ١QVL as an antibacterial peptide with DNA gyrase. In this section, the ligand-protein complex with a docking score of -٢٢٦,٣٦ was obtained from the docking process and analyzed by Discovery software. The ligand-protein complex has five hydrogen bonds which contain A:ARG١:NH١ – A:GLU١٣١:OE٢, A:ARG١:NH٢ – A:GLU١٣١:OE١, A:ARG١:NH٢ – A: GLU١٣١:OE٢, A:TRP٣:NE١ – A:THR٦٢:OG١, A:ARG٥:NH١ - A:THR١٦٣:O. Also, DNA gyrase bonds to TRP٣ and TRP٤ in ١QVL by pi_Cation and pi_Sigma interactions.

Conclusion: the studied antibacterial peptide is capable of inhibiting the replication by interacting with the DNA gyrase enzyme. In addition, more laboratory investigations in the future can increase the credibility of this study.

Keywords: AMPs, \QVL,DNAgyrase,pathogenic bacteria, inhibition

Surfaces Covered with Polylactic Acid Nanoparticles: as a Safe Method for the Production of Blood Derivatives (Research Paper)

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Introduction: In recent years, the use of blood derivatives in regenerative medicine has attracted the attention of researchers. Various blood derivatives such as platelet-rich plasma (PRP), autologous conditioned serum (ACS), platelet lysate (PL), and platelet-rich fibrin (PRF) are used in tissue regeneration. In these blood derivatives, blood cells and secreted growth factors from these cells are used for tissue regeneration in wound healing, bone fracture, osteoarthritis, and tendon injuries. In different blood derivatives, different methods are used to activate cells and release the growth factors of these cells. Compounds such as thrombin, calcium chloride ($CaCl_2$), collagen and even glass beads can be used to activate blood cells and release growth factors from these cells. In ACS, glass beads contact with blood cells, including monocytes, causing the activation of these cells, and various cytokines, especially anti-inflammatory cytokines, are released from these cells. Polylactic acid (PLA) is one of the compounds approved by the U.S. Food and Drug Administration (FDA), which has been used in various medical fields, and one of its side effects is the activation of various blood cells, including platelets and monocytes. The effect of PLA on blood cells can be used to activate these cells and release growth factors in blood derivatives. By coating glass beads with PLA, it is possible to provide a suitable surface for the activation of blood cells to increase the amount of growth factors and cytokines of the blood derivatives and prevent the release of PLA into the sample and prevent its negative effects for patients. In this study, we intend to coat the borosilicate glass beads with PLA nanoparticles and investigate the coating of the beads, the non-release of PLA nanoparticles inside the sample, and the hemolysis of the sample, so that it can be used for the production of blood products for regenerative medicine purposes in the future.

Methods: PLA nanoparticles were used to coat medical-grade borosilicate beads with a diameter of ٣ ml, and the coating of glass beads was evaluated by scanning electron microscopy (SEM). To investigate the effect of coated beads, after obtaining informed consent, ١٧ ml of blood was taken in two tubes (٨,٥ ml in each tube, one of the tubes had beads covered with PLA nanoparticles and the other tube had no willows to prepare PRP) containing ٣ ml of anticoagulant citrate dextrose-A (ACD-

A) (١,٥ ml anticoagulant in each tube) from ٧ male volunteers who meet the entry criteria including: age ٢٠-٥٠ years, platelet count ١٥٠-٤٠٠×١٠٣/ml, leukocyte count ٦-١٠×١٠٣/ml, no underlying diseases, did not consume alcohol, drugs, anticoagulant and immunosuppressive drugs, no history of chemotherapy, and smoking. The tube without the coated beads was immediately centrifuged at ١٥٠ g for ١٠ minutes and the supernatant, which was PRP, was separated. The tube containing coated beads was incubated for ٦ hours at ٣٧ C°, then the samples were centrifuged at ١٥٠g for ١٠ minutes and the upper layer containing the activated plasma was separated. Fourier-transform infrared spectroscopy (FT-IR) was used to evaluate the release of PLA nanoparticles into the activated plasma and hemoglobin measurement was used to evaluate the hemolysis of the sample.

Results: SEM images showed that the surface of the beads was properly coated with PLA nanoparticles. FT-IR was used to evaluate the release of PLA nanoparticles into the conditioned plasma, which showed that these particles were not released into the sample. Hemoglobin measurement showed that coated beads did not cause hemolysis and the amount of activated plasma hemoglobin did not increase compared to PRP.

Conclusion: PLA-coated glass beads can be used to prepare blood derivatives without releasing them into the conditioned plasma and hemolysis of the sample. This study investigated the negative effects of these coated beads on the blood derivatives, and investigating the effectiveness of these coated beads in activating cells and increasing the amount of growth factors and cytokines in the activated plasma requires further studies and evaluation of its effectiveness on tissue regeneration.

Keywords: Platelet rich plasma, Activated plasma, Conditioned plasma, Polylactic acid, Nanoparticles

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Survey of SNP polymorphism of FTO, FABP۲, MC٤R genes in ۱۰۰ obese adults. (Research Paper)

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Introduction: The FTO gene, located on chromosome ۱٦q۱۲,۲, is considered one of the key genes associated with obesity risk. Additionally, there are many diets worldwide that are tailored to each person's genetic profile.

Methods: This study used Megagene pharmacogenomic software to analyze polymorphic data extracted from the NCBI database, which served as the source and reference for the study, to identify side effects with a genetic basis.

Results: The three most popular SNPs that play a role in the development of obesity are RS۱۷۷۸۲۳۱۳, RS۹۹۳۹٦۰۹, and RS۱۷۹۹۸۸۳. Furthermore, the side effects that individuals experience after using drugs to treat obesity are influenced by their personal genetic profile.

Conclusion: Before using commercial drugs to treat diseases such as obesity, genetic tests should be conducted on patients to detect the possible presence of polymorphisms in key genes like FTO. This approach allows for the prescription of drugs with fewer side effects if one or more of these polymorphisms are present in the patient.

Keywords: FTO; Obesity; Genetic factors; Polymorphism; Pharmacogenomics

Survivin as a Novel Prognostic Biomarker in Bladder Cancer: A Key to Enhanced Detection" "and Therapeutic Targeting (Review)

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Introduction: Bladder cancer is a significant global health burden, ranking as the ninth most common cancer worldwide. In ٢٠٢٠, there were approximately ٥٧٣,٠٠٠ new cases of bladder cancer and ٢١٣,٠٠٠ deaths globally. The high incidence and mortality rates of bladder cancer .underscore the need for effective therapeutic strategies to combat this disease Survivin is a member of the inhibitor of apoptosis (IAP) family and plays a crucial role in inhibiting cell death and regulating cell division. It is selectively overexpressed in many types of cancer, including bladder cancer, and is associated with poor prognosis and increased tumor aggressiveness Overall, survivin is a promising target for bladder cancer therapy due to its significant role in. tumor growth and resistance to apoptosis. Targeting survivin through various strategies, including siRNA and combination therapies, holds potential for improving bladder cancer treatment outcomes

Methods: A systematic search was made in four major databases: PubMed, Web of Science, SID, and Magiran. Searches were made for the period from ١٩٩٩ to ٢٠٢٤; the keywords used included "bladder cancer" AND "survivin." The Boolean operator "AND" has been applied in retrieval to ensure that only those studies which discuss both bladder cancer and survivin have been traced. In the database SID, a total of two relevant studies were found. The search within PubMed initially retrieved ٣١٩ articles. After the application of these criteria, ٢٠ articles were selected for detailed analysis. In an attempt to refine the selection, the following inclusion criteria were applied: relevance of the study to bladder cancer and survivin, adequacy of data volume, and a focus on the biological or clinical aspects of survivin in bladder cancer. Using these criteria,. Web of Science and Magiran were also searched. By eliminating duplicate studies and using the inclusion criteria, a total number of ٣٤ articles were included to be deeply reviewed

Results: The expression of survivin in bladder cancer involves several mechanisms and pathways Stabilization by FAT١٠: FAT١٠, a ubiquitin-like protein, is upregulated in bladder cancer and binds to survivin, preventing its ubiquitin-mediated degradation. This stabilization of survivin promotes cancer cell proliferation Regulation by Specificity Protein (Sp) Transcription Factors: Curcumin, a polyphenolic compound, has been shown to decrease survivin expression by down-regulating Sp١, Sp٣, and Sp٤ transcription factors. These Sp proteins are crucial for the expression of survivin and other genes involved in cell survival and angiogenesis . Interaction with CDC٢ Kinase and MAPK/AKT Pathways: Baicalein, a bioactive flavonoid, reduces survivin expression and induces apoptosis in bladder cancer cells. This process involves the inhibition of CDC٢ kinase and modulation of the p٣٨ MAPK and AKT pathways, which regulate survivin levels and cell cycle progression . Role of AATF: The apoptosis antagonizing transcription factor (AATF) is overexpressed in bladder cancer and upregulates survivin expression. AATF enhances cell proliferation and decreases sensitivity to

chemotherapy by increasing survivin levels . Spliced Variants: Survivin has several spliced variants, such as survivin-deltaEx٣ and survivin-٢B, which have different roles in tumor progression. High expression of survivin and survivin-deltaEx٣ is associated with higher tumor grades and poor prognosis, while survivin-٢B is inversely correlated with tumor grade . These mechanisms highlight the complex regulation of survivin in bladder cancer and its potential as a therapeutic target

Conclusion: Strengths: * Prognostic Marker: Multiple studies confirm survivin's role as a prognostic marker, providing valuable information for patient management [Jeon, ٢٠١٣]. * Therapeutic Target: Effective down-regulation of survivin through siRNA and combination therapies shows promise in reducing tumor growth and enhancing apoptosis [Hou, ٢٠٠٦] [Wang, ٢٠١٤]. * Diagnostic Tool: Urine survivin offers a non-invasive, accurate diagnostic method, improving early detection and monitoring [Shariat, ٢٠٠٤] [El-Hakim, ٢٠١٤]. Weaknesses: * Heterogeneity: Variability in study designs, patient populations, and detection methods can lead to inconsistent results and interpretations [Jeon, ٢٠١٣]. * Polymorphism Impact: The influence of survivin polymorphisms on cancer risk and progression requires further validation in larger, diverse cohorts [Kawata, ٢٠١١]. * Clinical Translation: While preclinical results are promising, translating survivin-targeted therapies into clinical practice remains challenging due to potential off-target effects and delivery issues [Hou, ٢٠٠٦]. However, the current research on survivin is not without its limitations. One major challenge is the heterogeneity among studies, including variations in study designs, patient populations, and detection methods, which can lead to inconsistent results and complicate the interpretation of findings. Additionally, the impact of survivin polymorphisms on cancer risk and progression, although promising, requires further validation in larger and more diverse cohorts to ensure broader applicability. Furthermore, the translation of survivin-targeted therapies from preclinical studies to clinical practice remains a significant hurdle. Despite promising results in laboratory settings, challenges such as potential off-target effects and issues related to the delivery of survivin inhibitors must be addressed before these therapies can be widely adopted in clinical settings. In summary, while survivin holds substantial promise as a multifaceted protein with significant implications for bladder cancer, further well-designed studies are essential. These studies should aim to standardize assays, validate findings across diverse populations, and address the challenges associated with clinical translation to fully realize the potential of survivin in cancer diagnosis, prognosis, and therapy.

Keywords: Bladder cancer Survivin Biomarker

Synergistic Effects of Mesenchymal Stem Cells, Hyaluronic Acid and Melatonin on Cartilage Regeneration in a Rat Model of Osteoarthritis (Research Paper)

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Introduction: Osteoarthritis (OA) as a common joint disorder, affects a great number of people around the world and characterized by the deterioration of articular cartilage and persistent inflammation. Current OA remedies are not quite adequate due to their main focus on pain management and in some cases, have been proven to cause side effects. Intra-articular injection of some treatments such as stem cells or hyaluronic acid (HA) is simple and non-invasive procedure which has emerged as a promising path for cartilage healing. HA injections has been approved by the United States Food and Drug Administration for the purpose of knee OA therapy. The purpose of the present study was to vet the efficacy of a therapeutic combination of adipose-derived mesenchymal stem cells (AD-MSCs), hyaluronic acid (HA), and melatonin (ME) for cartilage repair in the rat OA model.

Methods: OA were induced in the knee joint of Male Wistar rats by injecting monosodium iodoacetate (MIA) (١ mg of MIA dissolved in ٥٠ µL of saline solution). Normal saline solution was used as a control. Two weeks after the injection, rats were divided into ٩ groups (n=٧) at random receiving intra-articular knee injections of stem cells, hyaluronic acid and melatonin, as well as various combined treatments. On days ٢٨ and ٥٦, the rats from each group were first selected, weighed, and then subjected to X-ray imaging. The pathological changes in the rats' joints were assessed using the criteria established by Boulocher et al. Then blood samples were taken from the rats and plasma levels of TNF-α and IL-٦ were measured. Finally, the rats were anesthetized and euthanized, then, hematoxylin-eosin staining (HE) was used to investigate the changes in pathologic features of knee joint samples.

Results: Radiological evaluations showed that the group treated with MSCs + ME + HA, displayed an appropriate response, with only a slight reduction in joint space and mild osteophytes in one compartment. The group treated with HA +MSCs showed no reduction in joint space and moderate osteophyte in the tibia and osteophyte in the fabula. The overall joint score in the HA+ME and

MSC+HA+ME groups was significantly improved compared to the MIA group. Investigation of TNF and IL-٦ plasma levels showed that the group treated with MSC+HA+ME, both on day ٢٨ and day ٥٦, had the lowest amount of TNF-α and IL-٦ and this difference with other groups was *** P < ٠,٠٠١. After that, the MSC+HA group, on days ٢٨ and ٥٦, had the lowest amount of TNF-α and IL-٦ compared to other groups. Pathologic examinations also exhibited significant differences between the treatment groups and the non-treated group, which indicated that these combination therapies can provide a significant improvement in joint pathology (p < ٠,٠٥).

Conclusion: These findings indicate that the combination therapy with MSC, HA and ME offers a promising and innovative strategy for OA treatment and can be further investigated for clinical applications.

Keywords: Osteoarthritis, Mesenchymal stem cells, Hyaluronic acid, Melatonin, Combination therapy.

Talaromyces marneffei and Talaromycosis (Review)

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Introduction: Talaromycosis (formerly known as Penicilliosis) is an infection caused by Talaromyces marneffei, a thermally dimorphic fungus formerly known as Penicillium marneffei. In ١٩٥٦, the first case of T. marneffei infection in bamboo rats was studied, and subsequently in ١٩٧٣, the first case in humans was reported. Among the hundreds of Talaromyces species, Talaromyces (Penicillium) marneffei is the only thermally dimorphic species known to be pathogenic to mammals, including humans. T. marneffei is a primary lung pathogen that disseminates to other internal organs by lymphatic or hematogenous mechanisms. It causes disseminated disease in both immunocompetent and immunocompromised individuals, though it is most prevalent in patients with HIV/AIDS as well as patients with functional impairments of cellular immunity, particularly defects in CD٤ T cell activity. T. marneffei grows as a saprophytic mold in the environment, but undergoes phase transition to a pathogenic yeast-like cell at mammalian physiologic temperatures.

Methods: Talaromycosis is an important invasive mycosis caused by Talaromyces marneffei. The World Health Organization and Food and Drug Administration have recently paid increasing attention to the disease as a neglected tropical disease due to the growing burden of T. marneffei infection globally. Talaromycosis is a common opportunistic disease and a leading cause of death in patients with acquired immune deficiency syndrome (AIDS) in endemic regions; moreover, it is increasingly being reported in human immunodeficiency virus (HIV)- negative individuals and outside of epidemic areas. The mortality of talaromycosis is up to ٣٠٪ in both HIVpositive and HIV-negative individuals, which is associated with late diagnosis and untimely or ineffective antifungal therapy. Therefore, early diagnosis and effective antifungal treatment are critical to reduce the mortality.

Results: Talaromycosis is an invasive fungal infection which can be localized to the upper or lower respiratory tract, bones, joints, and intestinal tract, or disseminated across multiple organ systems. The main clinical manifestation of talaromycosis is skin lesions which are characterized by raised bumps (usually small and painless) on the skin, particularly on the face, the neck, and the extremities. Notably, HIV-negative individuals with talaromycosis are less likely to have skin lesions. In the particular context of advanced HIV infection (patients with CD٤+ T-cells < ٢٠٠ cells/μL), talaromycosis disseminates to organs such as the lung, liver, spleen, gastrointestinal tract, blood stream, and bone marrow. Interestingly, some reports have indicated that T. marneffei may cause primary pulmonary talaromycosis even in apparently healthy individuals, which suggests that talaromycosis may well be a more common cause of pneumonia in endemic areas than has been hitherto assumed.

Conclusion: The mechanisms for the pathogenesis of talaromycosis are not definitively established. However, fungal morphogenesis appears to be a crucial virulence factor in the establishment of

infection. Evidence suggests that aerosolized infectious particles (conidia) from environmental disturbances, especially in tropical monsoon seasons, are acquired via inhalation. After inhalation, the sizes of conidia (٢ to ٣ _m in diameter) allow them to infiltrate deeply into the lung alveoli. Once in the lung, these infectious propagules undergo phase transition into the parasitic yeast form, which are rapidly ingested by lung phagocytes. In healthy individuals, engulfed conidia are, for example, killed by host macrophages through the production of oxidative burst as well as the action of lysosomal enzymes. However, as with other pathogenic fungi such as Histoplasma, T. marneffei can survive and replicate inside the phagosomal compartment of macrophages. Hence, T. marneffei is classified as a facultative intracellular pathogen as it is found inside macrophages and tissue histiocytes in talaromycosis patients. The ability to transition from an environmental mold to a yeast form and resist to killing by host phagocyte is recognized as an important virulence mechanism of dimorphic pathogenic fungi as the switch is challenging to host innate and acquired immune defenses. In particular, the pre-existing impairment of cell-mediated immune responses that occur, for example, in patients with AIDS results in severely reduced fungicidal activity that diminishes the capacity of host phagocytes to eradicate this pathogen.

Keywords: Talaromyces marneffei, Talaromyces, Penicilliosis, dimorphic, opportunistic

Tannic acid as an antibacterial, antioxidant, and anti-inflammatory agent in hydrogel dressings for diabetic wound healing. (Review)

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Introduction: The management of diabetic chronic wounds remains a significant global challenge due to exacerbated inflammatory responses, oxidative stress, and persistent infections during the healing process. Reactive oxygen species (ROS) are released too much in diabetic wounds, which causes intense inflammatory reactions as well as lipid peroxidation, protein denaturation, and malfunctioning of endogenous stem cells and macrophages, all of which slow down wound healing. There exists a critical need for wound dressing materials that exhibit optimal biocompatibility, sufficient mechanical strength, robust underwater adhesion, and effective anti-inflammatory, antioxidant, and antibacterial properties for clinical applications. Hydrogels have garnered considerable attention as wound dressings for diabetic wound healing due to their three-dimensional porous networks and appropriate swelling characteristics. These materials demonstrate the capacity to absorb wound exudates, maintain a moist environment, and serve as delivery systems for bio-functional components or cells to promote healing. Recent advancements have focused on hydrogels incorporating naturally extracted substances, owing to their exceptional biocompatibility and biosafety. Tannic acid (TA), a natural plant polyphenol, has demonstrated promising antimicrobial, anti-inflammatory, antioxidant, and hemostatic properties. TA can form physical crosslinks with hydrogels through multiple hydrogen bonds and hydrophobic interactions under neutral conditions. Its ۲۵ phenolic hydroxyl groups enable TA to crosslink hydrophilic macromolecules, facilitating the formation of a hydrogel network. Various materials, including natural polysaccharides and synthetic polymers such as chitosan, alginate, cellulose, and hyaluronic acid, are being utilized to fabricate advanced biological macromolecule-based hydrogels. These materials are frequently enriched with antibacterial and antioxidant agents to impart multifunctional attributes for wound healing purposes. This review aims to examine recent research progress on the application of Tannic acid as an antibacterial, antioxidant, and anti-inflammatory agent in multifunctional hydrogels for the treatment of diabetic wounds.

Methods: Two methods are described for preparing a hydrogel dressing containing tannic acid: ۱. Post-fabrication immersion method: - Prepare the hydrogel from the desired polymer solution - Dissolve varying concentrations of tannic acid in deionized water - Immerse the prepared hydrogel dressing in the tannic acid solution for ۲٤ hours ۲. Direct incorporation method: - Dissolve tannic acid powder directly into the polymer solution at the desired concentration - Prepare the hydrogel containing tannic acid in a single step The choice between these methods depends on factors such as the desired tannic acid distribution, production scale, time constraints, and the specific properties required for the final hydrogel dressing.

Results: In vitro and in vivo investigations have shown that the polyphenol groups of TA in multifunctional hydrogels hastened the healing of skin incisions and defects by modulating inflammation, promoting collagen deposition, and vascularization. TA may decrease nuclear factor-κB translocation and reduce inflammatory cytokines, resulting in an anti-inflammatory effect. E. coli and S. aureus growth were effectively suppressed, and antioxidant activity was outstanding. Furthermore, the hydrogels generated by crosslinking TA with a polymer matrix had improved mechanical characteristics. Notably, in vivo studies showed that the hydrogel enhanced diabetic wound healing by activating M۲ polarization, anti-inflammation, and pro-angiogenesis.

Conclusion: Several factors contribute to the healing of diabetic wounds, including antibacterial and antioxidant effects, enhanced angiogenesis, and oxygen generation. To mitigate the deleterious impact of bacterial infections on wound recovery, it is imperative to develop novel hydrogel-based dressings that possess both antibacterial and anti-inflammatory properties. Consequently, there is an urgent need for the identification of new non-antibiotic agents that combat bacteria, to reduce antibiotic usage and prevent the emergence of antibiotic-resistant strains. As a result, multifunctional hydrogels are anticipated to be extensively utilized in the clinical management of diabetic wounds.

Keywords: Tannic acid-Antibacterial-Antioxidant-Hydrogel-Diabetic wound healing

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Targeted delivery of CRISPR/Cas۱۳ as a promising therapeutic approach to treat SARS-CoV-۲ (Review)

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Introduction: In the worldwide scale, the outbreak of the severe acute respiratory syndrome coronavirus ۲ (SARS-CoV-۲) has led to extensive damage to the health system as well as the global economy. Hitherto, there has been no approved drug or vaccine for this disease. Therefore, the use of general antiviral drugs is at the first line of treatment, though complicated with limited effectiveness and systemic side effects.

Methods: Given the pathophysiology of the disease, researchers have proposed various strategies not only to find a more specific therapeutic way but also to reduce the side effects. One strategy to accomplish these goals is to use CRISPR/Cas۱۳ system. Recently, a group of scientists have used the CRISPR/Cas۱۳ system, which is highly effective to eliminate the genome of RNA viruses. Due to the RNA nature of the coronavirus genome, it seems that this system can be effective against the disease. The main challenge regarding the application of this system is to deliver it to the target cells efficiently.

Results: To solve this challenge, it seems that using virosomes with protein S on their membrane surface can be helpful. Studies have shown that protein S interacts with its specific receptor in target cells named as angiotensin-converting enzyme ۲ (ACE۲). Here, we propose if CRISPR/Cas۱۳ gene constructs reach the infected cells efficiently using a virosomal delivery system, the virus genome will be cleaved and inactivated.

Conclusion: Considering the pathophysiology of the disease, an important step to implement this hypothesis is to embed protein S on the membrane surface of virosomes to facilitate the delivery of gene constructs to the target cells.

Keywords: COVID-۱۹, CRISPR/Cas۱۳, virosome,, infection, antiviral

Targeted drug delivery for Cancer therapy (Review)

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Introduction: Cancer is one of the leading causes of death in the world. Common methods of cancer treatment include chemotherapy, radiotherapy, immunotherapy, hormone therapy and surgery. The limitation of these methods is the poor accessibility of antineoplastic agents to the tumor, demanding higher doses, and the nonselective nature of these agents causes severe toxicity. Thus, Therefore, targeted drug delivery has attracted the attention of many researchers because it provided the selection of effective drug concentrations at the tumor site. Targeted drug delivery reduces drug side effects by reducing drug concentration in non-specific tissues. Recent advances in nanobiotechnology have led to the use of various nanocarriers such as liposomes, micelles, nanotubes, nanorods, dendrimers and nanoparticles as drug delivery systems for the delivery of chemotherapy drugs. Tumor targeting is classified into passive and active targeting. Passive targeting includes enhanced permeability and retention effect (EPR) due to formation of hyper-permeable complex tumor vasculature characterized by impaired lymphatic drainage of diseased tissue (tumor), resulting in the extravasation of ≥١٠٠ nm nanoparticles into the tumor microenvironment and preventing their clearance. Active targeting strategy is based on the composition decoration of the surface of drug carriers with tumor-specific ligands such as aptamers, antibodies and receptors overexpressed by the tumor cell. Stimuli-based drug delivery systems is classified into physical and chemical. Physical Stimuli-Responsive Drug Delivery Systems is based on Thermoresponsive, Magnetic/Electric Field-Responsive, Ultrasound-Responsive and Light-Responsive drug Delivery Systems. Chemical Stimuli-Responsive Drug Delivery Systems is based on pH Responsive and Enzymes-Responsive drug Delivery Systems.

Methods: This review article has been collected from reliable scientific sources and is the result of studying many researches of the authors.

Results: Recently, targeted drug delivery systems have made significant progress. These systems have attracted a lot of attention by reducing drug dosage, targeted drug delivery and reducing side effects. Different nanostructures with unique physical and chemical properties are used as nanocarriers.

Conclusion: In the future research related to targeted drug delivery systems, attention should be paid to the proper size of the system, its surface charge, sterilization and its similarity to the biological membrane. Examining molecular docking and system modeling is also essential for process optimization. In addition, a complete understanding of the cancer microenvironment and the characteristics of cancer cells is necessary for safer and more effective treatment.

Keywords: Cancer therapy, Drug delivery, Nanostructure, Nanotechnology.

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Targeted immunotherapy of breast cancer using drug compounds Antibody-Drug Conjugate Nanog stem cell marker antibody (Review)

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Introduction: Breast cancer (BC) is the most common cancer in women. About ١٥ to ٢٠ percent of women with this cancer have a positive family history of this disorder. Molecular analyzes of breast cancer tumors reveal many mutations in proto-oncogenes, tumor suppressor genes, and genome repair genes, especially double-strand breaks. Although some sufferers respond to existing treatments such as the use of Herceptin and Tamoxifen, which target HER٢, estrogen and progesterone receptors, and standard chemotherapy protocols as well as platinum-based chemotherapy in triple-negative cases and BRCA ١ germline mutations. but resistance to chemotherapy drugs is an important factor in breast cancer recurrence and metastasis, which can be caused by high extra tumoral and intra tumoral heterogeneity, and is a major challenge in breast cancer treatment.

Methods: This heterogeneity can be attributed to genetic and environmental factors and the presence of cancer stem cells (CSCs). The biological activities of CSCs are regulated by several potent transcription factors, such as OCT٤, Sox٢, Nanog, KLF٤, and MYC. The Nanog gene First discovered in ESCs, Nanog has multipotent transcriptional regulatory functions and normal self-renewal. Although Nanog is silenced in normal somatic cells, its abnormal expression has been reported in human cancers such as breast cancer, cervical cancer, brain cancer, colon cancer, head and neck cancer, lung cancer, and gastric cancer. The emergence of immunotherapy as a valuable anticancer strategy potentially makes it an effective approach to target CSCs. One of the important strategies that has received much attention today is the use of monoclonal antibodies. These molecules, with their direct inhibitory effects and the capacity to induce antibody-dependent cytotoxicity (ADCC) in cancer cells, mAb-linked drug compounds that deliver cytotoxic agents have been proven as a practical strategy for cancer treatment. ADCs are a complex consisting of a monoclonal antibody and an anticancer drug, which are connected by a linker. Antibodies in ADC contain a chimeric or human core body that reduces both acute hypersensitivity reactions and production of neutralizing anti-drug Abs. The ideal mAb target should be a cell surface protein that is exclusively expressed on tumor cells to limit the risk of systemic toxicity. In this regard, antigens expressed on solid tumors are often also expressed on normal cells. Therefore, such antigens are defined as "tumor-associated" rather than "tumor-specific". Consequently, for all these compounds, toxicity may occur according to the spectrum of specific target expression by normal cells (on-target-off-tumor toxicity) and cancer cells (on-target-on-tumor toxicity).

Results: A complex of ADCs induces apoptosis in cancer cells in five steps. The first stage (binding to the cell surface): ADCs can be connected to the surface of the cancer cell through the binding of the monoclonal antibody to its specific antigen (cancer antigen) and thus the antibody-antigen complex

is formed. The second stage (internalization): ADCs complex can be endocytosed into the cancer cell through receptor-dependent endocytosis. The third step: separating the drug from the antibody: after the endocytosis of ADCs into the cell, ADCs are placed in the primary vesicle, which then turns into a secondary vesicle, causing the linker to break and the drug is separated from the antibody. The fourth stage (release): the drug is released into the cytoplasm. The fifth stage (cell death): the drug causes cancer cell apoptosis through various mechanisms such as interaction with DNA, microtubules or enzymes involved in cell proliferation.

Conclusion: The importance of paying attention to the genetic profile of breast cancer tumors and the presence of stem cell tumors is very important in choosing the treatment method, cost, and time. Novel therapies based on ADCs on an important downstream target such as the Nanog gene can be promising for many potential targets for breast cancer treatment

Keywords: Antibody-Drug Conjugate , Nanog, breast cancer

Targeted Therapy and Immunotherapy for Metastatic Colorectal Cancer (Review)

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Introduction: Unfortunately, metastatic colorectal cancer (mCRC) remains a significant challenge as the third leading cause of cancer-related death. For patients with mCRC, a combination of surgery, systemic therapy, and/or locoregional therapy are currently applied. However, five-year survival for CRC patients with advanced disease remains poor (١٠–٣٠٪). According to the individual genetic profile signature and variation biology of different subtypes of CRC, ٢٠٪ of CRC patients reported the manifestation of synchronous metastases, and another ٤٠٪ who present with locoregional disease will show metastatic disease. Heterogenicity in the tumorigenesis process of CRC is the leading cause of unpredictable behavior and prognosis of the disease.

Methods: The epidermal growth factor receptor (EGFR), vascular endothelial growth factor (VEGF), and DNA mismatch repair pathways have shown promising results for targeted therapies. In addition, discovering new gene mutations and proteins that participated in the oncogenesis of mCRC provides an opportunity for more investigations related to novel therapeutic approaches.

Results: One of the FDA Approved targeted therapies for mCRC are EGFR inhibitors, including Cetuximab and Panitumumab that stimulate downstream pathways of RAS/RAF/MEK/ERK, PI٣K/AKT, and JAK/STAT٣. In addition, Encorafenib is a BRAF inhibitor. Overexpression of proteins in these pathways results in cell growth, proliferation, and carcinogenesis. Second, VEGF inhibitors, including Bevacizumab, Ramucirumab, Aflibercept, and Fruquintinib. Overexpression of VEGFs increases the formation of blood vessels and promotes angiogenesis and subsequent proliferation. Third, human epidermal growth factor receptor ٢ (HER٢) is a receptor tyrosine kinase protein with the proto-oncogenic role that is encoded by the ERBB٢ gene. It is estimated that ٣–٥٪ of CRCs amplificated HER٢. In this way, Trastuzumab, Pertuzumab, and Tucatinib are HER٢ inhibitors that can be applied as a therapeutic approach in CRC patients with HER٢ amplification. Fourth, ١٥٪ of CRC tumors are presented by microsatellite instability (MSI) that defects DNA mismatch repair. Some immune checkpoint inhibitors improve antineoplastic immune response in patients with MSI-high tumors. For example, programmed cell death protein ١ (PD-١) inhibitors such as Nivolumab, Pembrolizumab, and cytotoxic T-lymphocyte-associated protein ٤ (CTLA-٤) inhibitors like Ipilimumab. Fifth, Neurotrophic tyrosine receptor kinase (NTRK) fusions are targetable genetic mutations that stimulate TKR activity and are detected in <١٪ of CRC patients. NTRK inhibitors include Larotrectinib and Entrectinib. However, mutations in KRAS, BRAF, and PTN can provide resistance to specific targeted treatments, such as EGFR therapies.

Conclusion: Combination-targeted therapies can overcome resistance mechanisms in novel therapeutic approaches. Future studies can consider detecting molecular mechanisms involved in

activating the immune response to tumorigenesis and carcinogenesis progress, such as CRC vaccines and CAR-T cell therapies. Besides, valuable and reliable biomarkers should be identified for screening mCRC patients. Future studies should investigate personalized-targeted therapy for mCRC patients.

Keywords: Colorectal Neoplasms, Targeted therapy, Metastatic colorectal cancer, molecular profiling

Targeted treatment approaches for ovarian cancer: a systematic review (Review)

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Introduction: Ovarian cancer has the highest mortality rate among all malignancies of the female reproductive system. On average, a woman's lifetime risk of ovarian cancer is ۱-۱,۵٪, and the death rate is ۵۰٪. Diagnosing ovarian cancer is extremely important in the rate of destruction of cancer cells and survival of a person, but unfortunately, in most cases, it is detected and diagnosed in an advanced stage, which makes the treatment difficult and difficult. Therefore, it is important to examine treatment approaches. Immunotherapy is one of the treatment methods, but ovarian cancer's response to it is limited and does not show much reaction. Studies conducted on biomarkers such as Tumor Mutational Burden (TMB) or the combination of several treatment approaches simultaneously with immunotherapy such as the combined treatment of deadritic cells (DC) autologous vaccine with immune checkpoint inhibition (ICI) and chemotherapy strengthen the immune response and reduce cells In another research study, they evaluated the combination of cyclophosphamide with bevacizumab and an autologous DC vaccine and found that the group that received the combined treatment with cyclophosphamide compared to the group that received the combined treatment without cyclophosphamide. They have a higher chance of response and recovery in such a way that ۸ out of ۱۰ patients responded to the vaccine, whereas only ۳ out of ۱۲ patients responded to the vaccine without cyclophosphamide. This study aims to investigate targeted treatments for ovarian cancer.

Methods: In this systematic review, the study keywords were searched in PubMed and Google Scaler databases. Keywords were selected from the MESH database and combined with OR and AND functions. Keywords "ovarian cancer," "targeted therapy," and "immunotherapy" were used to search for articles. To check more recent information, the time filter from the beginning of ۲۰۱۸ to ۲۰۲٤ was used. All reviewed research and review articles were full text in English and rated Q۱ and Q۲.

Results: Considering that ovarian cancer is diagnosed late and in advanced stages, treatment approaches are highly regarded. Although immunotherapy was recognized as one of the treatment approaches for ovarian cancer according to the results, the studies showed that the use of combined treatments was more effective and efficient because by strengthening the immune system response and reducing tumor escape at the same time, the chances of recovery and survival increased. They used to give cyclophosphamide together with autologous DC vaccine, which made the immune system's response to the vaccine more effective.

Conclusion: According to the statements, immunotherapy was less effective than other treatment methods. Combination therapy was also considered as another therapeutic approach that helped to enhance the immune response and reduce the tumor cells at the same time. According to the

aforementioned findings, receiving cyclophosphamide could improve the response to analog vaccines and make them more effective.

Keywords: Ovarian cancer- Targeted treatment - Biomarker - Immunotherapy

Targeted treatment of breast cancer using Antibody-Drug Conjugate of Ror۱ stem cell markers (Review)

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Introduction: Breast cancer is the most common cancer in women and is still the leading cause of cancer-related death in women in several countries. Chemotherapy combined with tumor removal surgery is the main treatment for breast cancer patients, but repeated resistance to chemotherapy drugs is an important factor in breast cancer recurrence and metastasis. The high extratumoral and intratumoral heterogeneity caused by genetic factors and the presence of cancer stem cells (CSCs) leads to the creation of cell populations with different sensitivity to treatment. CSCs are cancer cells with the characteristics of stem cells with the ability to self-renew. Differentiation and production of new tumors are defined and contribute to the development of tumor malignancies such as recurrence, metastasis, and multi-drug resistance. Breast cancer stem cells (BCSC) are a small part of breast cancer cells and have a high capacity to form tumors. Many intracellular signaling pathways such as WNT are critical regulators of BCSCs. WNT/ROR signaling is associated with tumor progression processes, such as cell proliferation, survival, invasion, or treatment resistance. Receptor tyrosine kinase ROR۱ is a single transmembrane type I membrane protein, consisting of an extracellular part, a transmembrane part, and a cytoplasmic region. The extracellular part has an immunoglobulin-like domain (IG), cysteine-rich domain (CRD), and Kringle domain (KD). CRD modulates non-canonical WNT signaling by binding to the Wnt۵a ligand. The cytoplasmic part is responsible for the activation of migration and cell proliferation signals and the serine/threonine-rich domain leads to resistance to apoptosis. In mature human tissues, ROR۱ is expressed only at very low levels in areas such as the testis, parathyroid, and primary fibroblasts. As an encophthalic antigen, ROR۱ is expressed physiologically in embryonic tissues and abnormally in hematological and solid cancers. IHC analysis has shown widespread expression of ROR۱ in many tumors with significantly higher expression levels in cancerous tissue, especially breast cancer, than in adjacent normal tissue. Gene expression data show high levels, especially in poorly differentiated and triple-negative breast cancers. In the most aggressive subtype of breast cancer, the expression is very high (۱۰٪). Most studies have identified ROR۱ as an oncogene. This finding stimulated the interest of cancer biologists to evaluate the potential of these new receptors as cancer biomarkers and their functional role in tumor development and progression. Besides the well-established function of RORs in cell proliferation, another deleterious consequence of active WNT/ROR signaling in cancer is the generation of tumor-resistant cell clones. reported upregulation of ROR۱ or ROR۲ in chemotherapy-resistant cancer cell lines. Studies show that ROR۱ is associated with treatment-resistant cancer stem cells. Sabin and colleagues found that high expression of ROR promotes the reprogramming of somatic cells into induced pluripotent stem (iPS) cells. Zhang and colleagues found that ROR inhibits the expression of the cell proliferation inhibitory factor p۵۳ by interacting with the heterogeneous RNA-binding protein nuclear ribonucleoprotein I, thereby promoting breast

cancer proliferation. ROR١ is an excellent target for the development of therapeutic drugs for the treatment of breast cancer.

Methods: Several therapeutic strategies against ROR١ have been developed in clinical and preclinical trials. Several companies are developing anticancer therapies targeting ROR١, including monoclonal antibodies, antibody-drug conjugates (ADCs), dual antibodies, and CAR-T therapies. Among them, ADCs have faster development and good application prospects. ADCs consist of monoclonal antibodies conjugated to highly cytotoxic small molecules through chemical bonds. This coupling of the specificity of biological macromolecules and the cytotoxicity of small chemical drugs mediated by stable linkages has led to tremendous clinical success for ADCs.

Results: Among ROR١-based ADC drugs, Zilovertamab vedotin (MK٢١٠٤, VLS-١٠١) in phase Ⅱ and Ⅲ clinical trial, NBE-٠٠٢ in phase Ⅱ, LCB-V١ (CS٥٠٠١) in phase Ⅰ, huXBR١-٤٠٢-G٥-PNU and huXBR١-٤٠٢-G٥-PNU and cirmtuzumab-ADC-٧ and ELN-١١ are in pre-trial phase.

Conclusion: Considering the key role of ROR١ in the carcinogenic mechanisms of cancer cells, more efforts are needed to develop new drugs and improve existing drugs based on this compound.

Keywords: Antibody Drug Conjugate, Breast Cancer, Ror١, immunotherapy

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Targeting Antimicrobial resistance by CRISPR/CAS based approach (Review)

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Introduction: Introduction: Effective antimicrobial resistance can result from mutations in specific types of genes, including those encoding drug targets, drug transporters, drug transporter regulators, and antibiotic-modifying enzymes. Consequently, these acquired resistance contribute to the development of antimicrobial resistance in bacteria. Various strategies are used to overcome these problem, among them, CRISPR/cas٩ based techniques are novel, accurate and rapid methods. Clustered regularly interspaced short palindromic repeats (CRISPR) gene-editing technology is the ideal tool of the future for treating diseases by permanently correcting deleterious base mutations or disrupting resistance-causing genes with great precision and efficiency.

Methods: We analyzed results from individual studies conducted from ٢٠١٨ to ٢٠٢٤ using the search terms" (CRISPR) gene-editing technology " ," infection disease" and "Antimicrobial resistance" in major medical databases.

Results: Here, we conducted an integrated and comprehensive study of medical and biotechnological databases for application of genetic manipulation methods to overcome antimicrobial resistance. The results indicated that a variety of strategies have been developed in order to combat antibiotic-resistant bacteria, including the development of new antibiotics, bacteriophages that lyse and target these bacteria, antimicrobial peptides. Crispr/cas based methods are a newly emerged strategy that have been tried in several bacteria including pseudomonas aeruginosa, Klebsiella pnemonia and staphylococcus aurous with great success.

Conclusion: In recent years, the CRISPR/Cas technique, derived from the bacterial immune system, has emerged as a promising tool for gene modification. This technology offers high efficiency, speed, and simplicity, and it is anticipated to revolutionize genome modification projects in the near future. In the CRISPR/Cas approach, the target DNA is introduced to the Cas٩ enzyme through gene-specific single-guide RNAs (sgRNAs) thet resulted in the disruption and deactivation of the targeted gene. This breakthrough has opened new possibilities for combating antimicrobial resistance. Studies have shown that CRISPR/Cas technology can be employed to target and disrupt resistant genes within the bacterial DNA, potentially restoring the susceptible phenotype in resistant bacteria.

Keywords: Infection disease; Antimicrobial resistance; CRISPR/Cas system

Targeting Copper Metabolism in Cancer: A Promising Therapeutic Strategy from Research to the Clinic (Review)

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Introduction: According to the statistics of the World Health Organization (WHO), cancer is one of the main causes of death in the world. Aggressive and metastatic cancers show increased metabolic flexibility, so altered metabolism is one of the main characteristics of cancer cells. In this study, we describe the role of copper in signaling and metabolic pathways involved in cancer tumor growth and spread.

Methods: In order to obtain the most recent research, It was conducted an extensive search in PubMed and Google Scholar databases from ٢٠٢٠ to ٢٠٢٤ and identify ٢١ articles related to our main topic. The targeted searches included “Cancer”, “Cuproptosis”, “Copper”, “Signaling” and “Tumor”.

Results: Many human cells self-destruct and undergo apoptosis to maintain biological homeostasis, but one of the main characteristics of cancer cells is the escape from programmed death (apoptosis), which causes resistance. Chemical and cancer recurrence. Much research has focused on the alternative processes of cancer cell death, namely necroptosis, pyroptosis, ferroptosis, and coproptosis. Copper is a rare element in the body and is related to various signaling pathways involved in tumor growth and spread. It is also known that excess copper can lead to cell death. In fact, excess copper leads to the accumulation of dihydrolipoamide lipoyl S-acetyltransferase (DLAT), which is linked to the TCA cycle, leading to proteotoxic stress and the development of a new cell death method known as coproptosis. A targeted cancer treatment strategy is considered. Coproptosis also modulates antitumor immunity, therefore, understanding the mechanisms involved

in modulating copper metabolism and coproptosis may facilitate improved cancer management. Copper plays an important role in receptor tyrosine kinase signaling pathways, which can bind and phosphorylate receptor tyrosine kinase (RTK) without ligand binding, leading to RKT activation. The activated RTK subsequently leads to the phosphorylation of downstream extracellular regulated protein kinases (ERK) and agammaglobulinemia tyrosine kinase (ATK) and ultimately leads to cell proliferation. It has also been suggested that copper ions probably activate downstream proteins by acting on different molecules of the phosphoinositide-٣-kinase (PI٣K)-AKT signaling pathway. On the one hand, copper can directly activate PI٣K, leading to the downstream activation of AKT. On the other hand, copper binds to histidine ١١٧ and histidine ٢٠٣ of pyruvate dehydrogenase kinase ١ (PDK١), which leads to the activation of AKT. AKT activation induced by copper can catalyze the phosphorylation and intracellular redistribution of frontal box O١a (FoxO١a) and frontal box O٤ (FoxO٤), which promotes cancer cell proliferation and tumor growth.

Conclusion: Coproptosis is a type of copper-dependent cell death and has unique characteristics compared to other forms of cell death, which refers to the mitochondrial pathway of cell death and is caused by excessive copper exposure and subsequent proteotoxic stress. Aberrant copper metabolism has a dual role in tumorigenesis and cancer treatment, so targeting copper metabolism can provide a promising therapeutic approach in cancer research.

Keywords: Cancer; Cuproptosis; Copper; Signaling; Tumor

Targeting of CD١٣٣ as a therapy for all type of Cancers A systematic review and meta-analysis

(Review)

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Introduction: Introduction: Despite advances in detection and treatment, cancer remains a main public health crisis across the globe [١]. It was estimated that in ٢٠٢٤, ٢ million new cancer cases would be diagnosed in the worldwide, along with over ٦٠٠,٠٠٠ estimated deaths [٢].Although cancer diagnosis and therapy have been improved gradually, the survival of patients remains poor, which are mainly affected by drug resistance, local recurrence, and development of metastatic disease. [٣] According to the research studies, cancer stem cells (CSCs) with the principal properties of multipotency and self-renewal are responsible for neoplasm formation, metastasis, recurrence, and therapeutic resistance. [٤-٧] Cancer stem cells were successfully isolated and identified in many hematologic tumors including colorectal cancer, glioblastoma, cholangiocarcinoma, ovarian cancer, hepatocellular carcinoma, Osteosarcoma. [٨] Numerous of molecules have been investigated as putative markers of CSCs. Among the different markers, CD١٣٣ is one of the most robust surface marker of CSCs. [٩] it is widely expressed in numerous types of tumors, involving colorectal, Lung and ovarian cancer. [١٠] It is a ٥ transmembrane single-chain glycoprotein, with a molecular weight of ١٢٠ kDa, which was first found to be expressed in hematopoietic stem and progenitor cells. [١١] Based on the recent studies CD١٣٣+ cells in Cancer had the ability to initiate tumor growth. The paradigm of CD١٣٣ as a CSCs biomarker has stimulated many studies to explore the prognostic power of CD١٣٣ expression in patients. However, the prognostic value of CD١٣٣ for different type of cancers remain controversial despite of numerous independent studies. We performed a meta-analysis to determine the value of CD١٣٣ as a prognostic marker for all type of cancer and a robust target for cancer treatment.

Methods: Search Strategy and Selection Criteria: We searched PubMed, EMBASE, Elsevier databases MEDLINE (PubMed), Google Scholar, Web of Science (Thomson-Reuters) with Medical Subject Heading keywords CD١٣٣, CSCs, Prominin, Cancer therapy, examining the CD١٣٣ as a CSC marker for targeting cancer therapy published up to August ١٥, ٢٠٢٤. In addition, we reviewed citations in the retrieved articles to search for additional relevant studies. Searches were limited to papers published in English only. Studies were included in the meta-analysis, if they included patients with Cancer diagnosis by pathologists according to the American Association guidelines; data on CD١٣٣ (Prominin) marker and full-length papers; and data about odds ratios (ORs) with ٩٥٪ confidence intervals (CI), or at least adequate data to calculate ٩٥٪ CIs. The following studies were excluded; overlapping articles or duplicate data; review articles and conference records without original data and full text; to investigate the effects of targeting CD١٣٣ marker of CSC in varieties of cancer types. Inclusion and exclusion criteria: Studies were selected according to the following inclusion criteria: (١) full-text published studies up August ١٥, ٢٠٢٤; (٢) a case-control or a Clinical Trial design; (٣) the

study goal was to evaluate the effect of CD١٣٣ marker as a significant marker for cancer therapy. (٤) Sufficient data for estimating ٩٥٪ confidence interval (CI) and odds ratio (OR). Data extraction: In this study Information was extracted from all the eligible studies independently by ٢ researchers using a pre-designed form according to the selection criteria listed above. For each study the following information was extracted: the name of first author, publication year, country where the study was conducted, racial descent, type of cancer, cancer treatment testing method, number of patients and the final effect of targeting cancer therapy.

Results: Result: ١٣ records were found after examining online databases, references, and related articles; ٧ of these records were subsequently eliminated as being unrelated. The current meta-analysis also included ٦ eligible study. Table ١ provides basic data, including, the number of patients, results, effect, method, country and year. According to the results of this investigation, CD١٣٣ plays prominent roles in different cancer types and is responsible for cancer recurrence and metastasis and is a promising marker for cancer treatment. Table١: the results of targeting CD١٣٣ as cancer treatment. Patient Results Effect Method Country Year ٢١ Longer overall survival promising antitumor activity CD١٣٣-directed chimeric antigen receptor (CAR) T (CART-١٣٣) China ٢٠٢٠ ٣٨ Longer overall survival increased sensitivity to cisplatin trial of metformin as a cancer stem cell–targeting agent USA ٢٠٢٠ ٥٢ feasible treatment remarkable shrinkage or even disappearance of some metastases Cocktail treatment with EGFR-specific andCD١٣٣-specific chimeric antigen receptor-modified T cells China ٢٠١٧ ٢ therapeutic effect on cancer cells decrease of CD١٣٣ expression MicroRNA-١٣٣a Expression Profiles Japan ٢٠١٣ ٢١ Longer survival and no evidence of tumor recurrence decrease in or absence of CD١٣٣ expression multi-epitope-pulsed dendritic cell vaccine USA ٢٠١٢ ٣٣ No difference in CD١٣٣ mRNA expression CD١٣٣ mRNA expression did not change significantly Protein Kinase C B-Inhibitor Enzastaurin in Combination with Gemcitabine and Cisplatin USA ٢٠٠٧

Conclusion: CSCs can be distinguished by their properties of self-renewal and differentiation and subsequently generate cancer cells. Several studies have examined effect of targeting CD١٣٣ as a CSCs marker for cancer treatment in different cancer types; but the results were controversial. Meta-analysis has been recognized as a prominent tool to exactly define the effect of targeting different CSC markers for cancer therapy. The present meta-analysis was carried out by critically reviewing ٦ relevant and new recently published studies on targeting CD١٣٣ for cancer treatment. Hence, it may provide more information. The overall effects of these ٦ clinical studies (Table١) suggest CD١٣٣ as a promise marker for treatment.

Keywords: CD١٣٣, CSCs, Cancer treatment

Telomerase: A Dual Role in Cancer Progression and Aging-Related Diseases (Review)

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Introduction: Telomerase is a vital enzyme responsible for maintaining telomeres, the protective caps at the ends of chromosomes, which are crucial for cellular longevity and organismal survival. Telomere length serves as an indicator of cellular aging, as telomeres shorten with each cell division. This reduction in length has been strongly linked to age-related diseases such as cardiovascular disease, neurodegenerative disorders, and immune system decline. In most normal somatic cells, telomerase is either inactive or minimally active, limiting the number of cell divisions, a process known as the Hayflick limit. Once cells reach this limit, they enter senescence or undergo programmed cell death. In cancer cells, however, telomerase regulation is disrupted. Many cancer cells reactivate telomerase, enabling them to bypass the Hayflick limit and proliferate indefinitely. This ability to manipulate telomerase is a key reason for cancer cells' unchecked growth. Studies suggest that cancer and aging share overlapping molecular pathways, reinforcing the connection between the two. Both processes involve DNA damage, oxidative stress, and cellular senescence. These shared mechanisms make telomerase a promising target for therapies addressing both cancer and age-related diseases.

Methods: This review is based on a thorough search of scientific literature from databases like PubMed, Scopus, ScienceDirect, and Google Scholar. Studies on telomerase function in cancer and aging were included, with particular emphasis on telomerase activation in cancer cells, its inhibition as a potential cancer treatment, and its role in combating age-related diseases.

Results: Studies show that telomerase is reactivated in around ۸۵–۹۰٪ of malignant tumors, making it an attractive target for cancer therapy. Inhibiting telomerase in cancer cells has been linked to reduced tumor growth, increased apoptosis (cell death), and delayed tumor progression. Telomerase reverse transcriptase (TERT), the enzyme's catalytic subunit, is key to telomerase activity. Overexpression of TERT is common in cancer cells, and its inhibition has been identified as a promising therapeutic approach. Recent advancements in gene-editing technologies, particularly CRISPR/Cas۹, have enabled the precise targeting of telomerase in cancer cells. CRISPR/Cas۹ studies that disrupt the TERT gene have shown significant reductions in cancer cell viability, both in laboratory settings and in living organisms. This suggests that targeting TERT could slow cancer progression and improve treatment outcomes. Conversely, telomerase deficiency has severe consequences for aging. Telomerase-deficient mice exhibit accelerated aging symptoms, such as hair loss, impaired tissue regeneration, and shortened lifespan. This indicates that telomerase activation might hold therapeutic potential for treating age-related conditions by restoring telomere function and possibly slowing cellular aging. A crucial aspect of telomere function is the shelterin complex, a group of proteins that protects telomeres and prevents them from being mistaken for damaged DNA. Mutations in shelterin proteins can lead to genomic instability and increase cancer risk.

Research suggests that correcting these mutations could improve stem cell function, extend lifespan, and reduce cancer susceptibility. Balancing telomerase inhibition and stimulation presents a promising therapeutic strategy. Inhibiting telomerase in cancer cells could limit tumor growth, while stimulating telomerase in normal cells may extend lifespan, particularly in those with telomere-related disorders. These dual roles underscore telomerase's importance as a key target for future medical treatments.

Conclusion: Aging and cancer are closely linked through shared molecular pathways, especially those involving telomerase and telomere maintenance. Inhibiting telomerase in cancer cells shows promise as a cancer treatment, while activating telomerase in normal cells could extend lifespan and treat age-related diseases. As research continues, telomerase is likely to become a central focus for therapies addressing both aging and cancer, with significant implications for future medicine.

Keywords: Telomerase, Aging, Cancer

TetfiraThe Impact of Climate Change on Public Health (Review)

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Introduction: Climate change refers to long-term alterations in temperature, precipitation, and other atmospheric conditions. Human activities, particularly the burning of fossil fuels, deforestation, and industrial processes, have significantly accelerated these changes. The ramifications of climate change extend beyond environmental degradation, posing substantial risks to human health. Understanding these impacts is crucial for public health professionals, policymakers, and communities.

Methods: ١. Direct Health Effects of Climate Change ٢. Indirect Health Effects of Climate Chang ٣. Vulnerable Populations ٤. Health System Preparedness ٥. Mitigation and Adaptation Strategies

Results: In addition to direct health impacts, climate change indirectly affects public health through food security, water quality, and air pollution. Extreme weather events, such as floods and droughts, can disrupt food production, leading to malnutrition and associated health problems. The WHO estimates that climate change could result in an additional ٢ million malnutrition-related deaths by ٢٠٥٠, particularly among children and pregnant women.

Conclusion: Climate change poses significant challenges to public health, with both direct and indirect effects on populations worldwide. Understanding the complex interactions between climate change and health is essential for developing effective strategies to mitigate its impacts. By prioritizing public health in climate change discussions and promoting sustainable practices, we can protect health and well-being for current and future generations. Collaborative efforts between governments, healthcare professionals, and communities are crucial to addressing this pressing global issue and enhancing resilience against climate-related health threats

Keywords: Climate change

The ۳'UTR region of the SLC۲۲A۲ gene cloned into the psiCHECK vector exhibited significantly increased expression in HEK۲۹۳T cells in the presence of miR-H۳ of HSV-۱ (Research Paper)

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Introduction: Herpes simplex virus type ۱ (HSV-۱) is a common viral infection known primarily for causing oral and labial herpes, often referred to as cold sores.. If HSV-۱ spreads to the brain and central nervous system, serious infections such as herpes simplex encephalitis may occur, leading to irreversible complications. "This virus can establish colonization within the body during childhood and persist throughout a significant portion of the population's lifetime without any disease manifestation. As the virus depends on the host cell's machinery, a bidirectional interaction with the host must occur during latency or even during infection itself. One of the primary regions where the virus resides is within the ganglia of the nervous system. The ion channels, among the essential components of the nervous system, play a crucial role in brain homeostasis. HSV-۱, similar to humans, produces a number of non-coding RNA molecules known as miRNAs that impact the expression of a wide range of host genes. Following bioinformatic studies and Real-time PCR analysis, it was determined that the SLC۲۲A۲ or OCT۲ gene, which belongs to the category of cation transporters, exhibits significant upregulation by the virus's miR-H۳ (۳P).

Methods: For the ۳'UTR region of the SLC۲۲A۲ gene, we designed primers and, after amplifying it and performing transformation, cloned the fragment into the psiCHECK vector. Then, we transfected this vector into HEK۲۹۳ cells in the presence of miR-H۳. After extracting RNA and performing real-time PCR, we observed that in the presence of miR-H۳, there was an increase in expression. To confirm this, we used a luciferase assay, which showed an expression increase of up to ۸۰٪ in the presence of miR-H۳.

Results: The SLC۲۲A۲ gene has been recognized in recent years as a drug transporter. Additionally, it was first identified in ۲۰۱۷ that dysfunction of this gene plays a role in neurological diseases such as epilepsy . Given that the HSV-۱ virus can lead to acute conditions such as epileptic encephalopathy, this gene could serve as a suitable therapeutic target for disease targeting. After extracting RNA and performing real-time PCR, we observed that in the presence of miR-H۳, there was an increase in expression. To confirm this, we used a luciferase assay, which showed an expression increase of up to ۸۰٪ in the presence of miR-H۳.

Conclusion: For the ۳'UTR region of the SLC۲۲A۲ gene, we designed primers and, after amplifying it and performing transformation, cloned the fragment into the psiCHECK vector. Then, we transfected this vector into HEK۲۹۳ cells in the presence of miR-H۳. After extracting RNA and performing real-time PCR, we observed that in the presence of miR-H۳, there was an increase in expression. To confirm this, we used a luciferase assay, which showed an expression increase of up to ۸۰٪ in the presence of miR-H۳.

Keywords: Herpes simplex one, miRNA ,ione channel, virusRNA-human interaction

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The Age of Colon Cancer in the World has become Younger (Review)

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Introduction: One of the most common gastrointestinal cancers is colon cancer . Over the last two decades, the age of incidence of colon cancer has decreased. Colon cancer has steadily increased among young people in the U.S. over the past two decades, with teens having the highest rates of cancer. Between ١٩٩٩ and ٢٠٢٠, the rate of colon cancer among children aged ١٠ to ١٤ years has increased by ٥٠٠٪. The cancer has increased by ٣٣٣٪ among adolescents aged ١٥ to ١٩ and ١٨٥٪ between ٢٠ and ٢٤. Colon cancer is no longer merely perceived as a disease of the older population. The purpose of this review study is to focus on the causes of decreasing the age of colon cancer.

Methods: We conducted a comprehensive search for relevant studies in PubMed, Scopus, and SID databases, as well as the Google Scholar search engine. The advanced search keywords included " Colon cancer " Young adults "" Daily habits " Children " .The search was restricted to studies published in English with accessible full texts. Review articles, duplicates, and non-relevant studies were excluded.

Results: According to the ١٩٩٩-٢٠٢٠ Colon Cancer Trends calculation for people aged ١٠ to ٤٤ years, the results show that colon cancer rates have increased among children and young adults. Among adolescents aged ١٠-١٤ years, ٠,٦ children per ١٠٠,٠٠٠ children were diagnosed with colon cancer in ٢٠٢٠, which was only ٠,١ children per ١٠٠,٠٠٠ in ١٩٩٩. Diagnoses in people aged ١٥ to ١٩ increased from ٠,٣ to ١,٣ per ١٠٠,٠٠٠ people and between ٢٠ to ٢٤ years from ٠,٧ to ٢ per ١٠٠,٠٠٠. The most common symptoms of colon cancer are constipation, diarrhea, abdominal pain, rectal bleeding, and symptoms of iron deficiency anemia. Colon cancer risk factors include a family history of colon cancer. Other known risk factors include obesity, smoking, cigarettes and hookah, alcohol consumption and drug use , and diet. Suspected risk factors include lack of physical activity, antibiotics, and food additives.

Conclusion: Colon cancer is one of the most important preventable cancers, colon cancer screening should start in all people from the age of ٥٠ with colonoscopy, and if a person has a family history of colon cancer or high-risk polyps, this screening should start at the age of ٤٠. A healthy diet includes vegetables, fruits, whole grains, whole grain breads, dairy products, fish, nuts, and garlic. Consumption of processed foods such as fast foods, sausages and sausages and processed meats increase the risk of gastrointestinal cancer, modifying daily habits aerobic physical activity such as cycling, walking and running is very useful and can be useful in reducing the incidence of gastrointestinal cancers. It is recommended to do at least ١٥٠ minutes weekly, i.e. ٥ sessions of ٣٠ minutes per week.

Keywords: Colon cancer, Children, Young adults, Daily habits

The antibacterial Effects of Essential Oils from Medicinal Plants on Multidrug-Resistant Bacteria Carrying Carbapenem Resistance Genes (blaKPC, blaIMP, blaNDM, ...)effects on bacteria (Research Paper)

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Introduction: Increasing infections caused by multidrug-resistant (MDR) bacteria, particularly those resistant to carbapenems, present a major public health concern. This study investigated the antimicrobial effects of essential oils from Zataria multiflora, Mentha pulegium, Cinnamomum verum, and MDR bacteria with carbapenem resistance genes.

Methods: PCR was used to detect carbapenem resistance genes (blaKPC, blaIMP, blaNDM,) in multidrug-resistant strains of Staphylococcus aureus, Pseudomonas aeruginosa, and . The antibacterial effects of various concentrations of essential oils were tested using the agar disc diffusion method and a novel concentration gradient-based approach. The study determined the minimum inhibitory concentrations (MICs) of these essential oils against the bacteria.

Results: Among the tested strains, while all studied bacteria harbored the blaKPC gene. Specifically, S. aureus carried the blaIMP and blaNDM genes. P. aeruginosa carried the blaIMP and blaNDM genes. The MICs of Z. multiflora against S. aureus, and P. aeruginosa were ٣,١, and ٩,٣ mg/ml, respectively. The MIC of C. verum against S. aureus, and P. aeruginosa was ٣,١, and ٩,٣ mg/ml, respectively, while the MICs of M. pulegium against S. aureus, and P. aeruginosa were ٢,٥, and ٠ mg/ml, respectively. Among the investigated bacteria, P. aeruginosa exhibited the highest resistance to the essential oils. Z. multiflora demonstrated the highest inhibitory effect among the essential oils.

Conclusion: This study highlights the high sensitivity of these bacteria to Z. multiflora, C. verum, and M. pulegium essential oils. Therefore, these essential oils present promising alternatives to chemical drugs for combating infections caused by carbapenem-resistant bacteria

Keywords: resistance to carbapenems, antimicrobial effects, Z. multiflora, C. verum, M. pulegium,

The Application of PET/MRI Imaging in Breast Cancer: A Systematic Review (Review)

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Introduction: Breast cancer is the most prevalent cancer among women globally. Early and accurate diagnosis of breast cancer is crucial, as it significantly improves the treatment outcome and increases survival rates. Imaging plays a crucial role in the screening, diagnosis, staging, and management of breast cancer. Positron emission tomography (PET) and magnetic resonance imaging (MRI) have been merged into an integrated PET/MRI system, a hybrid imaging technology that simultaneously acquires the metabolic information from PET and the high-contrast morphological details from MRI in a single examination, potentially enhancing the precision of breast cancer management. The current systematic review focused on the potential advantages of PET/MRI for clinical applications in breast cancer diagnosis.

Methods: A comprehensive review was conducted using the PubMed, ScienceDirect, Web of Science, and Google Scholar databases, focusing on studies published up to July ٢٠٢٤. Different combinations of keywords such as "PET", "MRI", "PET/MRI", "breast cancer" and "diagnostic accuracy", "hybrid imaging" were employed, resulting in the selection of ٣٠ pertinent records based on relevance and recent advancements.

Results: The systematic review demonstrates that PET/MRI imaging in breast cancer offers superior diagnostic accuracy, with sensitivity rates reported between ٩٠٪ and ٩٨٪ and specificity ranging from ٨٥٪ to ٩٥٪. The combination of PET and dynamic contrast-enhanced MRI (DCE-MRI) improves whole-body cancer staging, achieving approximately ١٥٪ higher diagnostic accuracy than conventional imaging techniques such as computed tomography (CT) and bone scans. The review also highlights the efficacy of PET/MRI in accurately detecting distant metastases, especially in bones, and assessing axillary lymph node involvement. Additionally, the PET/MRI system reduces false positives by around ١٠-١٥٪ compared to traditional methods, leading to a significant reduction in unnecessary mastectomies and extensive axillary dissections.

Conclusion: PET/MRI represents a transformative tool in the clinical management of breast cancer, offering significant advantages in diagnostic accuracy, radiotherapy treatment planning, and treatment response evaluation by combining metabolic and anatomical imaging for a comprehensive assessment. The superior soft tissue contrast and functional imaging features of this

imaging modality led to more tailored surgical and radiotherapy planning, improving patient outcomes. The high sensitivity and specificity of PET/MRI systems in assessing treatment response of breast cancer patients, enable early detection of residual disease or recurrence, facilitating timely adjustments to therapeutic strategies.

Keywords: Breast Cancer, Diagnostic Accuracy, Hybrid Imaging, MRI, PET and PET/MRI.

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The Application of Stem Cells in Tissue Engineering for Craniofacial Bone Regeneration (Review)

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Introduction: Stem cells exist in many tissues such as bone marrow, fat, and skin, but the isolation of cells that have the ability to transform into other tissues is very expensive and is done with invasive methods that may damage the cell. Another tissue from which stem cells with high potential can be extracted are dental follicles. Dental follicle stem cells are a group of dental mesenchymal cells that play a role in the growth and maintenance of teeth. These cells can be a good choice due to their ability to transform into different tissues. By studying a series of genes in these cells, it was shown that these cells have the capacity of self-renewal and have great potential to transform into all kinds of tissues. Researches mention that DFPCS possessed more similar protein profile cranial neural crest cells (CNCCs) compared with dental plup stem cell (DPSCs). The purpose of this study is to The Application of Stem Cells in Tissue Engineering for Craniofacial Bone Regeneration.

Methods: In the present review article, we studied both original and review studies published in PubMed, Science Direct, Scopus and Google Scholar database using the key words Tissue Engineering; Craniofacial Bone Regeneration; Stem Cells

Results: As we mentioned earlier, DFPC's are an important type of dental stem cells that originate from dental follicles, and they can be widely used due to the transformation into different types of cells like Osteoblasts, cement oblasts, adipocytes and (PDL) cells. Also, DFPC's can be harvested from discarded tooth conveniently and noninvasively, which has led to lower costs and easier access to these cells, these two reasons make these cells a very good source for obtaining cells with It has become highly versatile.

Conclusion: According to the previous material, we hope to use DFPC's because of the low extraction cost and easier access compared to other stem cell sources. It's hoped that in the near future we'll be able to use this method in treatment of facial defects.

Keywords: stem cell, Tissue Engineering, Craniofacial Bone Regeneration

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The Applications of Artificial Neural Networks in Clinical Biochemistry (Review)

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Introduction: Artificial neural networks (ANNs) are inspired by the biological nervous system and are designed as computational models to recognize patterns and relationships in data sets. In clinical biochemistry, ANNs have been employed to analyze complex biochemical data, leading to significant advancements in diagnosis, prognosis, and treatment of diseases.

Methods: Multilayer Perceptron(MLP) and Radial Basis Function (RBF) are two main methods of ANN. Feed forward MLP has the best performance in biochemical analysis.

Results: Applications of ANNs in Clinical Biochemistry ANNs can be widely used in diagnosing various diseases by analyzing biochemical markers. For instance, they have been used to predict the onset of diabetes by analyzing glucose levels and other related biomarkers. Similarly, ANNs have shown promise in cancer detection by identifying specific tumor markers. Predictive models which are using ANNs can forecast disease progression and patient outcomes. For example, ANNs have been used to predict acute kidney injury by analyzing patient data, including serum creatinine levels and other biochemical parameters. These models help clinicians make informed decisions about patient care and treatment strategies. The ability of ANNs to analyze large datasets allows for the development of personalized treatment plans. By examining individual patient data, including genetic information and biochemical profiles, ANNs can recommend tailored therapies that maximize efficacy and minimize adverse effects. Benefits on ANNS ANNs can process vast amounts of data with high precision and are leading to more accurate diagnoses and predictions. The accuracy is particularly beneficial in identifying subtle patterns that may be missed by human experts. The automation of data analysis through ANNs reduces the time required for diagnostic processes and allowing for quicker decision-making and improved patient outcomes. ANNs can handle large-scale data from diverse sources, making them suitable for widespread clinical applications. This scalability is crucial in modern healthcare settings where data volume is continually increasing. Challenges of ANNs The performance of ANNs is heavily dependent on the quality and quantity of data. Inconsistent or incomplete data can lead to inaccurate predictions and diagnoses. Ensuring high-quality data collection and management is essential for the effective use of ANNs. One of the significant challenges with ANNs is their “black box” nature, where the decision-making process is not easily interpretable. This lack of transparency can hinder clinical adoption, as healthcare professionals may be reluctant to rely on systems that they do not fully understand. The use of ANNs in clinical settings raises regulatory and ethical concerns, particularly regarding patient data privacy and the potential for biased algorithms. Establishing precise regulatory frameworks and ethical guidelines is necessary to address these issues.

Conclusion: Artificial neural networks have been considered as powerful tools in clinical biochemistry, offering significant advancements in disease diagnosis, predictive analysis, and personalized medicine. While challenges remain, the continued evolution of ANNs and their integration into clinical workflows hold the promise of transforming healthcare measures and improving patient outcomes.

Keywords: Clinical Biochemistery, Artificial Neural Network. Mutilayer Perceptron.

The Contribution of Long Non Coding RNAs (lncRNAs) to Alzheimer's Disease: Mechanisms and Therapeutic Potential (Review)

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Introduction: Alzheimer's disease (AD) represents a significant challenge to public health, characterized as a chronic degenerative condition of the central nervous system (CNS) and recognized as the most prevalent form of dementia. This multifaceted disorder profoundly impacts cognitive functions, including memory, learning, comprehension, language, and judgment. The pathogenesis of AD is intricate, involving numerous interlinked signaling pathways and diverse cell types. A multitude of hypotheses regarding its etiology have been proposed; however, current consensus points to the accumulation of amyloid-beta plaques and tau tangles as pivotal factors in the disease's progression. Despite ongoing research efforts, a definitive cure remains elusive, underscoring the urgent need for effective therapeutic interventions aimed at slowing disease progression or alleviating symptoms. This necessity highlights the importance of identifying reliable biomarkers that can enhance diagnostic accuracy, particularly in the disease's early stages. In this context, non-coding RNAs (ncRNAs) emerge as a promising area of investigation. Among these, long non-coding RNAs (lncRNAs) have been recognized for their significant roles in various pathological processes associated with AD, including amyloid production, tau hyperphosphorylation, and neuroinflammation.

Methods: Alzheimer's disease (AD) poses a formidable challenge to public health, necessitating a deeper understanding of its complex pathogenesis. The accumulation of amyloid-beta plaques and tau tangles remains central to current models of AD progression; however, the multifactorial nature of the disease calls for a broader exploration of contributing factors. Our review underscores the emerging role of long non-coding RNAs (lncRNAs) in the regulatory networks that govern key pathological processes in AD, such as amyloid production, tau hyperphosphorylation, and neuroinflammation. The identification of specific lncRNAs associated with these processes not only enhances our understanding of AD's molecular underpinnings but also opens avenues for novel diagnostic and therapeutic strategies. As potential biomarkers, lncRNAs could facilitate earlier and more accurate diagnoses, which is critical for timely intervention.

Results: The investigation into the role of long non-coding RNAs (lncRNAs) in Alzheimer's disease (AD) has revealed significant insights into their regulatory functions and potential as biomarkers and therapeutic targets. Our review highlights several key findings regarding the involvement of lncRNAs in critical pathological processes associated with AD. Firstly, lncRNAs such as BACE١-AS and ٥١A have been identified as promoters of BACE١ expression, which is crucial for the cleavage of amyloid precursor protein (APP) and subsequent amyloid-beta (Aβ) accumulation. This accumulation is a hallmark of AD pathology, and the association of lncRNA ١٧A with alterations in the Aβ ratio further underscores the role of lncRNAs in neurodegeneration. Secondly, the hyperphosphorylation of tau

protein, which leads to neurofibrillary tangle formation, is significantly influenced by lncRNAs. Specifically, Linc٠٠٥٠٧ has been shown to facilitate tau hyperphosphorylation by promoting tau kinase activation, thereby contributing to the neurodegenerative processes, characteristic of AD. Moreover, mitochondrial dysfunction, an early event in AD, is modulated by lncRNAs such as NEAT١. Dysregulation of NEAT١ has been linked to impaired autophagy and increased tau pathology, indicating a complex interplay between lncRNAs and mitochondrial health in the context of AD. Synaptic impairment, a critical factor in cognitive decline, is also associated with lncRNAs. BC٢٠٠ and BDNF-AS have been implicated in regulating synaptic dynamics, with disturbances in their expression correlating with cognitive deficits observed in AD patients. Neuroinflammation, a significant contributor to AD pathology, is influenced by lncRNAs like MALAT١ and MEG٣, which exhibit anti-inflammatory effects. This suggests that lncRNAs may hold therapeutic potential in modulating inflammatory responses in AD. Lastly, the role of lncRNAs in neuronal apoptosis is highlighted by EBF٣-AS and MALAT١, which modulate apoptotic signals and contribute to neuronal loss in AD.

Conclusion: In summary, our comprehensive review underscores the pivotal role of long non-coding RNAs in the pathogenesis of Alzheimer's disease. The evidence presented indicates that lncRNAs are intricately involved in key processes such as neuroinflammation, amyloid beta metabolism and tau pathology. Furthermore, their potential as biomarkers for early diagnosis and as therapeutic targets opens new avenues for intervention. Future research should focus on elucidating the precise mechanisms of lncRNA action and their clinical applicability in AD management, paving the way for innovative strategies in combating this devastating disease.

Keywords: Alzheimer’s disease, lncRNAs, nervous system, biomarkers, pathogenesis

The CRISPR-Cas۹ Mediated KRAS Mutation Targeting: Overcoming Immune Evasion in Lung Cancer (Review)

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Introduction: Lung carcinoma continues to be a predominant contributor to cancer-associated mortality on a global scale, with non-small cell lung carcinoma (NSCLC) representing the most widespread subtype. A considerable obstacle in the therapeutic management of NSCLC is the existence of KRAS mutations, notably the KRAS^G۱۲C variant. Recent progress in CRISPR-Cas۹ technology has facilitated novel strategies for targeting these mutations, thereby providing optimism for the potential to surmount immune evasion mechanisms in lung carcinoma.

Methods: Researchers engaged in an innovative exploration utilizing in vivo CRISPR-Cas۹ screening methodologies. They developed a bespoke library aimed at ۲٤۰ genes modulated by KRAS. This pioneering investigation was conducted within a murine model of KRAS-mutant lung cancer. Subsequently, they introduced the genetically modified cells into mice to assess the resultant impact on immune responses. Sequencing of the genomic DNA extracted from tumors facilitated the identification of active sgRNAs and revealed the underlying mechanisms contributing to immune evasion.

Results: The investigation revealed a critical observation: KRAS mutations significantly elevate COX۲ expression, which consequently enhances the synthesis of prostaglandin E۲ (PGE۲), a bioactive molecule that inhibits immune function. This PGE۲ pathway emerged as a central determinant in the resistance to immune checkpoint blockade (ICB) therapies, particularly those targeting PD۱. The PGE۲ compound fosters a tumor microenvironment that diminishes cytotoxic T-cell efficacy while facilitating the rise of myeloid-derived suppressor cells. Nonetheless, by targeting the COX۲/PGE۲ axis, researchers accomplished remarkable outcomes. The tumor microenvironment was successfully reengineered, creating a proinflammatory atmosphere in myeloid cells, which thereby facilitated the infiltration and activation of CD۸+ T-cells. This transformation markedly improved the efficacy of ICB therapies in KRAS-mutant lung tumors, resulting in more robust antitumor immune responses. Furthermore, the inhibition of COX۲ postponed tumor recurrence subsequent to the targeting of KRASG۱۲C, suggesting a potent synergistic interaction between these therapeutic modalities. Conversely, the study also indicated that the reinstatement of COX۲ expression precipitated tumor relapse following extended KRAS inhibition. This observation implies that persistent COX۲ activity may compromise the long-term efficacy of KRAS-targeted therapies, thereby underscoring the necessity for concurrent COX۲ inhibition.

Conclusion: This research highlights the complex mechanisms through which KRAS mutations facilitate immune evasion in lung cancer. The research highlights COX٢'s role as a key player in the challenges faced with immunotherapy, paving the way for combining COX٢/PGE٢ pathway blockers with therapies aimed at KRAS. This combinatorial strategy presents significant potential for overcoming resistance and enhancing treatment outcomes for patients afflicted with KRAS-mutant lung cancer. Future investigations should focus on refining these combination therapies and examining the broader implications of targeting immune evasion in oncological treatments.

Keywords: CRISPR-Cas٩, KRAS Mutation, Lung Cancer

The current progress on the antidiabetic, antibacterial, anticancer and antiAlzheimer properties of the genus Tamarix: A review. (Review)

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Introduction: The current progress on the antidiabetic, antibacterial, anticancer and antiAlzheimer properties of the genus Tamarix: A review. Introduction: Tamarix (T.) species are known as medicinal plants, used as the possible medications for some diseases and the value of the medicinal plant products is exceeding $ ١٠٠ per year. Traditionally, the genus Tamarix is known as "Gaz" in Persian culture, is mentioned in Quran as "Athl or "Manna" (Chapter Baqara: ٥٧ and Saba: ١٦) and is prescribed for several diseases in Persian medicine. The genus Tamarix (Tamaricaceae) includes ٧٠-١٠٤ halophyte species, grows as shrubs to trees up to ١٨ meters in the salty environments (soils etc.) and is considered as the potential medications for several diseases. The main objective of the review is to compile the most recent data on the effects of the methalonic, ethalonic and aqueous extracts of Tamarix species for antidiabetic, antibacterial, anticancer and antiAlzheimer treatments.

Methods: Methods: This review is based on the available data in PubMed, Science Direct and Google Scholar data, by keywords of Tamarix, medicinal plants, diabetes, cancer and Alzheimer from ٢٠٠٤-٢٠٢٤ and reviewing the abstracts and conclusions of the papers. Some irrelevant papers were excluded and the most related ones on the genus Tamarix were considered for this paper. Apart from the above data, in order to identify the Tamarix species in Kerman city, ٢٤ samples of Tamarix leaves and flowers around the Kerman city were collected during April ٢٠٢٤. The samples were dried under shade then pressed under carton papers for one month and finally, were submitted to the herbarium Laboratory of Biology Department, Shahid Bahonar University of Kerman, Iran for systematics of Tamarix species.

Results: Results: This investigation highlights that the main composition of the genus Tamarix are flavonoids (١٨,٠٪), phenols (١٣,٩٪), tanins (٩,٣٪), terpenoids (١٠,٥٪), essential oils (٣١,٠٪) and other organic components (١٧,٥٪). The results on the crude methalonic, ethalonic and aqueous extracts from the abovementioned compounds of the genus Tamarix show antioxidant and antidiabetic properties for the following diseases: Diabetes: It is recognized that diabetes mellitus is a metabolic disorder that has no well-defined treatment, yet treatment by commercial α-glucosidase may lead to acute hepatitis. To overcome this adverse side effect, the methalonic and ethalonic extracts of leaves in T. aphylla, T. nilotica, T. dioica, T. gallica, T. articulata and T. stricta give considerable antidiabetic treatment by inhibiting α-glucosidase as well as α-amylase activities, digestion of carbohydrates and regulating the blood sugar levels. Bacterial and Fungal diseases: As a results of allergic side effects caused by antibiotics, the extracts of leaves and flowers in T. gallica, T. africana, T. aphylla, T. dioica, T.arabica, T. tetragyna and T. nilotica give significant antibacterial and antifungal medications. Cancer : Notably, syringic acid extracted from the Tamarix species, in particular T. dioica, T. hispida and T. ramosissima inhibits cell proliferation, in

particular in rectal cancer cells. Alzheimer: The presence of antioxidants in the extracts of T. gallica, T. aphylla, T. africana, T. hispida and T. ramosissima diminishes the brain damages induced by the oxygen free radicals, thus provide a possible treatment for Alzheimers, s disease Rheumatoid Arthritis: It is noteworthy that ramosissimin or a flavonol extracts from the T. ramosissima is reported to induce cell death on the fibroblast-like synoviocytes and provide medicaments of rheumatoid arthritis. Liver fibrosis: There exist some data that methalonic and polyphenols extracts from T. ramosissima and T. hispida may have considerable potential for inhibiting the carcinogenesis of hepatocytes and protecting liver fibrosis. Lithiasis: Urinary minerals and stones are mostly of calcium-oxhalate. The acidic nature of extracts from T. hispida and T. ramaosissima can dissolve the minerals, thereby suppressing the nephroliths.

Conclusion: Conclusion: Tamarix species are salt-resistant plants that contain considerable components of flavonoids, phenols, tanins, terpentoids, volatile oils and others. The methalonic, ethalonic and aqueous extracts from the abovementioned species (e.g., T. ramosissima, etc.) offer potential medications for antidiabetic, antibacterial, anticancer, antiAlzheimer diseases. The occurrence of T. ramosissima and other species around the Kerman city merits further investigations on the DNA fingerprint atlas of these potential medicinal plants.

Keywords: Keywords. Tamarix species, T. ramosissima, Extracted medications, Tamarix DNA fingerprint atlas.

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The discovery of Exo-miRNAs presents a novel therapeutic strategy for patients with breast cancer

(Review)

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Introduction: Exosomes, or extracellular vesicles (EVs), are naturally occurring vesicles that carry specific biomarkers from their source cells. They contain a variety of biologically active substances, including lipids, proteins, nucleic acids, and non-coding RNAs like microRNAs (miRNAs). Exosomes facilitate intercellular communication, particularly between tumor cells and their surrounding environment, influencing cell functions during cancer progression. miRNAs are of particular interest as they can be taken up by nearby or distant cells, promoting oncogenic signaling and altering recipient cells. Research shows that exosomal miRNAs can induce malignant transformation in non-metastatic breast cells, highlighting their role in cancer development and positioning them as potential biomarkers for diagnosis and prognosis. Additionally, exosomal miRNAs offer promising opportunities for targeted cancer therapies and drug delivery systems.

Methods: We conducted a literature review to investigate the impact of EV-miR on breast cancer outcomes. To do this, we searched the PubMed database with the keywords "Exosome," "microRNA," "breast cancer," and "therapy." After evaluating the search results, we focused on the articles pertinent to therapy.

Results: Exosomes enriched with miR-٥٠٠a-٥p, miR-٣٧٨a-٣p, miR-٣٧٨d, miR-٣٤a, miR-١٤٥, miR-١٨١b-٥p, miR-٢١٨, miR-٣٤a-٥p, miR-٥٨٨, miR-٢٠٥, and miR-٣٨١ have the potential to significantly improve treatment efficacy, enhance anticancer properties, affect drug resistance, and demonstrate overall effectiveness in cancer therapy. Furthermore, these exosomes can act as efficient drug delivery systems. Our research suggests that exosomes containing various microRNAs may offer a promising approach for innovative therapies in breast cancer.

Conclusion: Our research indicates that exosomes containing a diverse array of microRNAs could represent a groundbreaking strategy for innovative therapies in breast cancer. By harnessing the potential of these exosomes, we may be able to develop novel treatment modalities that not only improve patient outcomes but also pave the way for personalized medicine approaches in oncology. This could ultimately lead to more effective and tailored therapies that address the unique characteristics of each patient's cancer, thereby revolutionizing the landscape of breast cancer treatment.

Keywords: Exosome - microRNA - Breast cancer - therapy-

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The EBV-Nasopharyngeal Carcinoma Connection (Review)

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Introduction: The majority of adults worldwide have been infected with the Epstein-Barr virus (EBV), a virus belonging to the gamma herpesvirus group. It can be regarded as the best-known oncovirus to some extent. EBV typically remains mostly inactive in persistent infection following initial infection, which usually occurs before adolescence. It has the potential to reactivate in specific circumstances, which could be linked to various cancers. Among human head and neck carcinomas (HNCs), nasopharyngeal carcinomas (NPCs) are distinguished by their consistent association with EBV, their unique geographic distribution, and their distinct histological features. NPC is currently the best-characterized human epithelial malignancy linked to EBV infection.

Methods: Scientific resources from PubMed, Science Direct, Springer, and Google Scholar were used to write this review study.

Results: Reports indicate that EBV infection is a significant risk factor and plays a crucial role in the development of NPC. Unlike its ability to transform primary B cells and render them immortal, EBV does not directly convert nasopharyngeal epithelial cells into proliferative clones. Instead, a hallmark of premalignant nasopharyngeal epithelial cells is latent EBV infection. Viral genes including Epstein–Barr virus–encoded small RNAs (EBERs) and Epstein–Barr virus nuclear antigen ١ (EBNA١), latent membrane protein ١ (LMP١), and latent membrane protein ٢A (LMP٢A) are expressed as a result of the latency program unique to epithelial cells. The changing state of premalignant nasopharyngeal epithelial cells is the first step toward the development of NPC. Through the deregulation of genes involved in DNA repair, cell cycle checkpoint, and anti-oncogenic activity, EBV causes genomic instability in infected premalignant cells. By preventing Chk١ activation, LMP١ causes a G٢ checkpoint malfunction. This allows unrepaired chromatid breaks to progress through mitosis, which spreads and builds up over time, ultimately resulting in chromosomal instability. High expression of EBV-miR-BART suggests its role in promoting epithelial cell survival. by affecting gene expression and leading to inappropriate epigenetic modifications, EBV also plays a role in non-mutational genetic instability. EBV-encoded latent proteins and microRNAs can compromise host immune responses by interfering with cytokine signaling networks and antigen presentation. This interference encourages the infiltration of immune-regulating cells, which can stimulate metastasis and tumor growth. LMP١, an EBV-encoded protein, enhances the epithelial-mesenchymal transition (EMT) by regulating transcription factors such as Twist and Snail. Additionally, it boosts calreticulin production through

the TGF-β pathway. In nasopharyngeal carcinoma (NPC), EBV induces angiogenesis by upregulating the expression of vascular cell adhesion molecule ١ (VCAM-١) with exosome-packaged EBERs. Furthermore, EBV regulates glucose metabolism in NPC by activating mTORC١ through LMP١, leading to NF-κB signaling and increased GLUT١ transcription. This process is mediated by the AKT/ERK/IKK signaling pathway.

Conclusion: Since EBV infection and NPC development are closely linked, EBV serology, which measures EBV DNA and antibodies against EBV oncoproteins, is a promising approach as a disease biomarker. It offers the potential to be used for minimal residual disease and therapeutic efficacy monitoring. Treatment options for NPCs differ according to stage. While radiation, chemotherapy, and surgery are standard treatments, surgical options are limited due to the deep placement of the tumor and the intricate anatomical features of the region where it is located. However, because NPC is a highly sensitive tumor to radiation and chemotherapy, the mainstay of care for patients with stage I/II NPC is either radiotherapy or chemotherapy, often administered alone or in combination. In the context of nasopharyngeal cancer, immunotherapy offers promising therapeutic potential. Key strategies in this area include immune checkpoint inhibitors, adoptive T-cell therapy, and EBV-directed immunization.

Keywords: Epstein-Barr virus (EBV), nasopharyngeal carcinomas (NPC), latent membrane protein ١ (LMP١)

The Effect of Adipose-Derived Mesenchymal Stem Cells on Neural Precursor Cell Differentiation and Motor Function Recovery in a Rat Model of Spinal Cord Injury (Review)

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Introduction: Spinal cord injury (SCI) often results in permanent neurological deficits and paralysis, presenting significant challenges for functional recovery. Various therapeutic approaches have been explored to promote repair and regeneration of the damaged spinal cord. Among these, cell-based therapies, particularly using mesenchymal stem cells (MSCs), have shown promise due to their potential to differentiate into various cell types and secrete neurotrophic factors. Adipose-derived mesenchymal stem cells (AD-MSCs) are of particular interest because they are readily accessible and possess robust regenerative properties. This study aims to evaluate the effect of AD-MSCs on the differentiation of neural precursor cells (NPCs) and the recovery of motor function in a rat model of SCI.

Methods: In this study, a total of ٦٠ adult Wistar rats (٣٠ males and ٣٠ females) were used. The mean age of the rats was ١٠ weeks, and the mean weight was ٢٥٠ grams. The rats were randomly assigned into three groups: control group (n=٢٠), SCI group (n=٢٠), and AD-MSC-treated SCI group (n=٢٠). The SCI was induced using a standardized contusion injury model at the T٩-T١٠ vertebral level. The AD-MSCs were isolated from the adipose tissue of healthy donor rats and expanded in vitro. Two weeks post-SCI, the AD-MSCs were transplanted into the injury site of the treatment group. Behavioral assessments, including the Basso, Beattie, and Bresnahan (BBB) locomotor rating scale, were performed weekly to evaluate motor function recovery. Immunohistochemical analyses were conducted to assess the differentiation of NPCs into neurons and glial cells within the injured spinal cord.

Results: The results demonstrated a significant improvement in motor function in the AD-MSC-treated SCI group compared to the untreated SCI group. The BBB scores of the AD-MSC-treated group increased from an average of ١,٢ ± ٠,٥ at one week post-injury to ٧,٨ ± ٠,٧ at eight weeks post-injury, whereas the untreated SCI group showed a more modest increase from ١,١ ± ٠,٤ to ٣,٩ ± ٠,٦ over the same period. Immunohistochemical analyses revealed a higher number of differentiated neurons and oligodendrocytes in the AD-MSC-treated group, with an average of ٨٥ ± ١٠ neurons and ٧٠ ± ٨ oligodendrocytes per mm² in the treated group compared to ٤٥ ± ٧ neurons and ٣٠ ± ٥ oligodendrocytes per mm² in the untreated group. Additionally, the presence of glial scar tissue was significantly reduced in the AD-MSC-treated rats.

Conclusion: The transplantation of adipose-derived mesenchymal stem cells significantly promotes the differentiation of neural precursor cells into neurons and oligodendrocytes, and enhances motor function recovery in a rat model of spinal cord injury. These findings suggest that AD-MSCs could be a promising therapeutic approach for the treatment of SCI, potentially aiding in the repair and regeneration of the damaged spinal cord and improving functional outcomes. Further studies are

warranted to elucidate the underlying mechanisms and optimize the therapeutic protocols for clinical application.

Keywords: Adipose-Derived Mesenchymal Stem Cells, Neural Precursor Cells, Spinal Cord Injury, Rat Model

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The effect of aerobic exercise with NBS supplementation on dopamine and DAT in male rats consuming methamphetamine (Research Paper)

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Introduction: Methamphetamine not only causes addiction but also induces abnormal alterations in dopamine and its transporter (DAT). These harmful effects remain even after relatively long periods of withdrawal. Therefore, this study aimed to investigate the impact of aerobic exercise intervention combined with NBS wheat supplementation on dopamine and DAT in male rats exposed to methamphetamine.

Methods: ٤٨ male Wistar rats, aged ٨ weeks, with an average weight of ٢٠٠±١٠ grams, were randomly divided into six groups: control (CO), methamphetamine (MA), withdrawal (W), withdrawal and aerobic exercise (W/TR), withdrawal and supplementation (W/SUP), and withdrawal combined with aerobic exercise and supplementation (W/TR+SUP). The rats were initially addicted to methamphetamine through intraperitoneal injections over six weeks, with the dosage increasing from ٢٠ mg/kg body weight in the first week to ٣٠ mg/kg in the final week. At the end of the intervention, the rats were sacrificed, and their brains were completely removed. Changes in DAT expression were measured using RT-PCR, and Dopamine level were assessed through Western blotting.

Results: The results of the ANOVA statistical test revealed significant differences between the groups for all markers (P = ٠,٠٠١). The LSD post-hoc test results showed that DAT expression in the withdrawal combined with aerobic exercise and supplementation group significantly increased compared to the control group, while it significantly decreased compared to the withdrawal and supplementation group (P = ٠,٠٠١ for both comparisons).

Conclusion: Overall, the findings of this study suggest that aerobic exercise combined with NBS supplementation can enhance mono-amine levels more effectively than either intervention alone, aiding in the recovery and normalization of monoamine transporter levels.

Keywords: Methamphetamine, Aerobic exercise, Wheat supplement, dopamine, dopamine transporter

The effect of aerobic exercise with NBS supplementation on serotonin and SERT in male rats consuming methamphetamine (Research Paper)

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2. University of Tehran, Iran

Introduction: Methamphetamine not only causes addiction but also induces abnormal alterations in serotonin and its transporter (SERT). These harmful effects remain even after relatively long periods of withdrawal. Therefore, this study aimed to investigate the impact of aerobic exercise intervention combined with NBS wheat supplementation on serotonin and SERT in male rats exposed to methamphetamine.

Methods: ٤٨ male Wistar rats, aged ٨ weeks, with an average weight of ٢٠٠±١٠ grams, were randomly divided into six groups: control (CO), methamphetamine (MA), withdrawal (W), withdrawal and aerobic exercise (W/TR), withdrawal and supplementation (W/SUP), and withdrawal combined with aerobic exercise and supplementation (W/TR+SUP). The rats were initially addicted to methamphetamine through intraperitoneal injections over six weeks, with the dosage increasing from ٢٠ mg/kg body weight in the first week to ٣٠ mg/kg in the final week. CO continued their normal routine for six weeks, while the withdrawal and aerobic exercise group performed aerobic exercises at ٦٠٪ of maximal running speed (MRS) for the first three weeks and at ٧٠٪ MRS for the next three weeks. The withdrawal and supplementation group received NBS wheat supplementation via gavage for six weeks, and the withdrawal combined with aerobic exercise and supplementation group followed both protocols. At the end of the intervention, the rats were sacrificed, and their brains were completely removed. Changes in SERT expression were measured using RT-PCR, and serotonin level were assessed through Western blotting.

Results: SERT in the W and W/TR+SUP group significantly decreased compared to the CO and MA groups (P=٠,٠٠١) (P=٠,٠٠١). Serotonin in the W and W/TR+SUP group significantly increased compared to all groups (P=٠,٠٠١).

Conclusion: Overall, the findings of this study suggest that aerobic exercise combined with NBS supplementation can enhance mono-amine levels more effectively than either intervention alone, aiding in the recovery and normalization of monoamine transporter levels.

Keywords: Methamphetamine, Aerobic exercise, Wheat supplement, ٥-HT, SERT

The effect of anti-thyroid cancer drugs on laminin protein by molecular docking method (Research Paper)

Mahdiyeh Gholaminezhad estalkhjani,[1,*]

[1]. -

Introduction: laminin protein is a target for thyroid cancer treatment. Sorafenib is an oral multi-kinase inhibitor that is used in the therapy of advanced renal cell, liver and thyroid cancer . Doxorubicin is an antibiotic in the treatment of cancer . These compounds are used to treat many cancers, including blood , breast, stomach , uterine , ovarian , lung and thyroid cancer. Vandetanib is a drug that is used to treat medullary thyroid cancer that cannot be treated with surgery or has spread to other parts of the body. Sunitinib is a medicine which is used in the treatment of gastrointestinal tract, kidney, pancreas and advanced thyroid cancer . The purpose of this research is to investigate the effects of anti-thyroid cancer drugs on laminin protein .

Methods: First, prepared the three-dimensional structure of the laminin protein by using the Uniprot site . Then, we obtain the three-dimensional structure of Sorafenib- Doxorubicin - Vandetanib and sunitinib drugs through the Pubchem site. In the next step, using the Chimera ۱,۱۰,۲ program, we include changes such as removing ions, adding hydrogen, removing extra chains, etc. in the original protein . Finally, with the PyRx program, we start docking by loading the modified protein file as macromolecule and the drug file as input .

Results: Drug Binding Affinity (kcal/mol) RMSD bound Sorafenib ۱۰- ۰ Doxorubicin ۹,۲- ۰ Vandetanib ۷,۸- ۰ Sunitinib ۷,٦- ۰

Conclusion: According to the investigations, sorfanib has the most effect on laminin protein, and Doxorubicin , Vandetanib and sunitinib have the most effect, respectively .

Keywords: Laminin , sorfanib , Doxorubicin , Vandetanib , sunitini

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The effect of case-based learning on self-directed learning and clinical self-efficacy in medical students (Review)

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Introduction: Today, the use of the case-based method in the education of medical sciences, especially in the era of basic sciences, is expanding in most universities worldwide. The reason for paying attention to this learning method is that it can cause the teacher's and student's active participation in the topics presented. The definition of case-based learning as a method to bring the educational environment closer to the real learning environment, case-based learning models and the application of each based on the academic environment, the principles of scenario design, and the results of studies on the effectiveness of this method in medical education are considered. took Creating and promoting self-directed learning is one of the important goals of higher education. Due to the benefits of self-directed learning, attention to this type of learning and basic training to promote it has been given attention in recent years. Self-efficacy in clinical practice was synonymous with acquiring clinical skills, examining the patient, planning and implementing, and evaluating care. Case-based learning (CBL) in medical education is an educational approach that engages students as learners through active learning in small, collaborative groups to solve clinical patient cases. The purpose of this study is to investigate the effect of case-based learning on self-directed learning and clinical self-efficacy in medical students.

Methods: The present study is a narrative review. After studying and evaluating ٤٢ original articles in Sid, PubMed, and Google Scholar databases through a simple and advanced search and using keywords "Case-based learning" "Self-directed learning" "clinical self-efficacy" and "Medical students" Between these retrieved articles in the stages of title, abstract and full text, finally ١٢ articles were selected and analyzed.

Results: The finding indicates that life-long self-directed learning is considered an integral part of the medical profession, and the best way to develop it in clinical education is still unknown. Case-based learning significantly improves self-directed learning and clinical self-efficacy in medical students. Studies report that CBL improves problem-solving abilities, critical thinking, and clinical

communication skills. Case-based learning has not only helped to increase students' theoretical knowledge but also strengthened their confidence in clinical situations. Using the case-based learning method prepares students with a variety of experiences in the classroom, including problem-solving, building knowledge together, communication, and group participation. CBL is an active teaching method that is effective for teaching medical students and helps to improve their performance and case analysis ability. Clinical performance self-efficacy is a person's belief about his abilities to perform a clinical skill. The higher the self-efficacy of clinical performance, the better the clinical performance.

Conclusion: Since the desire for lifelong learning is an important factor, medical schools and residency training programs should increase their efforts to develop this characteristic in learners. To realize their full potential as learners, students must have good self-directed learning skills. Rapid changes and developments in the field of science and knowledge necessitate the urgent need for higher education systems for self-directed and independent learners. Self-directed learning is one of the most important skills that make a person independent in learning and the foundation for lifelong learning. Self-efficacy is one of the important concepts for improving the clinical performance of medical students, so it is recommended to develop regular training programs with a supportive approach to strengthen all aspects of clinical performance self-efficacy.

Keywords: Case-based learning, self-directed learning, clinical self-efficacy, medical students

The effect of cell therapy in cancer treatment (Review)

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Introduction: Cancer is a major challenge to human health worldwide, and, while making some progress, traditional cancer treatments, such as chemotherapy, radiotherapy and surgery, often have a series of limitations and side effects (١). However, in recent years, chimeric antigen receptor (CAR)-T cell therapy, which is also known as the 'living drug', has emerged (٢). CAR-T cell therapy has garnered interest in the field of cancer treatment as a personalized cancer immunotherapy strategy (٢,٣). It works by altering the immune system of a patient, allowing it to recognize, attack and remove cancer cells (٤). Among the immune system, CAR-T cells are a special subpopulation of T cells that are genetically engineered to express specific antigen receptors, and to effectively recognize and destroy cancer cells (٥). However, this therapy also faces multifaceted challenges, such as antigen selection, treatment tolerance and safety .Tumor cells lacking specific antigens or displaying heterogeneity in antigen expression can impair the antigen selectivity of CAR-T cells (٨)

Methods: First, doctors screen patients to determine if the patients are eligible to receive CAR-T cell therapy (٥١). This typically includes evaluating the disease type, stage of disease, physical health and immune system status of the patient (٥٢). The peripheral blood of the patient is collected, and the T cells are isolated using centrifugation and immunomagnetic bead assay. In the laboratory, the T cells are genetically modified to introduce the CAR gene, which enables the T cells to recognize and attack specific tumor cells. The modified T cells are expanded and cultured in vitro to increase their number, which allows a sufficient number of CAR-T cells to be obtained for use in therapy

Results: Tisagenlecleucel (٨٩) (Novartis International AG) and axicabtagene ciloleucel (٨٩) (Kite Pharma; Gilead Sciences, Inc.) have been approved by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency. They are used for the treatment of relapsed/refractory B-NHL in adults (٩٠). In addition, Tecartus™ (٩١) is a CAR-T cell therapy drug, developed by Gilead Sciences, Inc., for the treatment of relapsed/refractory B-ALL in adults (Table I). Bristol-Myers Squibb Company developed Breyanzi (lisocabtagene maraleucel) for the treatment of adult relapsed/refractory large B-cell lymphoma

Conclusion: CAR-T cell therapy is a revolutionary immunotherapy that has achieved notable success in treating a number of B cell-associated malignancies. By targeting specific antigens on the surface of tumors, CAR-T cells are able to identify and destroy malignant cells, providing a new treatment option for those patients for whom conventional therapies have failed. However, CAR-T cell therapy still faces a number of challenges and limitations. Serious adverse reactions, such as CRS and neurotoxicity, may occur during treatment

Keywords: CAR-T-cell Therapy -Cancer

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The effect of consuming three types of tea along with combined exercise training on weight loss and health-related markers in overweight and obese men (Research Paper)

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Introduction: One of the most important health issues in the world is obesity, and the most effective factor in its prevention and treatment is physical activity. Physical activity has been shown to reduce obesity risk factors. In addition to exercise, pharmaceutical and nutritional interventions can be effective in obesity treatment. However, our aim was investigating of the effect of consuming three types of tea along with combined exercise training on weight loss and health-related markers in overweight and obese men.

Methods: ٦٠ overweight or obese men aged ٣٠ to ٥٠ (BMI ٣٥-٢٥) were randomly assigned to four groups of training + green tea (GT+T), training + white tea (WT+T), training + roselle tea (ST+T) and training (T) for ٨ weeks. Blood samples were measured ٤٨ hours before and ٤٨ hours after the last training session. leptin and adiponectin were measured using ELISA method. Also, body composition indices measured. Statistical analysis was performed using ANCOVA method at a significance level of ٠,٠٥.

Results: Results showed significant reductions in body composition indices (weight, BMI, FM) in intervention groups WT+T and GT+T compared to the control group, while FFM showing no significant changes. Weight, BMI, and FM variables in the WT+T group had a more significant reduction compared to ST+T, and weight and BMI variables in the WT+T group had a more significant reduction compared to the GT+T group. Additionally, Leptin and Adiponectin in the intervention group WT+T showed significant changes compared to the control group. Furthermore, Leptin and Adiponectin in the WT+T group had more significant changes compared to the ST+T group, and Leptin and Adiponectin variables in the WT+T group had a more significant reduction compared to the GT+T group.

Conclusion: In conclusion the consumption of white tea and green tea combined with combined exercise had a significant effect on body composition indices and adipokines, but no significant change was observed in the case of sour tea combined with combined exercise. The difference in the averages showed that the effect of white tea on the measured indicators is more than other interventions.

Keywords: Combined exercise training, Tea, Obesity

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The effect of endurance training and ketosis on brain lactate with magnetic resonance spectroscopy in people with Verne hypertrophy (Review)

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Introduction: Obesity is a growing global health problem, the prevalence of which is increasing in children and adults. More than ١,٤ billion adults are overweight and another ٥٠٠ million adults worldwide are classified as obese. Studying obesity is important because it is associated with an increased risk of developing a number of medical conditions. Overweight and obesity cause many diseases such as high blood pressure, diabetes, malnutrition, metabolic syndrome, inflammation, and neurological problems. It also increases the risk of cognitive decline and even the diagnosis of dementia in life. These findings are of considerable concern, as it is well documented that even the healthiest adults show age-related declines in basic cognitive operations, including processing speed, working memory, reasoning, and episodic memory. The effects of obesity are most prominent in brain aging. in old age and also this situation causes a further decrease in cognition.

Methods: Investigating the effect of endurance training and ketosis on brain lactate with magnetic resonance spectroscopy in people with hypervolemia Investigating the effect of endurance training and ketosis on weight in people with obesity Investigating the effect of endurance training and ketosis on fat percentage in people with excess fat

Results: A course of endurance training and ketosis has a significant effect on brain lactate by magnetic resonance spectroscopy in people with Verne's excess. A period of endurance training and ketosis has a significant effect on weight in people with overweight. A period of endurance training and ketosis has a significant effect on the percentage of fat in people with excess fat.

Conclusion: Pathological changes associated with obesity alter the uniformity of brain white matter neural networks, as demonstrated by diffusion tensor imaging (DTI). Increased mean diffusion (MD) and decreased fractional anisotropy (FA) in DTI observed in obese subjects may be due to degeneration of neural structures. This study aimed to investigate the effect of high-intensity interval training and ketogenic diet on brain aging in obese and overweight adults using DTI.

Keywords: endurance training, ketosis, Verne hypertrophy, magnetic resonance spectroscopy

The effect of environmental and genetic factors on infertility (Review)

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Introduction: Infertility is one of the most common reproductive health problems affecting the lives of millions of couples around the world. This problem can be caused by various factors, which are generally divided into two categories: environmental and genetic factors. Environmental factors include factors such as nutrition, stress, environmental pollution, and lifestyle habits, while genetic factors include chromosomal abnormalities, gene mutations, and hereditary disorders. Accurate identification and understanding of these factors can help improve the diagnosis and treatment of infertility. The purpose of this review study is to identify and categorize environmental factors affecting infertility, identify and categorize genetic factors affecting infertility, investigate the interaction between environmental and genetic factors in the occurrence of infertility, and evaluate the proposed strategies for the prevention and treatment of infertility related to these factors.

Methods: This research has been done as a systematic review. Studies published between ۲۰۰۰ and ۲۰۲۲ that investigated the effect of environmental and genetic factors on infertility. Data were collected by searching scientific databases such as PubMed, Scopus, and Web of Science. Search keywords included "infertility", "environmental factors", "genetic factors" and "gene mutation". Studies that investigated the effect of environmental and genetic factors on infertility and had valid methodology have been reviewed. Irrelevant articles, low quality studies and invalid articles were excluded from the review. The collected data have been reviewed and analyzed using the methods of content analysis and qualitative meta-analysis.

Results: The results of the review showed that factors such as poor nutrition, stress, environmental pollution (such as heavy metals and chemicals), smoking and alcohol consumption, and unhealthy lifestyle habits can significantly affect infertility. Chromosomal abnormalities such as Turner syndrome and Klinefelter syndrome, genetic mutations in fertility-related genes such as FMR۱, and inherited disorders such as metabolic abnormalities can lead to infertility. Some studies showed that there is a complex interaction between environmental and genetic factors. For example, people with certain gene mutations may be more sensitive to environmental factors, which can lead to an increased risk of infertility. Various strategies have been suggested for the prevention and treatment of infertility related to these factors. These strategies include changes in lifestyle, stress management, improved nutrition, genetic counseling and the use of advanced medical techniques such as IVF and PGD.

Conclusion: This systematic review study showed that infertility is influenced by multiple environmental and genetic factors. To prevent and effectively treat infertility, we need to accurately identify these factors and develop comprehensive and multifaceted solutions. Lifestyle changes, stress management, genetic counseling and the use of advanced medical techniques can help reduce

infertility and improve fertility. Also, further research on the interaction between environmental and genetic factors can help improve our understanding of this problem and develop new solutions.

Keywords: Infertility, environmental factors, genetic factors, gene mutation

The effect of Exercise in improving infertility factors in women (Review)

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Introduction: Exercise is one of the most important factors for maintaining health and well-being. Women are more at risk of diseases than men due to their specific metabolism. For this reason, it is necessary to try to prevent and strengthen their health in order to prevent the possible occurrence of dangerous diseases. By regulating weight and reducing obesity, reducing LDL (Low-density lipoprotein) and lowering blood pressure and regulating blood sugar, exercise has a direct effect on the functioning of organs. But in women, exercise has another special importance, and that is the treatment and prevention of its effect on infertility. In this way, it is effective in the prevention and treatment of polycystic ovary disease, menopause, premenopause and endometriosis and helps to maintain fertility. Physical activity, with its effect on the athlete's mood, has a special effect on the effectiveness of drugs used in the treatment of infertility, in addition, exercise leads to the release of hormones that are very effective in regulating menstruation and ovulation. During pregnancy, exercise also reduces inappropriate weight gain during pregnancy and helps to have a proper delivery by strengthening the pelvic floor muscles.

Methods: This study consolidates data from multiple research projects that focus on the effects of physical exercise on menopausal symptoms. The emphasis is on walking programs, which are compared to other forms of exercise such as aerobic workouts and resistance training. The study population comprised women aged ٤٥-٦٠ who were experiencing menopausal symptoms. The interventions varied in length, frequency, and intensity, but all involved regular, structured physical activity over a minimum of ١٢ weeks. Symptom severity was assessed using standardized surveys before and after the intervention.

Results: The data consistently reveal that women who engaged in walking and other physical activity programs reported a substantial decrease in menopausal symptoms. The most significant improvements were seen in the frequency and severity of hot flashes, sleep quality, and emotional stability. Participants who performed moderate to vigorous physical activity at least three times per week experienced the most notable benefits. Beyond symptom relief, participants also reported enhanced overall fitness and a greater sense of well-being.

Conclusion: Physical exercise, particularly walking, offers an effective and practical method for alleviating menopausal symptoms. This non-invasive intervention not only reduces physical discomfort but also improves mental health and overall life satisfaction. Future research should investigate the long-term effects of sustained physical activity on menopause and explore the potential advantages of combining exercise with other lifestyle modifications. By encouraging

regular physical activity, healthcare providers can adopt a holistic, patient-focused approach to managing menopause.

Keywords: physical activity, infertility,PCOS, obesity,۴. Endometrosis

The effect of exosomes derived from bone marrow mesenchymal stem cells on the osteogenesis process: effects based on the type of producing cells (Review)

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Introduction: Today, communities and their health systems are facing with several challenges associated with the population ageing. Growing number of bone disorders is one of the most serious consequences of aging. According to the reports bone disorders won't just affect the elderly population. Mesenchymal stem cells (MSCs) are multipotent cells that could be derived from a variety of tissues including bone marrow, Wharton's Jelly, adipose tissue, and others. MSCs have been utilized in different researches in the field of regenerative medicine because of their immunosuppression and anti-inflammatory mechanisms (like: inhibiting the activity of antigen presenting cells, and suppressing the activity of T lymphocyte cells, macrophages, and so on.), migration to injured areas, and participation in healing processes. Bone marrow mesenchymal stem cells (BMMSCs) are a type of these cells which can be commonly used in bone research with the promising results. These cells function by releasing a large number of extracellular vesicles (EVs). Exosomes are the most major EVs products produced by BMMSCs. They have the same contents and properties as their parent cells; however, these structures don't have the defects of cell therapy. Proteins (annexins, tetraspannins, etc.), lipids (cholesterol, phosphoglycerides, etc.), nucleic acids (micro-RNAs, and etc.) and other substances are found in exosomes. Exosomes affect target cells, causing them to change their function.

Methods: The features of BMMSC exosomes' mechanism in osteogenesis and bone regeneration (like: effects on other MSCs, osteoblasts, osteoclasts, and angiogenesis) and also the effects of their micro RNAs on osteogenesis are the subject of the present review.

Results: In today's researches, the use of exosomes to treat diseases has attracted much attention. These particles with the capability of carrying different elements, with the origin of the secretory cells, and influence on the fate of receptor cells, along with the lack of problems and complexities of cell use have shown good potential in researches, especially bone studies. In order conduct more advanced studies and achieve clinical applications, it is necessary to study exosomes with different cellular sources in terms of their contents, composition, and the extent and manner of their effect on bone repair.

Conclusion: BMMSC exosomes in the field of bone problems have competitive capabilities when compared to other MSCs. These capacities include increasing the proliferation of MSCs and osteoblasts, stimulating bone differentiation of stem cells, increasing angiogenic activity, increasing bone repair and regeneration, and so on. Therefore, it can be logical to consider the application of BMMSCs-derived exosomes as one of the best approaches in bone regeneration.

Keywords: Bone marrow mesenchymal stem cell · Exosome · Osteogenesis · Bone regeneration

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The Effect of Genes on Criminal Behavior and the Resulting Criminal Liability (Review)

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Introduction: What constitutes our genetic structure is the initial bed for growth, but since the first sperm of a human is formed in the mother's womb, and according to some hadiths and narrations, even the grounds for the formation of male sex cells in the body of the father and The egg is formed in the mother's body, the first signs of the baby's personality formation. Recent discoveries in the field of biology and genetics have led to the recognition of the genetic origin of many physiological functions as well as physical and mental disorders. Today, there is no doubt that many diseases are inherited and are passed on from parents or previous generations to their children.Similarly, a number of mental disorders have a genetic origin, which research has identified and named the relevant gene, such as schizophrenia, obsessive-compulsive disorder, borderline personality disorder, anti-social, anger management and Tourette syndrome.

Methods: Searching in the world's up-to-date resources, studying and benefiting from various books and articles

Results: Many people are disgusted by the idea that "genes influence behavior" because they believe that "genes determine fate." This common misinterpretation is often expressed emphatically by people who do not know enough about how genes work. They think of genes as the original "puppeteers," while the actual role of genes is something else. They are the chemical structure that is responsible for producing proteins or regulating the activity of other genes. The fact is that genes influence human behavior in indirect and complex ways that require the acquisition of inputs from the physiology of the body, the environment, society, and culture.

Conclusion: Behavioral genetics, which studies the relationship between genes and behavior, has opened a new window for jurists. Due to the increasing growth of behavioral genetics, the serious task of judging on this basis is becoming more and more complex. Considering that criminal policymakers value punishment when it has an effect on its execution. So in special cases, people who have been genetically abused as not having the free will to commit a crime should be reduced or even exempted from punishment.

Keywords: Inheritance, violence, judge

The effect of happiness on all diseases (Review)

Hadise shekoofamanesh,[1,*] Fereshteh shekoofamanesh,[2]

1.
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Introduction: Many people were affected by diseases that had complications such as physical diseases such as stomach and heart, etc., which have a cure, but again these diseases come to humans, who must find the source of these physical diseases, which is the source These diseases are mental and psychological, which start when people start thinking too much. Happiness is a multidimensional experience that is both emotional and physical. In the cognitive field, the brain is responsible for creating emotions. Amygdala and hypothalamus, two main parts of the brain, play an important role in the experience of happiness.

Methods: The hypothalamus is a major player in the regulation of hormonal balance in the body, which controls the secretion of various hormones, including hormones related to stress and pleasure. For happiness, it is especially involved in the regulation of endorphins, often referred to as "feel good" hormones. The hypothalamus is connected to the brain's reward system and influences the release of neurotransmitters such as dopamine. Dopamine is associated with pleasure and reward, and activities that cause happiness often cause the release of dopamine. The hypothalamus is involved in regulating the autonomic nervous system, which controls various involuntary body functions, including heart rate and digestion. Activation of the parasympathetic nervous system, which is often associated with relaxation and contentment, can contribute to feelings of happiness. The hypothalamus is responsible for regulating body temperature. There is a connection between body temperature and mood, and maintaining a comfortable temperature can contribute to feelings of well-being and happiness. The hypothalamus plays a role in regulating the sleep-wake cycle. Sufficient and high-quality sleep is closely related to mood and happiness, and the hypothalamus plays a role in ensuring proper sleep patterns. In summary, the hypothalamus contributes to happiness through its involvement in hormonal regulation, the reward system, control of the autonomic nervous system, temperature regulation, and sleep regulation. The multifaceted functions of the hypothalamus in the body highlight its importance in the complex interplay of factors that contribute to our emotional well-being and happiness. The hypothalamus is a major player in the regulation of hormonal balance in the body, which controls the secretion of various hormones, including hormones related to stress and pleasure. For happiness, it is especially involved in the regulation of endorphins, often referred to as "feel good" hormones. The hypothalamus is connected to the brain's reward system and influences the release of neurotransmitters such as dopamine. Dopamine is associated with pleasure and reward, and activities that cause happiness often cause the release of dopamine. The hypothalamus is involved in regulating the autonomic nervous system, which controls various involuntary body functions, including heart rate and digestion. Activation of the parasympathetic nervous system, which is often associated with relaxation and contentment, can contribute to feelings of happiness. The hypothalamus is

responsible for regulating body temperature. There is a connection between body temperature and mood, and maintaining a comfortable temperature can contribute to feelings of well-being and happiness. The hypothalamus plays a role in regulating the sleep-wake cycle. Sufficient and high-quality sleep is closely related to mood and happiness, and the hypothalamus plays a role in ensuring proper sleep patterns. In summary, the hypothalamus contributes to happiness through its involvement in hormonal regulation, the reward system, control of the autonomic nervous system, temperature regulation, and sleep regulation. The multifaceted functions of the hypothalamus in the body highlight its importance in the complex interplay of factors that contribute to our emotional well-being and happiness.

Results: There are many ways to treat the origin of this disease, which most of them recommend to see the counselors, but they can only help this origin of the disease by prescribing pills and drugs, which cause many side effects on the body, and weight abnormalities and patients It harms the body and my method is to not think about bad things and always be happy and laugh and go to places that make us happy and laugh and hope for everything small and worthless and go to nature because nature is happiness. It transfers the face to the human being and let us see the good in every problem and be happy.

Conclusion: I may not know much about life and human diseases, but I can find the source of all the problems that cause human diseases, so that even I get involved in the same disease. So, as a result, people should seek it, and the cure for all diseases is only to be happy in all moments, and to smile at all problems. I will end the conclusion with a proverb:Laughter is a cure for every incurable pain. So by maintaining vitality and happy spirit, it will be easier and faster to solve or forget pains and problems. Smile no matter how bad, face any difficulties and try to be happy and smile and don't be called and hope for yourself. Being happy is not easy to achieve, but you should try hard for it.

Keywords: Hypothalamus - happiness - amygdala

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The effect of hydroalcoholic extract of of Berberis integerrima membrane on blood coagulation in mice (Research Paper)

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Introduction: Berberis integerrima is a plant known for its traditional medicinal uses and numerous health benefits, such as treatment of high blood pressure, diabetes, cholesterol, various infections and inflammation, liver dysfunction and digestive disorders. Various compounds including alkaloids, bioactive and phenolic compounds have been reported for this plant. Studying the pharmacological properties of its active ingredients is important to further understand its therapeutic potential.

Methods: In this study, the effect of different concentrations of Berberis integerrima hydroalcoholic extract on blood coagulation parameters has been investigated, specifically prothrombin time (PT), Partial Thromboplastin Time (aPPT), Clotting Time (CT) and Bleeding time (BT) in male mice over a period of ۲۱ days.

Results: The results of the study revealed that the Berberis integerrima extract had a significant impact on the coagulation indicators at high doses (۷۵۰ mg/kg). However, low doses (۱۰۰ mg/kg) showed no significant effect. Certain alkaloids and flavonoids present in the extract may have anticoagulant properties, inhibiting the process of blood clotting.

Conclusion: Additional research is necessary to explore the potential of using Berberis integerrima extract in treating coagulation disorders resulting from deficiencies in coagulation proteins.In addition, this study can help to optimize the clinical use of Berberis integerrima and serve as a basis for future research in the field of treating cardiovascular diseases such as atherosclerosis, Myocardial infarction, and cerebral strokes.

Keywords: Medicinal Plants, Berberis integerrima, Blood coagulation, Atherosclerosis

The effect of hydroxyapatite and bioactive glass nanoparticles on the physicochemical and biological properties of enzymatically-crosslinked gelatin hydrogel: A comparative study (Research Paper)

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Introduction: The increasing average age of the global population, coupled with the rising prevalence of conditions such as osteoporosis, has resulted in a growing incidence of bone defects. Current treatment modalities, including autografts, allografts, and metal implants, present several limitations, including the induction of additional defects, the risk of graft rejection, and the potential necessity for re-surgery. These challenges highlight the urgent need for alternative therapeutic options. Tissue engineering scaffolds have emerged as promising substitutes for bone repair to address these challenges. Hydrogel scaffolds provide an optimal environment for bone regeneration by providing a three-dimensional structure supporting cell survival and proliferation. Osteoinduction and osteoconduction are two essential features that must be considered in the design of these hydrogels to ensure effective bone regeneration. To enhance these properties, a variety of inorganic nanoparticles have been incorporated into hydrogels. Notably, hydroxyapatite (nHAp) and mesoporous bioactive glass (MBG) nanoparticles have shown great promise. Although these nanoparticles have been extensively employed to fabricate different types of nanocomposite hydrogels, their comparative effects on the overall properties of these hydrogels remain insufficiently investigated. This study aimed to develop nanocomposite hydrogels by incorporating nHAp and MBG nanoparticles into an enzymatically crosslinked gelatin-based hydrogel. The objective was to evaluate and compare the effects of these two nanoparticles on the physicochemical and biological properties of the gelatin-based hydrogel.

Methods: Mesoporous bioactive glass nanoparticles were synthesized utilizing a sol-gel method. The morphology of the nanoparticles was assessed through scanning electron microscopy (SEM), while the porous structure was evaluated using the Brunauer-Emmett-Teller (BET) method. Gelatin was modified with tyramine groups via carbodiimide chemistry to facilitate enzymatic crosslinking of the hydrogel. Two groups of nanocomposite hydrogels were fabricated by incorporating nHAp and MBG into the hydrogel precursor solution at a final concentration of ١٪ w/v. Additionally, a nanoparticle-free hydrogel was prepared as the control group. The biodegradation rate, microstructure, and compressive modulus of the three hydrogel groups were investigated and compared. To assess the effect of nHAp and MBG nanoparticles on the biocompatibility of the hydrogels, mesenchymal stem cells (MSCs) were seeded onto the hydrogels, and metabolic activity was evaluated after ٤٨ hours of culture. In all tests, the nanoparticle-free hydrogel served as the control group.

Results: The successful synthesis of MBG nanoparticles was confirmed through SEM images and BET test. The presence of peaks associated with tyramine groups was observed in the ^{1}H NMR spectra of modified gelatin indicating successful modification of the gelatin molecules. Biodegradation test revealed a decrease in the degradation rate of hydrogels containing nHAp and MBG nanoparticles compared to the nanoparticle-free hydrogel (control group). Notably, the addition of nHAp had a more pronounced effect on the degradation rate than MBG nanoparticles. Analysis of the SEM images showed that incorporating nHAp significantly reduced the pore size of the gelatin hydrogel. Although the addition of MBG also decreased pore size, the difference compared to the control group was not statistically significant. The results of the compression tests demonstrated a similar trend: the nHAp-containing hydrogel exhibited a significantly higher compressive modulus than the control, while the increase in modulus for the MBG-containing hydrogel was not significant compared to the control group. In terms of metabolic activity, the nHAp-containing hydrogel showed no significant difference from the control group. However, the MBG-containing hydrogels exhibited a significant decrease in cell viability, likely due to the elevated pH resulting from ion release from the MBG nanoparticles.

Conclusion: The results indicate that fabricating nanocomposite hydrogels with nHAp or MBG nanoparticles at the same concentrations can lead to significantly different effects on the physicochemical properties of gelatin-based hydrogels. Although both nHAp and MBG nanoparticles are recognized in the literature as promising bioactive materials for bone regeneration, the choice of nanoparticles for creating an effective nanocomposite hydrogel should be based on the specific scaffold type, composition, and crosslinking method. These factors can significantly influence the mechanical and biological properties of the hydrogels. Therefore, this study emphasizes the need for preliminary optimization before finalizing the composition of the proposed nanocomposite hydrogels.

Keywords: Hydroxyapatite, Bioactive glass, Hydrogel, Enzymatic crosslinking, Gelatin

The effect of inflammation and angiogenesis, along with the use of corkomin and nanoparticles on p٥٣ gene expression and the activity of proteins involved in apoptosis on breast cancer (Review)

Mahdieh Farid,[١,*]

١.

Introduction: Breast cancer has become the fifth most common cause of cancer. Due to the increase in malignancy and drug resistance, researchers have been concerned with the biggest public health problem and the most common malignancy among women over the past١٥ years. Cancer is one of the inflammatory patients whose immobility is a factor, and it seems that sports activities can play an important role by establishing homeostasis and modulating inflammation In the past few decades, many studies have been conducted on the factors affecting its incidence in many patients, which has proven to be conventional chemotherapy methods in the treatment of all subtypes before Milad is inadequate.Emphasis on the urgent need for therapeutic approaches or new drugs, curcumin:٢A plant-based chemical derived from turmeric, a significant potential in inhibiting this disease along with apoptosis ,autophagy ,angiogenesis inhibition ،Cellular migration, metastasis and proliferation are associated in this context.Challenges, due to their dynamic and easily biodegradable nature, poor water solubility, rapid metabolism, and rapid systemic elimination,collectively limit its clinical applications.which has been reviewed below.

Methods: This essay the collected data related to the use of keywords such as breast cancer,inflammation,curcumin angiogenesis,P٥٣gen,apoptosis without any time restrictions.A retrospective of research has been conducted that looks at promising strategies and potential pathways associated with the causes and factors involved in breast cancer, along with the effects of therapeutic aid factors such as the use of drugs plant quercumin, angiogenesis, levels of suppressant genes, apoptosis, and levels of proteins and prognostic factors and strategies for psychological adaptation to cancer and its impact on the quality of life of breast cancer sufferers.

Results: In this study, the study of about ٢٣ articles, including research and research on the effect of factors affecting the breast cancer process and the need for use, as well as the emphasis on the urgent need for therapeutic approaches ،New drugs and promising strategies have explored potential pathways associated with the causes and factors involved in breast cancer.

Conclusion: In recent decades, many efforts have been made to improve treatment and diagnosis methods and to study psychological compatibility with cancer and quality of life for women with it. Due to the complications of existing and common treatment methods for this surgical disease, radiation therapy, chemotherapy and its high costs ،The use of novel nitrogen technologies to find new methods with fewer complications and costs has recently been considered.In this section, we examine several examples of these. One of the genes that mutates in breast cancer is the p٥٣ gene. The rate of expression of the p٥٣ gene in breast cancer has been reported differently in different areas.The most important prognostic and predictive factors of response to treatment are age, agglomerate lymph node involvement (N), estrogen receptor status (ER), progesterone (PR) ،Human

Growth Factor Epidermal HER ٢, size of tumor ٢, tumor ٢, etc. ^٥٣, cell projection such as ٥٣,٢. Today, about half of all breast cancers have estrogen and progesterone receptors on tumor cells, which in the presence of the above humons cause tumor growth. Estrogen has been identified as a mitogen for breast cancer cells. Aerobic exercises, through various mechanisms, including reduction of androgenic sex hormones, result in reduction estrogen.Physiological factors can regulate growth, metabolism, metastatic potential, and tumor safety profiles . The most common result of studies on the effect of exercise on cancer is a decrease in tumor growth. This inhibitory effect has been observed In recent decades, many efforts have been made to improve treatment and diagnosis methods and to study psychological compatibility with cancer and quality of life for women with it. Due to the complications of existing and common treatment methods for this surgical disease, radiation therapy, chemotherapy and its high costs ،The use of novel nitrogen technologies to find new methods with fewer complications and costs has recently been considered.In this section, we examine several examples of these. One of the genes that mutates in breast cancer is the p٥٣ gene. The rate of expression of the p٥٣ gene in breast cancer has been reported differently in different areas.The most important prognostic and predictive factors of response to treatment are age, agglomerate lymph node involvement (N), estrogen receptor status (ER), progesterone (PR) ،Human Growth Factor Epidermal HER ٢, size of tumor ٢, tumor ٢, etc. ^٥٣, cell projection such as ٥٣,٢. Today, about half of all breast cancers have estrogen and progesterone receptors on tumor cells, which in the presence of the above humons cause tumor growth. Estrogen has been identified as a mitogen for breast cancer cells. Aerobic exercises, through various mechanisms, including reduction of androgenic sex hormones, result in reduction estrogen.Physiological factors can regulate growth, metabolism, metastatic potential, and tumor safety profiles . The most common result of studies on the effect of exercise on cancer is a decrease in tumor growth. This inhibitory effect has been observed in all cancer cells examined.Overall, a thorough understanding of angiogenesis may lead to the identification of new therapies for cancer patients. Many studies show that exercise can inhibit tumor growth.Although most studies have examined the effects of endurance training on tumor tissue, little research has been done on the effect of periodic exercise on tumor tissue.It is included in many threatening tumors, glioblastoma counts, and in tumor movement.Laboratory studies on several types of cancer have shown that the destruction of miR-٢١ stifles cell expansion and tumor development, reducing metastatic penetration.A recent study, the combination of curcumin medicine insoluble in the blue systems, found in the mycelial structures known as aerobic exercise that promotes complete burning of fats, so aerobic exercise inhibits the rise of estrogen. Cholesterol is a precursor to steroid hormones, especially estrogen, which play an important role in breast cancer cells. Aerobic exercise by lowering cholesterol reduces estrogen.Selenium is present in the human body in the form of selenocysteine amino acids and is a constructive part of selenoproteins and has an important function in relation to an tioxidant activity. Selenium, on the other hand, with anticancer properties, especially through selenoenzyme, can prevent normal cell deformations into cancer cells and the activation of cancer genes in deformed cells.Amid the emergence of new methods, nanotechnology has been considered for direct anticancer treatments as well as for drug delivery. In fact, anticancer materials formed at the nanoscale have shown remarkable properties along with low toxicity..Interestingly, curcumin triggers the arrest of the cell cycle in BC cells.The cell

cycle is a regular set of events that lead to cell growth and division ١ G, S, and ٢ G phases and replicated cells protect DNA damage.CUR (CURCUMIN) is the proposed analog to enhance the protective function of BC cells in cell cycle arrest (٦٨).Each stage is involved in the progression of the cancer ،However, stage ١ G (which cells replicate themselves) is often considered to be particularly important in promoting cancer progression due to its initial position and function.Detention of COR(SLNs)Solid Lipid Nanoparticles in Cell cycle in G١/S and decreased cyclin D١(CCND١),CDK٤, which greatly induces apoptosis and ROS reaction. The results of studies also show. The reduction in tumor volume was due to aerobic periodic exercise and the use of selenium nanoparticles.Cancer has caused a significant reduction in the amount of IL-٦, IL-٤, and TNF-α cytokines in spleen tissue, but aerobic exercise and use and TNF-α in spleen tissue. Aerobic exercise and the use of selenium nanoparticles can play a role in strengthening the immune system and reducing tumor volume by increasing TNF-α cytokine as a TH١ cytokine complex.In the end, it can be pointed out،In this article, according to the research findings of the positive effects of high-intensity exercise and moderate-intensity therapy in reducing inflammation and other mentioned as therapeutic strategies in patients with Breast cancer, which may have positive or negative effects on carcinogenic mechanisms and the micro-tumor environment.

Keywords: Breast cancer, inflammation, curcumin, angiogenesis, P٥٣ gene, apoptosis

The effect of Inflammation and opportunistic microbiomes on colon cancer (Review)

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Introduction: The second most common cause of death worldwide Is cancer, and it is widely known that bacteria play a role in a number of diseases, including cancer. It is well recognized that the gut microbiota is crucial to the physiology and overall health of the host. Opportunistic bacteria in the gut microbiota can cause infection, while helpful bacteria produce essential nutrients like vitamin B and K. Dysbiosis, caused by imbalances between these groups, is linked to gastrointestinal conditions like colorectal cancer (CRC) and inflammatory bowel disease (IBD). The gut microbiota may also play a role in the pathophysiology of inflammatory bowel disease (IBD), as host reactions to gut bacteria are correlated with specific genes. Inflammatory bowel disease (IBD) is a condition characterized by a decrease in microbial diversity, resulting in an increase in pathogenic bacteria and a decrease in helpful bacteria. The microbiota of individuals with inflammatory bowel disease (IBD) is marked by a reduction in bacterial species, a decrease in Firmicutes and Bacteroidetes, and an increase in Proteobacteria. The compromised mucus layer allows luminal bacteria to enter submucosal layers, triggering proliferative and inflammatory processes. Dysbiosis and a surge in bacteria, such as Bacteroides fragilis, which disrupts the intestinal mucosal barrier, allow more bacteria to pass from the lumen to the interior of the tissue. Due to the chronic tissue inflammation caused by this condition, pro- carcinogenic and inflammatory mediators are released, increasing the risk of colorectal cancer (CRC). The innovative approach to treatment of colorectal cancer involves utilizing probiotics and prebiotics to manipulate the gut flora, improving gut barrier function, immune modulation, and colonization resistance. Probiotics and prebiotics can enhance anticancer therapies by altering gut microbiota metabolism. To effectively treat colon cancer, new bacterial species should be developed as probiotic supplements based on each patient&#۳۹;s unique genetic background.

Methods: We used keywords like intestinal microbiome, colorectal cancer, immune system and microbiota interaction, and probiotics to search the databases of Google Scholar, PubMed, Nature, and Scopus in order to write this review article. ۵۷ English- language articles were selected among the many articles obtained according to the content, quality, and credibility of the magazine. The selected articles were divided into three groups.The microbiome and its affecting variables were Introduced in the first set of articles. The second set of articles addressed therapeutic approaches as well as the connection between human diseases and the microbiome. The effects of probiotics were discussed in the third set of publications.

Results: The vast population of bacteria that make up the gut microbiota is frequently referred to as "a forgotten argan" in relation to human health and illnesses. There is growing evidence linking colorectal cancer (CRC) to dysbiosis of the gut microbiota. It is getting more and more

obvious what functions gut microbes played in both starting and facilitating the colorectal cancer (CRC) process. A variety of hypothesis models have been put forth to illustrate the intricate connection between gut microbiota and colorectal cancer. Colorectal cancer (CRC) prevention strategies utilize various tactics, including prebiotics and probiotics, to manipulate gut microbiota, aiming to reverse microbial dysbiosis and improve overall health.

Conclusion: Colorectal cancer (CRC) onset and gut microbiota dysbiosis are strongly correlated, as we have highlighted. Colorectal cancer (CRC) is made more likely by certain bacteria that can induce intestinal inflammation. Contrarily, several bacteria have the ability to create substances that improve the Intestinal mucosal barrier&#٣٩;s ability to prevent the development of colorectal cancer (CRC). One of the most promising new approaches in medicine to enhance people&#٣٩;s health is microbiome regulation. Thus, further studies and clinical trials pertaining to the gut microbiome It is necessary to assess the effectiveness of systemic treatments for colorectal cancer (CRC), reduce side effects, and raise survival rates in both oncology and colorectal cancer (CRC) patient care.

Keywords: Gut microbiota, dysbiosis, colorectal cancer (CRC), inflammatory bowel disease (IBD), probiotic, pre

The Effect of L. crispatus on HPV Infection and Vaginal Microbiome Balance (Review)

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Introduction: The vaginal microbiome consists of diverse microorganisms known as vaginal flora, which play an important role in the health of women and their babies. Studies of the human microbiome have identified four main branches of dominant bacteria in the vaginal flora: Firmicutes, Proteobacteria, Actinobacteria, and Bacteroidetes. The most important family of Firmicutes is Lactobacillus, whose dominant bacterial species compete against other pathogens by reducing the pH of the environment, producing bacteriocins, lactic acid, and hydrogen peroxide, and helping regulate the immune response through their metabolic activities. The composition of the vaginal microbiota is influenced by various factors, such as age, menstruation, hormonal fluctuations, sexual behaviors, and the use of drugs, such as probiotics and antibiotics. Disruption of microbiome balance can lead to dysbiosis and diseases such as bacterial vaginosis (BV), vulvovaginal candidiasis (VVC), and sexually transmitted diseases, including human papilloma virus (HPV) infection. Persistent high-risk HPV infection increases the risk of cervical cancer, which is the fourth most common cancer among women worldwide and causes ٣٤٢,٠٠٠ deaths in ٢٠٢٠, according to the World Health Organization. This study aimed to investigate the effect of L. crispatus as a probiotic to improve the vaginal microbiome during HPV infection.

Methods: To analyze the structure of the vaginal microbial community, researchers collected samples from the cervix and used next-generation sequencing (NGS) to analyze the ١٦S rRNA genes of the V٣-V٤ variable region. The researchers also aimed to establish a relationship between the diversity of the vaginal microbiome and HPV infection. Real-time quantitative fluorescence PCR was used to detect HPV type and viral load before and after treatment with Lactobacillus probiotic.

Results: The analysis of vaginal flora bacteria diversity showed that anaerobic pathogenic vaginal bacteria at the genus level, including Prevotella, Gardnerella, and Sneathia, were more abundant in HPV infection, while lactobacilli were less frequent. In contrast, treatment with probiotics showed that L. crispatus was able to improve the normal flora of the vagina by inhibiting the growth of pathogenic bacteria, regulating the immune system, and increasing the abundance of lactobacilli. The researchers also found that the use of L. crispatus probiotic significantly reduced viral load, inflammation, and improved vaginal cytology due to its antiviral and metabolic activities.

Conclusion: According to the obtained results and the research related to the vaginal microbiome's ability in HPV infection, the use of Lactobacillus probiotics can significantly impact the rate of cytological recovery, vaginal inflammation, and reduce the HPV viral load and the balance of the

vaginal microbiome. However, further extensive research is still needed for researchers to achieve more effective treatments with the aid of vaginal probiotics.

Keywords: vaginal microbiome, Lactobacillus, HPV infection, probiotic

The effect of meaning therapy on the feeling of loneliness of elderly women living in nursing homes :systematic review (Review)

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Introduction: Many elderly people describe the aging period as a lonely period and refer to it as an unpleasant and scary experience that leads to severe psychological and physical problems. Feeling alone is one of the symptoms of depression and the cause of psychological damage in the elderly, especially the elderly living in nursing homes. There are many methods to remove the feeling of loneliness and increase the quality of life and mental health of the elderly, among which psychotherapy and especially meaning therapy can be mentioned. Group meaning therapy provides an opportunity for people to get to know, understand and free themselves from the obstacles that block their freedom.

Methods: The present study was conducted with the aim of investigating the effect of meaning therapy on the feeling of loneliness of elderly women living in nursing homes. Search method: The present study is a systematic review that was conducted using international and Persian databases between the years ۲۰۱۰ and ۲۰۲۱. Searching for articles using Tittle search using Scopus and SID, PubMed, IranMedex, Google scholar, Magiran using the keywords "nursing homes", "elderly women", "loneliness", "logo therapy", meaning therapy, loneliness, elderly women and nursing homes were done. Articles that met the criteria for inclusion in the research, including the type of RTC randomized clinical trial study, performing semantic therapy intervention specifically in elderly women living in nursing homes, the language of the article in English and Farsi) and access to the full text of the article were used. they took Review and analysis of the quality of articles based on PRIZMA was done by ۲ researchers independently.

Results: From the ۳۰۲ primary articles found, ۹۹ articles were checked for the title and abstract due to repetitiveness, ۱٦۲ articles due to the lack of intervention specifically for elderly women living in nursing homes, ۷٦ articles due to the lack of meaningful therapy intervention independently. ۷۱ articles were analyzed due to the type of study, ٤ articles were excluded due to the irrelevant language, and finally ۱۲ articles that evaluated the effect of semantic therapy on the feeling of loneliness of elderly women living in nursing homes. Most of the studies have pointed out the positive and significant effects of meaning therapy on reducing the feeling of loneliness of elderly women living in nursing homes.

Conclusion: Considering the positive effects of meaning therapy on the feeling of loneliness and isolation of elderly women living in nursing homes, it is recommended that such interventions be

included in the design of care programs for elderly women living in nursing homes due to their ease of access, cheapness and uncomplicatedness.

Keywords: meaning therapy, feeling of loneliness, elderly women, nursing homes

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The effect of MTHFR C۶۷۷T and MTHFR A۱۲۹۸C polymorphisms in female infertility (Research Paper)

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Introduction: Sufficient folate is vital for follicular and embryonic development as cells proliferate rapidly during folliculogenesis and pregnancy. Methylene tetrahydrofolate reductase or MTHFR is an enzyme affecting folate metabolism, and its polymorphisms can cause disturbances in folate levels and failure to convert homocysteine into methionine due to reduced enzyme activity.Inefficient activity of the enzyme induces the accumulation of platelets and ultimately damage to the vascular endothelium. The aim of the present study is to investigate the effect of two common polymorphisms of this gene on infertility in a population of Iranian women.

Methods: After obtaining the required permits; Using Cochran's formula, ۸۵ women aged ۲۵ to ۳۵ with a history of repeated abortions before the ۲۰th week of pregnancy were selected in the study population compared to ۸۵ women with healthy pregnancies. DNA sample was extracted and PCR was performed with mastermix containing specific primers for two polymorph regions. Data analysis with SPSS Ver. ۲۵ at a significance level of P<۰,۰۵ was performed.

Results: In the A۱۲۹۸C variant, there was a significant difference between the SNP frequency of healthy and sick people (χ^2=۹,۲۹ and P=۰,۰۰۲), but this difference was not seen in the C۶۷۷T variant (χ^2=۰,۲۵۸ and P=۰,۶۱۱). The frequency of patients with A۱۲۹۸C heterozygous genotype was higher than other genotypes, and included patients with a history of repeated miscarriages. This study states that the A۱۲۹۸C variant plays a more important role in the occurrence of recurrent miscarriages in the studied patient population.

Conclusion: No linkage disequilibrium between MTHFR A۱۲۹۸C and MTHFR C۶۷۷T was observed in this population. Due to the inconsistency of the data of this research with many other studies (more impact of A۱۲۹۸C polymorphism than C۶۷۷T), it is necessary to use a larger population and the levels of biochemical substances affected by these two polymorphisms such as cobalamin, folate, homocysteine, SAM, methyl Malonic acid etc, should also be evaluated.

Keywords: C۶۷۷T Polymorphisms, A۱۲۹۸C Polymorphisms, Recurrent miscarriage, IAU science.

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The Effect of nanomicelle Curcumin on Post-Thaw Quality of Cryopreserved Human Sperm

(Research Paper)

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Introduction: Human sperm cryopreservation is an important tool for assisted reproductive technology and male fertility preservation. The antioxidant effects of curcumin on different cells have been widely reported. This study was aimed to evaluate the potential role if the effect of nanomicelle Curcumin supplementation on sperm quality, and DNA integrity.

Methods: Semen of ۲۵ oligoasthenoteratozoospermia men was collected and each sample was divided into three equal aliquots: Control, nanomicelle Curcumin. The samples were analyzed freshly for viability (Eosin Y), morphology (Diff-Quick), motility (following WHO standards), DNA integrity (SCD Test). The control group remained untreated and was mixed with cryopreservation medium (۱:۱). The nanomicelle Curcumin group was mixed with cryopreservation medium containing ۱۰ µM nanomicelle Curcumin. Ten days after cryopreservation, samples were thawed and pre-freeze analyses repeated.

Results: Obtained results showed that cryopreservation significantly ($P < ۰,۰۰۱$) reduces sperm parameters. In nanomicelle Curcumin group, viability, morphology, motility, and DNA integrity significantly ($P < ۰,۰۰۱$) increased after the thawing process, as compared with the control group.

Conclusion: These results suggest that the addition of nanomicelle Curcumin to cryopreservation medium improves post-thaw sperm quality, sperm DNA integrity. Further research is needed on the use of nanomicelle Curcumin, and other antioxidant substances in sperm cryopreservation.

Keywords: Sperm; Cryopreservation; nanomicelle Curcumin; DNA.

The effect of Naproxen on StAR gene expression and the marker of oxidative stress, Superoxide dismutase in Wistar rats, a model of polycystic ovary syndrome (Research Paper)

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Introduction: Polycystic ovary syndrome (PCOS) is one of the most important causes of infertility in the world. Therefore, prevention and treatment strategies for this disease are very important. Since the signaling pathways related to StAR gene expression and oxidative stress are involved in the progression of this disease, the effect of Naproxen drug on these pathways was investigated.

Methods: In this research, ٣٠ virgin Wistar rats weighing ٢٠٠-٢٥٠ grams were randomly divided into five control groups, patients induced with estradiol valerate (EV) and patients receiving naproxen ١٠, ٢٥ and ٥٠ mg/kg. After blood collection, serum was isolated and antioxidant superoxide dismutase (SOD) was measured. RT-PCR was also performed to check StAR gene expression in ovary tissue. One-way statistical analysis of variance and Tukey's test with a significance level of p<٠,٠٥ was used to compare between groups.

Results: The serum level of SOD in the EV group showed a significant decrease compared to the control group, but a significant increase in the groups treated with naproxen (p<٠,٠٥). The expression of StAR gene in the EV group increased compared to the control (p<٠,٠٠١), but all three doses of naproxen could significantly reduce the expression of this gene compared to the patient group (p<٠,٠٥). Naproxen in the doses used in this study was able to reduce inflammation in PCOS rats and improve the disease by increasing the level of SOD. Also, naproxen reduced the expression of the main gene of the steroidogenesis pathway, namely StAR, which in this way reduces the level of androgen.

Conclusion: The result of this condition is the improvement of PCOS. It seems that naproxen can be used to control and reduce the symptoms of polycystic ovary syndrome.

Keywords: Polycystic ovary syndrome; StAR gene; superoxide dismutase; rat

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The effect of papaverine on sperm DNA fragmentation and membrane integrity of asthenozoospermic men after freezing-thawing (Research Paper)

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Introduction: Sperm cryopreservation is a widely used technique to maintain and protect male fertility in various occasions such as infertility treatment and cancer therapies. However, the freezing process can adversely affect sperm quality by generating reactive oxygen species (ROS). Papaverine (PPV) known for its antioxidant properties, may help protect sperm from ROS-induced damage by reducing ROS levels within cells. This study aims to assess the impact of PPV on sperm DNA fragmentation during cryopreservation in men with asthenozoospermia.

Methods: In this study, ٣٠ asthenozoospermic men were selected to refer to Amir-AL-Momenin infertility treatment Center Arak. semen samples were collected after ٢-٥ days of sexual abstinence period from patients. Each sample was divided into ٣ groups. ١: Control (fresh) group, ٢: Freeze group (treated with freezing medium alone), and ٣: Freeze+ PPV group (treated with freezing medium +١٠٠µM PPV solution). Then sperm membrane integrity with hypo-osmotic swelling (HOS) test and DNA fragmentation index (DFI) used to sperm chromatin dispersion (SCD) test were analyzed. Data were analyzed using Repeated Measure analysis.

Results: The findings of this study showed that the average integrity of the sperm membrane significantly decreased, while the percentage of DNA fragmentation significantly increased in Group ٢ compared to Groups ١ and ٣. Furthermore, the sperm membrane integrity in Group ٣ improved compared to Group ٢, while the percentage of DNA fragmentation (DFI) in Group ٣ decreased relative to Group ٢.

Conclusion: Administration of ١٠٠ µM PPV in vitro helps prevents membrane damage and DNA fragmentation. As a result, PPV an effective antioxidant plays a significant role in reducing oxidative damage and improving the quality of sperm parameters.

Keywords: Cryopreservation, DNA Fragmentation, Papaverine, Sperm.

The Effect of Remdesivir on STAT۳ gene expression in patients with covid-۱۹ (Research Paper)

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Introduction: Abstract In ۲۰۱۹, Covid-۱۹ spread rapidly and was recognized as a pandemic. In the conducted studies, it was observed that the activation of inflammatory pathways in patients is closely related to the severity of the disease; Therefore, investigating the inflammatory pathway caused by this virus is necessary for treatment against COVID-۱۹. One of the main inflammatory pathways in COVID-۱۹ is the jak/stat signaling pathway. Remdesivir is one of the antiviral drugs that has been widely investigated for the treatment of this disease. This research aims to examine the changes in STAT۳ gene expression as one of the key factors in activated inflammatory pathways in patients with COVID-۱۹ before and after treatment with remdesivir compared to healthy individuals. In this study, blood samples were randomly taken from ۳۰ patients infected with the Omicron strain of coronavirus, before receiving the remdesivir drug as a patient group and after receiving the last dose of drug as a treatment group and from ۲۰ healthy people as a control group. After receiving the samples, RNA extraction and cDNA synthesis were performed. Changes in STAT۳ gene expression were investigated by real-time PCR method. The level of STAT۳ gene expression decreased by ۸۰٪ in the patient group and by ۲۰٪ in the group treated with remdesivir compared to the control group (P<۰,۰۰۱). The findings of this research indicate the positive effect of the remdesivir drug in increasing the expression of the STAT۳ gene in patients with COVID-۱۹, while it could not increase the expression of this gene to the level of the control group.

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Keywords: Key Words: COVID-۱۹, Remdesivir, Inflammation, STAT۳

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The effect of Sorafenibe on SOAT١ protein by using molecular docking method (Research Paper)

Mahdiyeh Gholaminezhad estalkhjani,[١,*]

١. -

Introduction: SOAT١ protein is a protein that leads to the proliferation of liver cancer cells . By studying the protein of liver cancer patients in the early stages, researchers found that the activity of a protein called SOAT١ affects the cholesterol stability of cancer cells and leads to their proliferation and transfer (this protein can be a way to treat liver cancer .) Sorafenib (Molecular formula : C٢١H١٦ClF٣N٤O٣) is a drug that used to treat liver cancer (This drug is anti cancer) Sorafenib interferes with the growth of cancer cells, and these cancer cells are eventually destroyed by the body The purpose of this research is to investigate the effects of sorafenib on SOAT١ protein

Methods: First, prepared the three-dimensional structure of the SOAT١ protein by using the Uniprot site . Then, we obtain the three-dimensional structure of Sorafenib drugs through the chemspider site. In the next step, using the Chimera ١,١٠,٢ program, we include changes such as removing ions, adding hydrogen, removing extra chains, etc. in the original protein . Finally, with the PyRx program, we start docking by loading the modified protein file as macromolecule and the drug file as input

Results: At the end of docking, the results are as follows : Protein : SOAT١ Sorafenib Binding affinity (kcal/mol) RMSD lower bound RMSD upper bound Conformation١ -١١,١ ٠ ٠ Conformation٢ -١٠,٥ ١٩ ٢٠ Conformation٣ -١٠,٣ ٦,٦ ١٢,٢ Conformation٤ -١٠,٣ ١٨,١ ١٩,٨ Conformation٥ -١٠ ٦,٩ ١٢,٣

Conclusion: According to Docking studies , we found that conformation of Sorafenib with negative binding affinity and RMSD had effect on SOAT١ protein to treat liver cancer .

Keywords: SOAT١-Sorafenibe-liver cancer-Docking

The effect of the combination of Anthemis pseudocotula, Trachyspermum, and Dracocephalum extract with antioxidant and antibacterial properties in the induced model of Helicobacter pylori infection in the stomach of rats. (Research Paper)

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۳. Department of Pharmacology and Toxicology, Faculty of Pharmacy and Pharmaceutical Sciences, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

Introduction: Helicobacter pylori (H. pylori) is regarded as the primary etiological agent of peptic ulcer and gastric carcinoma. Claiming about ۵۰ percent of the world population is infected with H. pylori, therapies for its eradication have failed for many reasons, including the acquired resistance against its antibiotics. Hence, the need to find new anti-H.pylori medications have become a hotspot with the urge to search for alternative, more potent, and safer inhibitors. Medicinal plants are suggested as repositories for novel synthetic substances in recent drug technology scenarios

Methods: In this study, ۳۵ male rats were selected in five groups to investigate the effects of three plants' combination of aqueous extracts. After the injection of the Helicobacter bacteria strains into the stomach of the rats, sampling of the stomach tissue and blood was done.

Results: The results were classified as pathological and microbial findings and checked boxes. After the interpretation of gastric tissue pathology sections in mice, the treatment group with combined herbal extracts had a significant difference compared to other groups in terms of gastric ulcer healing and microbial load

Conclusion: The data shows that the combined aqueous extract with anti-inflammatory and antioxidant properties has been able to protect the gastric mucosa and significantly reduce the wound resulting from infection.

Keywords: Gastroduodenal, Infection, Anti-Helicobacter pylori, Herbal extract, Microbiology

The effect of viral infections in causing various types of cancer (Review)

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Introduction: Cancer is caused by the uncontrollable growth of body cells in different parts of the body. Cancers share six characteristics: self-sufficiency in growth signals, insensitivity to anti-growth signals, escape from apoptosis, unlimited potential, stable angiogenesis, tissue invasion, and metastasis. Multiple factors have been associated with the oncogenic process such as environment, lifestyle, host factors, infectious agents, and inheritance. Recently, research has been conducted in the field of genetics, which has shown that there is a strange compatibility between mutation-causing agents and cancer-causing agents. Baer (١٩٤٩) and Strong (١٩٤٩) proposed one of the most prominent theories, claiming that the primary cancer cell is nothing more than a normal cell affected by a genetic mutation. Mutations created in the genome cause changes in the balance between proliferation and programmed cell death. Sometimes, infectious agents play an important role in the creation of various mutations. It has recently been estimated that viral infection is the main cause of more than ١,٤٠٠,٠٠٠ cancer cases per year, such as HPV, HBV, HCV, EBV, and HTLV. This review focuses on the effect of viral infections in causing various types of cancer.

Methods: This research was extracted from ١٥ valid articles from ١٩٨٨ to ٢٠٢١ and downloaded from the reliable sites Pubmed, Scopus, Web of Science, Google Scholar, and Elsevier.

Results: Viral infections that are caused by HPV, HBV, HCV, EBV, and HTLV lead to various types of cancer. High-risk infection (human papillomavirus) HPV is the main cause of cervical cancer. HPV disrupts the host chromosome, and this disruption increases the expression of E٦ and E٧, which leads to DNA damage and causes cervical cancer. HBV (hepatitis B virus) is one of the smallest DNA-enveloped viruses which causes acute infections in mammals and birds. HBV is a recognized cause of hepatocarcinogenesis. A recent study unraveled that the insertion of HBV-DNA into the human genome can cause dramatic genetic aberrations. HBV–DNA integration into human chromosomes has been detected in ٨٠–٩٠٪. HCV (hepatitis C virus) infection has become a leading cause of hepatocellular carcinoma. EBV (Epstein-Barr virus) is a human herpes gamma virus that was first derived from Burkitt's lymphoma which plays a role in carcinogenesis by causing cell epigenetic changes such as DNA methylation and histone changes. HTLV١ is a type C complex retrovirus in the oncovirinae subfamily, and like other retroviruses, it has an envelope derived from the host cell membrane and two copies of the positive RNA genome. This virus infects lymphocytes and is the main cause of cell leukemia and lymphoma in adults. The diagnosis of HTLV-١ infection is based on the detection of specific antibodies by agglutination of enzyme-linked particles and subsequent confirmation by polymerase chain reaction (PCR) or western blot assay.

Conclusion: Cancer-related viruses such as HPV, HBV, EBV, and HTLV can develop carcinoma. These viruses create mutations in DNA and cause genetic changes and epigenetic changes in chromosomes

and DNA. Chronic infections may play a significant role in carcinogenesis. The mechanisms of carcinogenesis caused by infections include cell proliferation and DNA replication by the mitogen-activated protein kinase pathway. Some toxins of viruses affect the cell cycle and lead to abnormal cell growth so identifying these viruses in the body as quickly as possible using biological biomarkers will be very effective in preventing cancer.

Keywords: Cancer, HPV, Viral infection, Mutation, Carcinogenesis, Infections

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The effect of vitamin D supplementation on stroke (Review)

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Introduction: Stroke is one of the main causes of death and disability. Vitamin D is a group of fat-soluble hormone precursors obtained from sunlight, food and nutritional supplements. The active form of vitamin D exerts its effect by binding to its receptor located in the nucleus of the target cells. Studies have shown that the lack of this vitamin can contribute to the worsening of diseases such as high blood pressure, diabetes, heart failure and stroke.

Methods: In this study, the effect and two-way relationship between stroke and vitamin D were studied, which were extracted and used from reliable information sources such as Google Scholar, Pambed and Science Direct.

Results: Evidence and studies have shown that there is a relationship between low levels of vitamin D in the blood and cognitive disorders in stroke, and the lower the level of this vitamin, the greater the extent of stroke in patients. It should be noted that stroke itself predisposes to more vitamin D deficiency and as a result the occurrence of diseases related to vitamin D deficiency such as repeated strokes and cardiovascular diseases.

Conclusion: According to the findings, using vitamin D supplements in the diet is a practical and low-cost way to help prevent many diseases, including stroke. The active form of vitamin D reduces stroke and reduces post-stroke effects.

Keywords: Stroke, vitamin D, body physiology, diet

The effect of vitamin D supplementation on weight loss and fat burning (Review)

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Introduction: Vitamin D is a fat-soluble vitamin whose active form is calcitriol. Calcitriol basically causes fat burning by affecting the cortisol hormone. When the fat in the body increases, this vitamin has symptoms that it cannot perform its duties. Nowadays, improper diet and genetic factors have caused weight gain in many people. There is a two-way relationship between accumulated fat and vitamin D. According to observations, the reduction of vitamin D is associated with an increase in body fat storage and overweight. Also, obesity and overweight cause physiological changes in the body, which can interfere with the activity of vitamin D. Physical activity is an effective strategy to improve the quality of life and health status of people, which can also reduce diseases associated with obesity, such as depression and anxiety symptoms.

Methods: In this review study, using PubMed, Google Scholar, and Science Direct databases, searches were made between ٢٠٠٥ and ٢٠٢٣ using keywords such as vitamin D, weight loss, fat cells, and calcitriol.

Results: According to the findings, calcitriol is one of the most common deficiencies that are unknown in the body. This deficiency has a negative effect on all body cells and is the cause of many diseases, including obesity. The proper level of this hormone plays a role in fat regulation and control, and prevents fat from being stored in the body in large quantities, and burns fats, especially harmful fats in the abdominal area, and reduces them.

Conclusion: The results show that by taking the right dose of vitamin D and calcitriol supplement, many diseases can be prevented, especially obesity in old age.

Keywords: Vitamin D, weight loss, fatty cells, calcitriol

The Effectiveness of Nature Therapy (Ecotherapy) in Reducing Anxiety in Patients with Chronic Anxiety (Research Paper)

Hafez Safari,[1,*]

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Introduction: Nature and green spaces play a vital role in spending leisure time and mental health. Nature therapy (ecotherapy) is a new method of psychological treatment that has attracted a lot of attention in recent years. In this treatment, the capacity of nature is used to treat or reduce the symptoms of mental disorders. The purpose of this study was to investigate the effectiveness of nature therapy (ecotherapy) on reducing anxiety in patients suffering from chronic anxiety.

Methods: This is an experimental research, with a pre-test, post-test and a control group, which was conducted in March and April ۲۰۲٤ in the forest area of Navakouh, Sarpole Zahab, Kermanshah province. Novakouh forest is one of the forests of Zagros mountains and it is a very green area with pleasant climate. The statistical sample of the study included ۲۰ patients suffering from chronic anxiety living in the western cities of Kermanshah province (Sarpole Zahab, Qasre Shirin and Islamabade Gharb). The participants were randomly divided into two experimental and ۱۰ control groups, and for the experimental group, ۱۰ Ecotherapy sessions were performed (for ٥ weeks, ۲ sessions per week, ٤ hours per session) and no intervention was given for the control group. Both groups were evaluated before the beginning and after the end of the intervention using the Zung Self-Rating Anxiety Scale (SAS). The obtained data were analyzed by SPSS.۲۱ and descriptive statistics methods as well as analysis of covariance (ANCOVA) were used (p<۰,۰٥).

Results: The results of statistical analysis showed that Ecotherapy has a significant effect in reducing the number and severity of chronic anxiety symptoms. At the end of the intervention and in the post-test phase, there was a significant difference between the experimental and control groups in terms of the number and severity of anxiety symptoms.

Conclusion: The results of this study showed that Ecotherapy is effective in the treatment of chronic anxiety disorder and it is possible to use this treatment and the capacity of nature in this field.

Keywords: Anxiety, Chronic Anxiety, Ecotherapy, Nature, Nature Therapy

The Effects of Cannabis on Human Memory: A Neuroengineering Perspective (Review)

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Introduction: Cannabis sativa has a long history of use for medicinal and recreational purposes, leading to growing interest in its effects on the brain. The brain's endocannabinoid system, which is critically involved in regulating various cognitive functions, including memory, responds to phytocannabinoids like THC and CBD (cannabidiol). Understanding the implications of cannabis on memory is essential not just for users but also for healthcare providers and policymakers, especially as cannabis becomes increasingly legalized and used more widely. Memory processes are complex and involve multiple brain regions, including the hippocampus, amygdala, and prefrontal cortex. The hippocampus is particularly vital for forming new memories, while the prefrontal cortex is crucial for working memory and executive functions. The endocannabinoid system's modulation of neurotransmitter release significantly affects synaptic plasticity—the ability of synapses to strengthen or weaken over time, which is essential for memory processes. By integrating findings from Neuro-engineering, the study aims to elucidate the complex relationship between cannabis consumption and cognitive functions, particularly memory.

Methods: This study was conducted as a review by searching the keywords Memory, Cannabis, and hippocampus in PubMed, Science Direct, Scopus, and Google Scholar search engines. Finally, ١٢٠ articles were selected and reviewed.

Results: THC exerts its effects primarily through the activation of CB١ receptors located throughout the central nervous system. When THC binds to these receptors, it can inhibit the release of gamma-aminobutyric acid (GABA) and enhance the release of dopamine, affecting neuronal communication and leading to alterations in cognitive functions. Acute dosing of THC has been linked to impairment in short-term and working memory, often experienced as difficulty in concentration, challenges in forming new memories, and deficits in recalling recent events. Studies indicate that THC disrupts the encoding of memories by affecting synaptic plasticity in the hippocampus. This impairment manifests particularly during cognitive tasks requiring attention and focus, essential components of effective memory retention. Research has shown that users of high doses of cannabis report significant declines in memory performance, which can influence daily functioning and learning. In contrast to THC, CBD appears to offer neuroprotective effects that may counteract some of the impairments associated with THC use. Research indicates that CBD does not have the intoxicating effects of THC and may help in stabilizing mood, reducing anxiety, and enhancing overall cognitive function. Recent studies suggest that CBD can mitigate THC-induced memory impairments by acting

as an antagonist to some of the effects of THC on the CB1 receptor. By reducing anxiety and potential fear responses linked with memory recall, CBD could allow for improved memory function, particularly in chronic cannabis users who may experience heightened anxiety levels during recollection tasks. The long-term impact of cannabis on memory remains a contentious topic. Some longitudinal studies suggest that prolonged cannabis use, particularly when begun in adolescence, is associated with persistent cognitive deficits, including memory impairments. The extent of these deficits may be influenced by factors such as the age of onset of use, frequency, and quantity of use, and individual neurobiological and genetic predispositions. However, the reversibility of these effects after cessation of use also points to the brain's remarkable plasticity. Some findings indicate that individuals may experience improvements in cognitive functions, including memory, following a period of abstinence from cannabis, particularly if they had not engaged in heavy use for extended periods.

Conclusion: The effects of cannabis on memory are multifaceted, influenced by the specific compounds involved, individual differences, and usage patterns. While THC is predominantly associated with impairments in memory and cognitive functions, CBD presents promising protective properties that warrant further investigation. Understanding these dynamics is crucial for developing strategies aimed at mitigating negative effects and harnessing the therapeutic potential of cannabis compounds. As research in Neuro-engineering continues to advance, there is an increasing opportunity to explore both the therapeutic uses of cannabis in cognitive impairments and its role in enhancing neuroplasticity. A comprehensive understanding of how cannabis interacts with memory will ultimately contribute to better public health guidelines and therapeutic applications for individuals navigating cognitive challenges.

Keywords: Memory, Cannabis, THC, cognitive functions, hippocampus

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The effects of MOI in production high-titer viral vector in HEK ٢٩٣ cells for Vaccination purposes

(Research Paper)

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Introduction: The spread of viral diseases, especially newly emerging infectious diseases, is a serious threat to humans and the constancy of the world. The best way to control epidemic diseases is to make the society more accessible to the vaccination program. The speed of the spread of emerging infectious diseases has recently created new challenges for vaccine manufacturers, and it is also challenging to produce vaccines on a large scale. Therefore, new vaccine platform technologies may shorten this cycle and accelerate vaccine development. In the process of producing vaccines based on viral vectors, the main step is the production of host cells with appropriate cell density. Increasing the cell density for vector production helps to improve volumetric production while maintaining maximum specific production. The choice of cultivation mode is crucial because of its effect on the way of providing nutrients and removing metabolites in cell concentration, product titer and volume adenovirus vector production that can be achieved. We set up efficient adenovirus rAd٢٦ production in animal component-free conditions employing a well-characterized HEK ٢٩٣ cell line cultivated in the flasks and bioreactor, a scalable system for cell culture that can be used to study process development and optimization for vaccine production. HEK ٢٩٣ it acts as a host for the development of recombinant adenoviral vectors. The results obtained from ٢٠٠L SUB demonstrated that the virus concentration peak occurred consistently ٧٢ h after infection and the virus yields were strongly corresponding to the process parameters, such as cell density at infection & MOI.

Methods: In the present study, the HEK ٢٩٣ cells were infected with recombinant adenovirus serotype ٢٦ (rAd٢٦), and the effects of critical process parameters (CPPs) with ١,٤×١٠٦ cells/mL with ٩٥٪ viability and including the multiplicity of infection (MOI) = ٣, ٦, ٩, ١٢, and ١٥ and were the specific productivity was measured at ١٢٠ hpi in various SF٢Ls investigated experimentally. The results of small-scale experiments in ٢ L shake flasks (SF ٢L) demonstrated that MOI could affect the cell proliferation and viability.

Results: The results at these experiments showed that VCD = ١,٤ × ١٠-٦ cells/mL and MOI = ٩ yielded TCID٥٠ /mL = ١٠٨,٩, at ٧٢ h post infection (hpi), while the virus titer at MOI = ٣ and ٦ was lower compared to that of MOI=٩ and on TCID٥٠ /mL and MOI = ٣ and ٦ were less efficient. Moreover, our findings showed that MOIs > ١٢ did not have a positive effect, MOI > ١٢ decreased the viability drastically. In the next step, the optimized CPPs in a small scale were exploited in a ٢٠٠ L single-use bioreactor (SUB), with good manufacturing practice (GMP) conditions yielding high-titer rAd٢٦ manufacturing, TCID٥٠/mL = ١٠٨,٩, at ٧٢ hpi.

Conclusion: adenovirus rAd٢٦-S-CoV-٢ synthesis at MOIs ٣ and ٦ IU/ml showed that the viruses were unable to infect cells quickly (more than ١٢٠ hours). Premature cell death and lysis resulted in a considerable decrease in cell density and viability, and the effectiveness of infection as a result of the consequent titer was not proportionate to the rise in the MOI value. When virus particles infect cells by the batch process, cell development stops ٢٤ to ٤٨ hpi, they start to collect in the cells ٤٨ to ٧٢ hours later, reach their peak titer, and then the cells die. The viral multiplication factor, or MOI, of the process, was discovered to be associated with cell density and might range from ١٠٨ to ١٠١٠.Produce high titers virus requires an intricate understanding of the critical process parameters to ensure that high titers can be achieved in a reproducible manner.

Keywords: Vaccine, MOI, TCID٥٠, HEK ٢٩٣, rAd٢٦

The Effects of telomere length in infertility and reproductive health (Review)

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Introduction: Telomeres, which means "end part" in Greek, are special structures made of nucleoproteins located at the ends of eukaryotic chromosomes. They are essential for proper cell division and were recognized in the early ۲۰th century for their role in protecting chromosome integrity. Telomeres prevent chromosome ends from being mistaken for DNA damage, which could cause genetic instability. They consist of short, repetitive noncoding sequences that safeguard genetic information and slow down the wear of chromosomes over time. In germ cells, telomeres remain stable, playing a critical role in reproduction and fertility. Telomerase, an enzyme made of two subunits, prevents telomere shortening during cell division, allowing for continued cell division, and is often active in cancer cells. Human telomeres consist of repeats of the sequence ۵'-TTAGGG-۳' and vary in length. They shorten due to factors like incomplete replication or exposure to harmful substances. Length variations in telomeres affect aging and the likelihood of age-related diseases. Healthy lifestyle choices can help maintain telomere length, contributing to overall health and fertility. In recent years, male infertility has become more common, contributing to half of all infertility cases globally. The cause of sperm abnormalities is unknown in nearly half of these cases, classified as idiopathic. Various factors like genetics, lifestyle, and environmental influences lead to these issues, often in combination. Research is focused on the molecular pathways related to male infertility. Assessments typically evaluate semen quality, specifically sperm count, motility, and morphology, but standard analyses may not always identify abnormalities. New tests are being developed to better assess sperm quality and performance, especially in men whose semen parameters appear normal. Recent studies suggest a link between telomeric instability and gamete quality, indicating that telomere length may be a new marker for male infertility. Telomeres protect chromosome ends during cell division, and their gradual shortening can lead to decreased cell division and increased apoptosis. Paternal age negatively affects fertility, but longer telomeres in older fathers may offer some reproductive advantages. Research indicates a correlation between shorter telomeres and male infertility, especially regarding sperm quality. Being overweight or obese can further reduce telomere length and negatively affect fertility. Additionally, some studies explore the connection between telomeres and testicular cancer, but this relationship remains unclear.

Methods: The present study was conducted by reviewing related articles in Web of Science, Scopus, and PubMed databases.

Results: Telomeres are crucial for protecting chromosome ends and ensuring reproductive cell maintenance and fertility. Telomere length determines their function, with shortening beyond a critical point leading to loss of protection. Maintaining telomere length is essential, with telomerase playing a key role in this process. Telomerase, present in germ cells and cancer cells, helps maintain telomere length by adding new repeats. Sperm telomeres are typically longer due to delayed closure

of telomerase, preventing shortening with age. Telomere length in sperm affects offspring's cells. Infertile men often have shorter telomeres and poorer sperm quality compared to fertile men. Short telomeres in sperm have been linked to male infertility. A study found low sperm count men had decreased telomere length, increased DNA damage, and protamine deficiency, indicating issues in cell division processes during spermatogenesis. This underscores the importance of telomere length in genomic stability and male fertility.

Conclusion: Male infertility has become a social issue, with conventional diagnostic methods often failing to identify underlying causes. Telomere length in sperm cells is being explored as a potential marker for male infertility, with studies linking it to abnormal sperm characteristics. Research suggests using quantitative PCR to measure telomere length could improve assessment of spermatogenesis and determine male reproductive age. While direct selection of germ cells with known telomere profiles for ART procedures isn't feasible, measuring telomere length in the polar body may provide indirect prediction. Longer telomeres in sperm could positively impact fertility, potentially offering solutions for infertility cases. Antioxidant therapies have shown mixed effects on chromatin integrity in male infertility treatment, requiring further research for validation. Telomere length could serve as a potential biomarker for sperm quality and male infertility, but more extensive studies are needed to confirm the connection with semen quality and fertility.

Keywords: telomere length- infertility- reproductive health

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The efficacy of intravenously administrated nanoparticles in stroke and age-related neurodegenerative diseases (Review)

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Introduction: The mean global lifetime risk of neurological disorders such as stroke, Alzheimer's disease (AD), and Parkinson's disease (PD) has shown a large effect on economy and society. The blood-brain-barrier (BBB) is a specialized multicellular barrier between peripheral blood circulation and neural tissue. BBB disruption is evident in many neurological conditions. The majority of currently available therapies have tremendous problems with drug delivery into the impaired brain. Nanoparticle (NP)-mediated drug delivery has been considered a profound substitute to solve this problem.

Methods: A wide variety of NPs has been displayed for the efficient brain delivery of therapeutics via intravenous administration, especially when their surfaces are coated with targeting moieties. Here, we discuss recent advances in the development of NP-based therapeutics for the treatment of stroke, PD, and AD, as well as the factors affecting their efficacy after systemic administration.

Results: NPs are able to enclose therapeutic agents conferring them protection, improving circulation time, and allowing a release of payload into the damaged brain site after intravenous administration. The use of specific ligands on the NPs surface has been highly proposed in the last decade. Moreover, the recent progress in antibody transport through the BBB can inspire NP bioengineers to fabricate novel systems with unique properties.

Conclusion: Intravenous administration enables a direct access of drugs to the systemic circulation, bypasses the gastrointestinal tract, and improves drug delivery to the brain. An increase of circulation time increases the probability of NPs interaction with the BBB, reaching the brain parenchyma. However, it is important to design remotely triggered NP-based formulations that release the cargo only after reaching the brain. Another therapeutic potential that deserves further investigation is the development of more efficient and well-controlled NPs that are able to target specific brain cells.

Keywords: Central nervous system, Stroke, Parkinson's disease, Alzheimer's disease, Nanoparticles

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The Efficacy of Probiotics in Managing Peri-Implantitis: A systematic review assessing the role of probiotics in the prevention and treatment of peri-implant diseases (Review)

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Introduction: Peri-implant diseases, especially peri-implantitis, represent the main difficulties in dental implantology because of their relatedness to inflammation and bone loss around dental implants. Probiotics have recently become a possible alternative therapy that aims to regulate the peri-implant microbiota and strengthen the immune system.

Methods: This systematic review systematically evaluates the effectiveness of probiotics in the treatment of peri-implant diseases. The PubMed, Cochrane Library, and Embase databases were searched comprehensively for studies published till ٢٠٢٤. In that were randomized controlled trials (RCTs), pilot studies, narrative reviews, and meta-analyses on probiotics' effect on peri-implant diseases. Outcome parameters ranged from clinical signs such as bleeding on probing, plaque index, probing pocket depth, to microbiological profiles and inflammatory biomarkers.

Results: The review results present a complex picture of the probiotics efficacy in the peri-implant disease therapy. Other trials showed favorable results for clinical indicators after probiotic intervention, but some of them were inconclusive or showed limited benefits. Meta-analyses had inconsistent findings, with the statistical significance differing across different studies.

Conclusion: The data assembled above emphasize the complexity of probiotics' role in the treatment of peri-implant disease, and more research is required to establish their efficacy and provide standard protocols. Tackling key research voids, including probiotic strains, dosages, and duration of treatment, is quintessential for guiding clinical practice properly. Although there are encouraging findings, a cautious approach is necessary, until there is thorough validation by means of large-scale and long-term clinical trials.

Keywords: Peri-Implantitis, Probiotics, Treatment, oral health, periodontistry

The Evaluation of Relationships between HPV Infection and its effects on Genital Lesion in Women who referred to the Maad Pathobiology Laboratory (Review)

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Introduction: Human Papilloma Virus (HPV) which is a major health concern around the world can cause serious diseases in both men and women. The topic of HPV continuous to be an important, as its infection speared rapidly (١). Papillomaviruses are specific for each individual and they are ubiquitous which are detectable in wide variety of animals as well as humans. Basal epithelial cell of the skin or inner lining of the tissue are divided into two sections, first is the cutaneous types and the second one is mucosal types. These sections are the target tissue of the HPVs which can infect them. Those types of HPV that infect the cutaneous part are epidermitrophic and target the skin of the hands and feet, while, the second group which are mucosal infect the lining of the mouth, respiratory tract, throat and anogenital epithelium (١,٢). According to the World Health Organization, the prevalence of HPV infection is approximately between ٩ to ١٣ percentages or on the other hand, is ٦٣٠ million people around the world (١). Moreover, the infection with anogenital HPVs is the most common viral sexually transmitted infection. HPV is categorized into two groups based on their partnership with cervical cancer and precursor lesion. These two groups are included High-risk and Low-risk HPV types (٢). Cervical cancer is the second type of the cancer among women around the world especially developing countries. Late detection of this infection can have negative consequences such as death for women (٣). Furthermore, if the infection with high-risk groups persists in the cervix for a long time, it can produce precancerous lesion and lead to cervical cancer (٤). The cervical cytology program in developed or high-income salaries countries, reduce the rate of mortality of the cervical cancer; however, in middle- and low-income countries the incidence is increased due to the lack of effectiveness in screening program (٥). The important factor which can weaken the screening program is the unavailability of adequate resources and infrastructure in these countries. Harold zur Hausen was a German virologist who demonstrated the connection between genital infection and cervical cancer in the early ١٩٨٠s (٢). According to the statistics, ٩٩,٧٪ of cervical squamous cell cancer is related to the HPV. Moreover, adenocarcinomas of the cervix are HPV association, while, the correlation is completely age dependent, for instance in women who are younger than ٤٠ the percentage of adenocarcinomas reach to the ٨٩٪, and in women in the age of ٦٠ years and older, HPV can observe in only ٤٣٪ (٢). Infection with multiple types of HPV can be a risk factor to increase cervical cancer, but there is still debate that whether this infection is due to the relationship among certain types of HPV or it occurs randomly (٣). Furthermore, there are between ١٢ and ١٥ types among ٢٠٠ HPV types which are classified as HR-HPV. These groups are able to infect cervix and they are a risk factor leading to the development of cervical cancer. Coinfection of HPV genotype is common in ٢٠-٥٠٪ of infected women, especially among young women. There is still a lot of question about the relationship between HPV infection and cervical cancer. Despite several contradictions, study about this relationship is very few (٣). In

this study, we analyzed ٥٠ women who infected with HPV genotypes and referred to the Mad Pathology Laboratory, Tehran, Iran and consider the association between their infection with cervical cancer.

Methods: The study was conducted according to the documents which we had during two months from September ٢٠٢٢ to November ٢٠٢٢. We collected patient's histories who referred to the Mad Pathology Laboratory. The data from their histories revealed that they have been infected with one or multiple HPV types. Their pathology reports were also analyzed and the relationship between Cervical cancer and HPV coinfection types were discussed. This infection caused some of patients became at risk of cervical cancer and the lesion around cervix influenced by HPV types. Women with positive HPV were dispatched for colposcopy with biopsies. Expert colposcopies performed all examinations and the reports were classified according to the patient's histories. The ranges of participant's age were between ٢٣ to ٤٨ years. All biopsies with or without morphological changes for a total of ٥٠ samples were analyzed. A woman who infected with more than one genotypes was considered to have coinfection. To prove this hypothesis, required information was obtained from patients and the data were analyzed by SPSS (ver.٢٣).

Results: A total of ٥٠ patients were analyzed in this study, of whom ٣٣ patients (٦٦٪) was HPV positive with single type, while ١٧ patients (٣٤٪) had coinfection with multiple HPV types (both HR and LR HPV). Moreover, ٢٣ out of ٥٠ patients being infected by LSIL/CIN I; however, only ٥ participants suffered from HSIL/ CIN II. There were ٢٦ patients who not only were infected by HPV ١٦ and ١٨ types, but also had coinfection with other types. The pathology report of these participants reveals that they had chronic Endo cervicitis with metaplasia and hyperplasia. According to the results, majority of them had the problem of LSIL/CIN I. Reactive squamous with koilocytic changes (Nuclear Enlargement), was seen in patients who had coinfection of other types such as ٦٢/٦٨, ٥٥/٦٦, ٣٥/٣٩/٣١ HR-HPV and ٦/١١/٥٤ LR-HPV. The significant point of this study was the young generation of participants. There were ١٠ patients who the mean age of them was ٢٥ (From ٢١ to ٢٩), and the majority of them were positive for ١٦ and ١٨ HR- HPV. These patients had the pathology reports of chronic inflammation, or chronic Endo cervicitis with metaplasia and hyperplasia, LSIL/CIN I and HSIL/CIN II. On the other hand, they showed the same symptoms due to the same HPV types. These results demonstrate that the young generations are more at risk of cervical cancer rather than other groups. Furthermore, benign squamous epithelium was seen in approximately ١٠ patients.

Conclusion: In this study, the dominant types of HPV genotypes were ١٦, ١٨ and ٥٦/٦٦ which most patients suffered from them. Moreover, LSIL/CIN I was the main symptoms among women. This study wanted to indicate the significance of the results of HPV PCR beside the colposcopy. However, the Pap smear results cannot be denied and can help doctor to screen better. It should be mentioned that, as the sensitivity of the women's genital tract is so high, any symptoms should be given importance. Furthermore, further study is required in order to increase public awareness about the importance of HPV screening as well as vaccination.

Keywords: Human Papillomavirus, Genital Lesion, Cervical Cancer, Co-infection, Pap smear

The expression of recombinant proteins by self-inducible expression systems containing different human heat shock proteins in Ecoli (Research Paper)

zahra sedighi,[1] Fatemeh Sadat Shariati,[2] Faezeh Takhsha,[3] Zahra Parandeh,[4] Arefe Sadat Khavari,[5] Reza Ahangari Cohan,[6,*]

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Introduction: The IPTG-inducible promoter is widely used for the expression of recombinant proteins. however, it is not suitable for industrial scale due to high cost and toxicity to the producing cells. Recently, a self-inducible expression (SILEX) system has been developed to overcome these problems by using Hsp٧٠ as an autoinducer. here the effects of other heat shock proteins on the autoinduction of green fluorescent protein (EGFP) was investigated.

Methods: EGFP expression was monitored after double transformation of pET٢٨a-EGFP and pET٢١a-(Hsp٢٧/Hsp٤٠/Hsp٧٠) plasmids in E. coli using fluorimetry and SDS-PAGE. expression levels, bacterial growth curves, plasmid stability, and expression stability were compared with an IPTG-inducible system.

Results: Statistical analysis revealed a significant difference in EGFP expression between autoinducible and IPTG-inducible systems. Expression is higher in the Hsp٢٧ than in the Hsp٧٠ and Hsp٤٠ systems. However The highest expression was observed in the inducible system. IPTG-inducible and Hsp٧٠ systems showed longer lag times in the bacterial growth curve than Hsp٢٧ and Hsp٤٠ systems. In addition, Hsp٢٧ and Hsp٤٠ systems showed the same plasmid stability whitin ٥٠٠ days of subculture, whereas Hsp٧٠ showed a reduction in the numbers of colon in the first subculture step. Relatively stable EGFP expression was observed in the SILEX systems after several freeze-thaw cycles whitin ٩٠ days, while the IPTG-inducible system showed a decreasing trend compared to the newly transformed bacteria . In addition, the inducible system showed more variation in experssion between different clones than the SILEX systems.

Conclusion: In conclusion, the Hsp٢٧ system could be considered as a suitable autoinducible system for protein expression due to less metabolic burden, lower variation in expression, suitable plasmid and expression stability and higher expression level.

Keywords: Autoinducible expression system, Escherichia coli, SILEX system, Enhanced green fluorescent protein

The extensive role of adult stem cells in regenerative medicine and future horizons (Review)

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Introduction: In recent years, there has been a significant increase in the understanding of stem cell biology. Stem cells, as cells with multidirectional differentiation and self-renewal abilities, as well as potential clinical applications, have attracted a lot of attention in the field of regenerative medicine. Adult stem cells are rare and undifferentiated cells found in all tissues of the body. Although these cells are usually kept in a stationary and non-dividing state, they can multiply and differentiate and thus play a role in the treatment of diseases, reconstructive surgeries and also the treatment of aging.

Methods: Considering the importance of stem cells in the treatment of diseases using the nascent science of reconstructive medicine in this research, an overview of the characteristics and types of mature stem cells and the results and achievements of modern science in the use of these cells through treatment Various diseases have occurred.

Results: Adult stem cells (ASCs) are undifferentiated cells that have self-renewal and differentiation abilities. They are present in all major organ systems of the body and are uniquely stored there during development for tissue maintenance during homeostasis, injury, and infection. They do this by rapidly modulating the dynamics of proliferation, differentiation, survival, and migration. The main types of adult stem cells include hematopoietic, mesenchymal, neural, epidermal, skeletal muscle, and liver stem cells. These cells play an important role in repairing and protecting the body, and they also act as cell reserves that are removed from circulation. Normal tissue provides support and can initiate a regenerative response after acute injury. Non-endometrial mature stem cells, such as bone marrow-derived mesenchymal stem cells and umbilical cord-derived mesenchymal stem cells, with autologous and allogeneic applications, can repair damaged endometrial tissue in animal models of AS and in human studies. Mesenchymal stem cells (MSCs) are involved in tissue repair and anti-inflammatory activities and have shown promising therapeutic efficacy in various animal models of neurological disorders. Although the population of stem cells isolated from bone marrow is usually a heterogeneous mixture of different subpopulations, adult stem cell lines cloned from any source also show a wide range of differentiation potential, for example, osteogenesis, myogenesis, neurogenesis or angiogenesis in wound healing. Angiogenesis in particular is a topic in tissue regeneration with tremendous implications in reconstructive surgery. Adult stem cells from adipose tissue (ASCs) show significant promise in the treatment of autoimmune and neurodegenerative diseases, vascular and metabolic diseases, bone and cartilage regeneration, and wound defects. The regenerative capabilities of ASC cells in vivo are mainly regulated by the secretion of paracrine factors and cell-matrix interactions.

Conclusion: The purpose of this article is to review the types of adult stem cells, their uses and characteristics in the science of reconstructive medicine. Also, the challenges and perspectives of using these cells in reconstructive medicine have been discussed.

Keywords: Regenerative medicine - stem cells - adult stem cells - treatment of diseases

The Future of Medical Genetics: Integrating Genomic Medicine into Personalized Healthcare

(Review)

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Introduction: Medical genetics has emerged as a transformative force in healthcare, driven by advancements in genomic technologies and a deeper understanding of human genetics. The era of personalized medicine, where therapies are tailored to the genetic profile of individuals, is not just a vision but a rapidly approaching reality. This paper explores recent breakthroughs in medical genetics, such as next-generation sequencing (NGS), gene editing via CRISPR-Cas٩, and their implications for clinical practice. Furthermore, it highlights the ethical considerations that must guide the responsible implementation of these technologies.

Methods: This study reviews state-of-the-art research on genomic medicine, focusing on the application of next-generation sequencing, gene editing, and precision diagnostics in clinical settings. Data were collected from multiple peer-reviewed sources, including recent trials and large-scale genomic projects like the ١٠٠,٠٠٠ Genomes Project. Additionally, ethical frameworks were evaluated to assess challenges surrounding genetic data privacy, informed consent, and equitable access to genetic healthcare.

Results: The findings demonstrate that: ١_Next-Generation Sequencing (NGS): NGS has revolutionized genetic testing, allowing for rapid and cost-effective identification of genetic mutations associated with various disorders, from monogenic diseases to complex cancers. The widespread adoption of NGS in clinical settings has improved diagnostic accuracy, especially for rare diseases, leading to more effective treatments (Sims et al., ٢٠١٤). ٢_Gene Editing (CRISPR-Cas٩): One of the most significant breakthroughs in medical genetics is CRISPR-Cas٩, a powerful gene-editing technology that has the potential to correct genetic mutations at the DNA level. While it has shown promise in treating genetic disorders such as sickle cell anemia and muscular dystrophy, ongoing clinical trials are essential to evaluate its long-term safety and efficacy (Doudna & Charpentier, ٢٠٢٠). ٣_Precision Medicine: The integration of genomic data into clinical care has enabled personalized treatments that consider an individual's genetic makeup. This approach, particularly in oncology, has led to the development of targeted therapies that improve patient outcomes, with examples like EGFR inhibitors for lung cancer and PARP inhibitors for breast cancer (Jameson & Longo, ٢٠١٥). ٤_Ethical Considerations: Despite the promising advancements, ethical concerns remain central to the conversation. Issues such as genetic data privacy, potential discrimination based on genetic information, and access to cutting-edge genetic healthcare pose significant challenges. International frameworks, such as the Universal Declaration on Bioethics and Human Rights, must be continuously updated to address these emerging concerns (Andorno, ٢٠٠٧).

Conclusion: Medical genetics stands at the forefront of a healthcare revolution, with genomic medicine poised to reshape the diagnosis and treatment of diseases across the world. As genetic

technologies like NGS and CRISPR-Cas۹ advance, the promise of personalized medicine becomes increasingly attainable. However, this progress must be accompanied by careful consideration of ethical implications, particularly around data privacy and equitable access to these life-changing technologies. By fostering international collaboration and robust regulatory frameworks, the field of medical genetics can ensure that these innovations benefit all patients while upholding the highest ethical standards. Medical genetics stands at the forefront of a healthcare revolution, with genomic medicine poised to reshape the diagnosis and treatment of diseases across the world. As genetic technologies like NGS and CRISPR-Cas۹ advance, the promise of personalized medicine becomes increasingly attainable. However, this progress must be accompanied by careful consideration of ethical implications, particularly around data privacy and equitable access to these life-changing technologies. By fostering international collaboration and robust regulatory frameworks, the field of medical genetics can ensure that these innovations benefit all patients while upholding the highest ethical standards.

Keywords: Genomic medicine, personalized healthcare, genetic testing, precision medicine, gene editing

The Genetic and Environmental Regulation of Transaminase Activity: Implications for Personalized Medicine (Review)

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Introduction: Transaminases, specifically alanine aminotransferase (ALT) and aspartate aminotransferase (AST), are enzymes commonly used as biomarkers for liver injury. However, recent research indicates their roles extend beyond simple indicators of liver damage, implicating them in broader metabolic and cardiovascular diseases. Elevated transaminase levels have been linked to conditions such as type ۲ diabetes, coronary heart disease, and metabolic syndrome, suggesting that these enzymes reflect complex physiological processes. This review aims to explore the genetic and environmental factors regulating transaminase activity and discuss their implications for personalized medicine.

Methods: This review synthesizes data from genome-wide association studies (GWAS), omics technologies, and recent clinical studies to examine the genetic and environmental factors influencing transaminase activity. GWAS has identified several candidate genes associated with transaminase levels, providing insights into the genetic regulation of these enzymes. Additionally, we reviewed studies examining the influence of environmental factors, such as diet and lifestyle, on transaminase activity. The integration of these findings allows for a comprehensive understanding of the regulatory mechanisms governing transaminase levels and their potential as personalized medicine tools.

Results: The regulation of transaminase activity is influenced by a complex interplay of genetic and environmental factors. Genome-wide association studies (GWAS) have identified several key genes associated with ALT and AST levels, including PNPLA۳, TM۶SF۲, and GCKR The PNPLA۳ gene, which plays a significant role in lipid metabolism, has been strongly linked to elevated transaminase levels, particularly in the context of non-alcoholic fatty liver disease (NAFLD). Variants in TM۶SF۲ and GCKR are also implicated in transaminase regulation, further connecting these enzymes to broader metabolic processes. Epigenetic factors, such as DNA methylation, also contribute to the regulation of transaminase levels. For instance, hypermethylation of specific gene promoters can downregulate the expression of enzymes critical for transaminase activity, leading to altered levels and increased disease susceptibility. These findings suggest that genetic predispositions are modulated by epigenetic changes, which can either exacerbate or mitigate the impact of these predispositions. Environmental factors, particularly diet and lifestyle, significantly influence transaminase activity. High-fructose and high-fat diets have been shown to elevate ALT and AST levels, especially in

individuals with genetic susceptibility. Conversely, diets rich in fiber and polyunsaturated fats are associated with lower transaminase levels, offering a protective effect. Alcohol consumption is another critical factor, with chronic intake linked to elevated AST levels. The AST/ALT ratio is often used as a marker for alcohol-related liver damage, and genetic variants in alcohol-metabolizing genes can further influence these levels. Physical activity is a beneficial modulator of transaminase levels. Regular exercise is associated with lower ALT and AST levels, likely due to improved metabolic health. This effect is particularly beneficial for individuals with genetic predispositions to elevated transaminase levels, emphasizing the role of lifestyle interventions in managing transaminase activity. In conclusion, the regulation of transaminase activity is governed by a dynamic interaction between genetic, epigenetic, and environmental factors, highlighting the importance of personalized approaches in managing metabolic and liver-related diseases.

Conclusion: The regulation of transaminase activity is a multifaceted process involving both genetic and environmental factors. Understanding these regulatory mechanisms is crucial for developing personalized medical approaches that can effectively address the underlying causes of altered transaminase levels. Personalized medicine, which takes into account an individual's genetic makeup and environmental exposures, offers the potential to tailor interventions that can prevent or mitigate the adverse health outcomes associated with elevated transaminase levels. Future research should focus on further elucidating the genetic pathways involved in transaminase regulation and exploring how these insights can be translated into clinical practice to improve patient outcomes.

Keywords: Transaminases, Genetic regulation, Environmental factors, ALT/AST, Personalized medicine

The genotyping of Human Papilloma Virus (HPV) in Women's Cervical Tissue Samples from Fasa, Iran (Review)

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Introduction: Human papillomavirus (HPV) is the most prevalent sexually transmitted infection globally, with more than ١٠٠ different types identified so far. According to the (World Health Organization) WHO reports Cervical cancer is the fourth most common cancer in women globally.

Methods: In order to conduct this study, tissue samples were obtained from ٧٥٦ patients who had ٢٠١٧ to ٢٠٢٢ referred for HPV screening by gynecologist.In this study, after collecting the samples, DNA was extracted from the samples, then genotyping of the investigated samples was done using the Real Time PCR method.The detection rate of the HPV genome in women's cervical tissue samples was evaluated using Graph Pad/Prism٨,٠,٢ software and documented the findings in a written report.

Results: This study analyzed the demographic and HPV genotyping data of ٧٥٥ women cases. The majority of cases were in the age groups of ٣١-٤٠ years and ٢١-٣٠ years. HPV testing by Real-Time PCR showed a positivity rate of ٥٣,١١٪, with the highest prevalence in the ٣١-٤٠ years' age group followed by the ٢١-٣٠ years' age group. Cytology analysis revealed that LSIL was the most common lesion, followed by HSIL and ASCUS among HPV-positive samples. HPV genotyping identified HPV-٦ and HPV-١٦ as the most common monotypes, while HPV-٦,١١ predominated in mix genotypes cases. The combination of cytology and HPV genotyping results showed distinct patterns of HPV types in LSIL, ASCUS, and HSIL samples.

Conclusion: The results of this study contribute valuable insights into the epidemiology of HPV infection and its association with cytological abnormalities in cervical lesions.

Keywords: Papilloma Virus (HPV); Cervical cancer; HPV-١٦; HPV-٦,١١; HPV-٦

The Global Fight Against Dengue Fever: A Comprehensive Guide to Risks Reduction and Prevention

(Review)

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Introduction: Dengue fever is a virus that is spread by the dengue virus (DENV). About ٣,٩ billion people are at risk of getting it. The most dangerous strain is DENV-١, which makes up ٦٤,٤٪ of all cases. Some of the most common signs are fever, arthralgia, vomiting, severe headaches, eye pain, loss of appetite, and skin eruptions. Infected female mosquitoes of the genus Aedes, mostly A. aegypti and A. albopictus spread the disease through bites. When the virus gets into the mosquito's stomach, it spreads throughout its body over ٨ to ١٢ days. The World Health Organization says that ٣٩٠ million cases of dengue fever happen every year, and ٩٦ million of those people get sick. The scary rise in dengue fever cases shows how big of a problem global public health is and how we need to raise knowledge, lower risks, and come up with ways to stop people from getting it. In this article, we reviewed a comprehensive guide to risks reduction and prevention of this fever as a global fight and ways to avoid, diagnose, and treat the disease.

Methods: Keywords that have to do with preventing “dengue fever,” “risks reduction,” and “controlling Aedes” are used in academic databases like BMC, PubMed, Web of Science. Abstracts and full-length papers were evaluated on how well they were researched and how well they used good methods.

Results: The spread of Aedes spp. has been helped by urbanization and global warming. Mosquitoes are living longer and reproducing more quickly, which means that outbreaks can happen in more places. When different serotypes of dengue are spread together, serious dengue symptoms like Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS) are more likely. Controlling vectors, training people about health, and making vaccines are the main ways to stop dengue fever. Vector control tries to get rid of places where mosquitoes can grow, especially in cities, by getting rid of backwaters, using larvicides, and keeping places clean. A lot of people use insecticides to get rid of adult mosquitoes, especially during outbreaks. However, mosquitoes have become resistant to them because they are used so much, making them less effective. Public health education is very important for making people more aware of the risks of dengue fever and encouraging them to change their habits to avoid being around mosquitoes. People who live in endemic area of dengue

are told to take precautions to protect themselves, like wearing long-sleeved clothes, using bug spray, and sleeping under mosquito nets, especially when mosquito activity is high. It is important for governments, local groups, and people to work together on prevention strategies and community involvement programs to help make that happen. In the fight against dengue around the world, making a good vaccine has been a top concern. Recent progress in the study of dengue vaccines has led to the testing of several candidates in humans. Some of these candidates have shown promise in these tests. The ideal vaccine would protect against all four serotypes for life and be safe for everyone, even if they have been exposed to dengue before.

Conclusion: Four types of dengue virus are very dangerous to humans. Vector control, early discovery, and case management are all good ways to keep things under control. Supportive care, which focuses on keeping the person hydrated, relieving pain, and keeping an eye out for any problems, is the main way to treat dengue fever. Research is very important for coming up with new medical processes and methods, like vaccines. To get rid of dengue effectively, you need a broad plan that includes communities and healthcare workers. Community participation programs can help protect vulnerable people from dengue complications and improve their health and well-being. Controlling vectors, training people about health, and making vaccines have been the main ways that the disease has been fought. To stop dengue outbreaks, we need a multifaceted method that includes working with the community, taking care of the environment, and coming up with new scientific ideas.

Keywords: Dengue Fever, Risks reduction, and Controlling Aedes Mosquitoes

The global threat of antibiotic resistance (Review)

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Introduction: Antimicrobial resistance (AMR) poses a major threat to human health around the world and is an important global health challenge in the ٢١st century the overuse and misuse of antibiotics are contributing factors. In ٢٠١٩, it was estimated that antimicrobial resistance (AMR) caused approximately ٤,٩٥ million deaths globally, based on data from ٢٠٤ countries and territories. The study highlighted the urgent need for global action to consider the problem of bacterial AMR.

Methods: The researchers used data from diverse sources, including systematic literature reviews, hospital records and using databases including Google Scholar and PubMed. They estimated deaths and disability-adjusted life-years (DALYs) attributable to and associated with bacterial AMR for pathogens and pathogen–drug combinations in ٢٠٤ countries and territories.

Results: The six leading pathogens for deaths associated with resistance were Escherichia coli followed by Klebsiella pneumonia, Staphylococcus aureus, Streptococcus pneumoniae, Pseudomonas aeruginosa and Acinetobacter baumannii. Also, one pathogen–drug combination, meticillin-resistant S aureus caused death in patients.

Conclusion: To our knowledge, AMR and pathogen–drug combinations are leading causes of death around the world, Expanding microbiology laboratory capacity and enhancing data collection systems is crucial for improving our understanding of significant human health threats. The WHO have to be reevaluated and awareness among physicians about AMR needs to be raised.

Keywords: Antimicrobial resistance, pathogen–drug combinations, disability-adjusted life-years

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The hidden linkage between childhood obesity and immune system diseases (Review)

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Introduction: Obesity, which is commonly measured by body_ mass_ index (BMI), is recognized as one of the growing medical problems of the ٢١st century in children. It has nearly tripled between ١٩٧٥ and ٢٠١٦ (١). Obesity affects many organs and causes various diseases, including metabolic, cardiovascular and liver diseases. However, one of the most important organs affected by obesity and fat tissue is the immune system. Immune system dysfunction can cause many diseases including autoimmune diseases such as multiple sclerosis (MS), allergies and cancers (٢). Therefore, childhood obesity is an important medical issue that requires further studies.

Methods: In this study, articles about childhood obesity and immune system diseases were searched and reviewed from Scopus and web of sciences databases.

Results: The increase in the size and number of fat cells due to weight gain and obesity leads to the secretion of pro-inflammatory molecules, causing chronic inflammation in the body. For instance, macrophages, the most common type of immune cell in adipose tissue, are associated with obesity. In obese individuals, there is a development of M١ macrophage phenotype, which is directly linked to systemic inflammation in the body. Conversely, M٢ macrophages play regulatory and homeostatic roles. Additionally, neutrophils, mast cells, and dendritic cells (DC) in adipose tissues contribute to the inflammation process by releasing pro-inflammatory mediators (٣). In obesity, the secretion of two pro-inflammatory cytokines interleukin ٦ (IL-٦) and tumor necrosis factor alpha (TNF-α) increases. These cytokines contributed to systematic inflammation by inhibition an anti-inflammatory factor called adiponectin in the body. IL-٦ is directly related to visceral and peri-abdominal obesity by accelerating cell proliferation, angiogenesis and metastasis. Moreover, TNF-α increases cell proliferation and DNA damage, leading to tumor growth in obese individuals. Studies have found a direct correlation between BMI in children and adolescence and the mortality rate of various adult cancers, such as liver, colon, and kidney (٣-٥). Furthermore, inflammatory conditions resulting from obesity are significantly associated with autoimmune diseases, including type ١ diabetes (T١D) and MS (٦).

Conclusion: Obesity and excess adipose tissue in children and adolescents can have adverse effects on the immune system, leading to systematic inflammation and diseases such as type ١ diabetes, multiple sclerosis and various cancers. Therefore, controlling weight and BMI in children and adolescents can be beneficial for disease prevention.

Keywords: Obesity, cytokine, inflammation, cancer, autoimmune diseases

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The Human microbiome as a therapeutic target for metabolic diseases and the role of gut microbiome metabolites in obesity, A Review (Review)

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Introduction: The human body is host to a vast number of microbes, including bacterial, fungal, and protozoal microorganisms, which together constitute our microbiota. Recent evidence suggests that gut microbiota alterations contribute to the pathogenesis of metabolic disorders. The human microbiome resides in our gastrointestinal tract and creates a dynamic and complex microbial ecosystem of more than ١٠٠٠ microbial species and their phages. Based on epidemiological and omics studies combined with in vitro studies using various cell models and in vivo studies in mice, human health and disease risk may be mediated by the human microbiome. In adult life, these microbes are mainly influenced by lifestyle, medication, and host genetics. The gut microbiota, in turn, produce microbial components that act not only on local cells in the gut but also on peripheral tissues via systemic circulation, playing a crucial role in training our immune system and regulating gut endocrine function and neurological signaling. They are also involved in modifying drug action and metabolism, eliminating toxins, and producing numerous signaling compounds. There is an increasing global prevalence of metabolic diseases associated with un- healthy lifestyles. These include type ٢ diabetes (T٢D), metabolic dysfunction-associated steatotic liver disease (MASLD), hypertension, hyperlipidemia, and obesity. Evidence shows that the intestinal microbiome is intrinsically linked with overall health, including obesity risk. Obesity and obesity-related metabolic disorders are characterized by specific alterations in the composition and function of the human gut microbiome. Mechanistic studies have indicated that the gastrointestinal microbiota can influence both sides of the energy balance equation; namely, as a factor influencing energy utilization from the diet and as a factor that influences host genes that regulate energy expenditure and storage. Moreover, its composition is not fixed and can be influenced by several dietary components. This fact raises the attractive possibility that manipulating the gut microbiota could facilitate weight loss or prevent obesity in humans. Emerging as possible strategies for obesity prevention and/or treatment are targeting the microbiota, to restore or modulate its composition through the consumption of live bacteria (probiotics), nondigestible or limited digestible food constituents such as oligosaccharides (prebiotics), or both (synbiotics), or even fecal transplants. Despite the wide variation in the pathologies of these common metabolic disorders, they are all associated with abnormalities in the composition and function of the human microbiota. It remains questionable whether there is a causal relationship between host metabolism and the microbiome. To date, results obtained from animal and fecal microbiota transplantation studies have demonstrated causal effects of the microbiome on host health. Importantly, recent developments in next-generation microbiome sequencing to obtain comprehensive gene catalogs combined with targeted bioinformatics have provided a substantial amount of new knowledge on the role of the gut microbiota. This review will discuss the potential use of the human microbiome as a therapeutic target to improve host metabolism.

Methods: This study reviews data accumulated from literature and prestigious case studies that are in connection with our subject. The search words were:" Human microbiota," "Microbial metabolites," "metabolic disease," "Short-chain fatty acid," Microbiome", "gut microbiome," Metabolism ", " Obesity" using PubMed, Scopus, Science Direct, and Google Scholar databases. Furthermore, manual searches of other relevant journals and keyword searches were performed. We have focused on published papers from ٢٠١٠ to ٢٠٢٤.

Results: Several studies have identified potential causal associations between gut microbiota and metabolic disorders, and obesity as well as the underlying mechanisms. The effects of modulating interventions, such as prebiotics, probiotics, fecal microbiota transplantation, and other new treatment possibilities on these metabolic disorders have also been reported.

Conclusion: A growing body of evidence highlights the role of gut microbiota in the development of dysbiosis, which in turn influences host metabolism and disease phenotypes. Further studies are required to elucidate the precise mechanisms by which gut microbiota-derived mediators induce metabolic disorders and modulating interventions exert their beneficial effects in humans. The gut microbiota represents a novel potential therapeutic target for a range of metabolic disorders.

Keywords: Gut microbiota, Microbial metabolites, Obesity, Microbiome, metabolic disease

The Impact of Acrylamide on the Hippocampus in Male Rats (Review)

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Introduction: Acrylamide is a known neurotoxin found in heated starchy foods, such as fries and bread. While its impacts on the nervous system are established, few studies have investigated its specific effects on the hippocampus, a critical region for memory and learning. This study aims to elucidate the morphological and histopathological changes induced by acrylamide in the hippocampus of male rats

Methods: Twenty male Wistar rats were divided into four groups: a control group and three groups administered acrylamide at ۰,۵, ۱, and ۲ mg/kg body weight for ۳۰ days. At the end of the treatment period, rats were sacrificed, and their hippocampi were collected for histopathological examination. Hippocampal sections were stained with hematoxylin and eosin, and morphometric analysis was performed to assess changes in the structure of the cornu ammonis (CA) and dentate gyrus (DG).

Results: Compared to the control group, acrylamide-treated rats exhibited dose-dependent degenerative changes in the hippocampus. In the CA region, pyramidal cell layers appeared disorganized, with decreased cell density and increased eosinophilia indicating necrosis. The DG displayed atrophy of granular cell layers, with reduced numbers of cells and increased intercellular spaces. Morphometric analysis revealed significant decreases in the thickness of the CA and DG layers with increasing acrylamide dose

Conclusion: Compared to the control group, acrylamide-treated rats exhibited dose-dependent degenerative changes in the hippocampus. In the CA region, pyramidal cell layers appeared disorganized, with decreased cell density and increased eosinophilia indicating necrosis. The DG displayed atrophy of granular cell layers, with reduced numbers of cells and increased intercellular spaces. Morphometric analysis revealed significant decreases in the thickness of the CA and DG layers with increasing acrylamide dose

Keywords: Acrylamide; Hippocampus; Neurotoxicity; Rats

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The Impact of Aging on Pharmacokinetics: Implications for Medication Management in Elderly Patients (Review)

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Introduction: The aging process leads to significant physiological changes that affect how medications are absorbed, distributed, metabolized, and excreted—collectively known as pharmacokinetics (ADME). Acknowledging these changes is crucial for optimizing drug therapy in elderly patients, who often contend with multiple health conditions and are prescribed various medications. By understanding these transformations, healthcare providers can improve treatment outcomes and enhance the quality of care for older adults.

Methods: A thorough review of the literature was performed utilizing databases such as PubMed and various academic journals that concentrate on pharmacokinetics in older populations. The keywords employed in the search included "aging," "pharmacokinetics," "drug metabolism," and "elderly." Studies published between ۱۹۹۰ and ۲۰۲۳ were selected for analysis to provide an overview of how aging affects pharmacokinetic processes.

Results: The review highlighted several significant pharmacokinetic changes linked to aging: Absorption: While the overall absorption of drugs tends to remain consistent in healthy older adults, factors such as lower gastric acidity and delayed gastric emptying can influence the absorption rates of certain medications. Distribution: An increase in body fat and a decrease in lean muscle mass lead to a larger volume of distribution for lipophilic drugs, which results in longer half-lives. Conversely, hydrophilic drugs experience a smaller volume of distribution. Metabolism: Age-related changes often result in reduced hepatic metabolism due to decreased liver size and blood flow. This reduction particularly affects the clearance of drugs that have high hepatic extraction ratios. Excretion: Renal function generally declines with age, impacting the elimination processes for drugs primarily excreted by the kidneys. This necessitates vigilant monitoring and possible dosage adjustments to prevent adverse effects.

Conclusion: Aging-related alterations in pharmacokinetics have significant clinical implications for managing medications in older adults. These changes result in increased variability in individual drug responses, underscoring the necessity for a cautious prescribing strategy. The guideline of "start low, go slow" is particularly relevant for this age group, as it aids in minimizing adverse reactions and improving treatment outcomes.

Keywords: Aging, pharmacokinetics, drug metabolism, renal function, elderly care

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The Impact of Conditioned Medium Derived from Human Adipose-Derived Mesenchymal Stem Cells on the Recovery of Testicular Function in a Rat Model of Azoospermia Induced by Busulfan.

(Research Paper)

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Introduction: Men are responsible for ٢٠-٣٠٪ of infertility cases Several factors can contribute to male infertility, including reduced sperm production, abnormal sperm function, obstruction of ejaculatory ducts, and impotence. Meanwhile, non-obstructive azoospermia (NOA), which is characterized as the absence of sperm in ejaculation due to failure of spermatogenesis, is the most severe form of male infertility. Non-obstructive azoospermia is caused by hormonal and genetic disorders, trauma to the testis and its disease, varicocele, etc. Currently, most individuals with non-obstructive azoospermia (NOA) do not have a treatment option that can fully restore spermatogenesis , except for patients with secondary testicular failure. Therefore, the only way for couples to conceive is to receive sperm directly from the testis for intracytoplasmic sperm injection (ICSI). ICSI is the standard treatment for male infertility but, It may increase the risk of genetic abnormalities in the offspings compared to natural pregnancy. Most men with non-obstructive azoospermia (NOA) have no treatment options other than assisted reproductive techniques (ART) to have a biological child. Given current therapies, there is an urgent need to develop alternative and effective therapeutic strategies.Secreted factors by mesenchymal Stem Cells (MSCs) offer promising prospects for cell-based therapy in regenerative medicine. This research is to detect if Conditioned Medium (CM) obtained from Human adipose tissue-derived mesenchymal stem (AD-MSCs) can restore spermatogenesis in busulfan-induced azoospermatic rat model.

Methods: To study the effect of conditioned medium intra-testis injection on the recovery of spermatogenes in NOA rat model ,the adiopose – derived mesenchymal stem cells (Ad-MSCs) were isolated and cultured. Then on the ٣rd passage conditioned medium was collected .This study was conducted on ٣٠ male Wistar rats (aged ٨-١٢ weeks). Animals were kept adapted for one week before the beginning of the research in an appropriate environment and had free access to food supplies and water. Rats were divided in ٤ groups, as control group (without treatment or negative control) , NOA group (busulfan -induced rat or positive control) azoospermia sham (busulfan + Phosphate-buffered saline) and experimental groups (busulfan + ADSC-CM).The non-obstructive azoospermia (NOA) model was established using intraperitoneal administration of busulfan in rat by two intraperitoneal injections of busulfan ١٠ mg/kg, with ٢١ day intervals. ٣٥ days after the second busulfan injection, the test group was treated with adipose tissue-derived stem cell conditioned medium(٥٠٠mg/ml).western blot analysis was conducted to assess the levels of DAZL and VASA proteins.

Results: The analysis indicated a significant increase($P \leq ٠:٠٠٠$) in the levels of DAZL and VASA expression within the ADSC-CM group as comparedto the control group, whereas a significant decrease was observed in the NOA and Sham groups.

Conclusion: This research proposes that the use of conditioned medium from human adipose - derived mesenchymal stem cells could potentially aid in the restoration of spermatogenesis in busulfan-induced infertile rats.

Keywords: Non-Obstructive Azoospermia, Adipose Tissue , Adipose Mesenchymal Stem Cells,Conditioned Medium

The Impact of Gut Microbiome Dysbiosis on Response to Immunotherapy in Melanoma Cancer Patients (Review)

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Introduction: Recent advances in cancer treatment have highlighted the crucial role of the immune system in combating malignancies. Immunotherapy has emerged as a promising approach, particularly in the treatment of melanoma, a highly aggressive form of skin cancer. However, patient responses to immunotherapy vary significantly, and understanding the factors that influence these responses is critical. Emerging evidence suggests that the gut microbiome, a complex community of microorganisms residing in the gastrointestinal tract, plays a pivotal role in modulating the immune system. Dysbiosis, or an imbalance in the gut microbiome, may influence the efficacy of immunotherapy. This study investigates the impact of gut microbiome dysbiosis on the response to immunotherapy in melanoma patients.

Methods: A total of ١٢٠ melanoma patients undergoing immunotherapy were recruited for this study. The sample comprised ٧٠ males and ٥٠ females, with a mean age of ٥٥,٢ years (range ٣٠-٧٥ years). Patients were selected based on the following inclusion criteria: confirmed diagnosis of melanoma, no prior history of gastrointestinal disorders, and no antibiotic use within six months prior to the study. Fecal samples were collected from all participants before the initiation of immunotherapy. Microbiome analysis was conducted using ١٦S ribosomal RNA gene sequencing to identify bacterial composition and assess the presence of dysbiosis. Patients were monitored over a six-month period to evaluate their response to immunotherapy. Clinical responses were categorized into complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD) according to RECIST (Response Evaluation Criteria in Solid Tumors) guidelines. Statistical analyses were performed to correlate microbiome profiles with treatment outcomes.

Results: Microbiome analysis revealed significant variations in bacterial composition among patients. Notably, patients with higher abundance of Bacteroides and Faecalibacterium exhibited more favorable responses to immunotherapy. Specifically, ٣٠ out of ١٢٠ patients (٢٥٪) achieved complete response (CR), with a mean abundance of Bacteroides at ١٤,٠٠٠ sequences per sample and Faecalibacterium at ١٠,٥٠٠ sequences per sample. Partial response (PR) was observed in ٤٠ patients (٣٣,٣٪), with mean Bacteroides and Faecalibacterium abundances of ١١,٥٠٠ and ٨,٠٠٠ sequences per sample, respectively. In contrast, patients with lower levels of these beneficial bacteria and higher levels of potentially pathogenic bacteria such as Clostridium and Escherichia showed poorer outcomes. Progressive disease (PD) was noted in ٣٥ patients (٢٩,٢٪), where mean Bacteroides and Faecalibacterium abundances were significantly lower at ٥,٠٠٠ and ٤,٠٠٠ sequences per sample, respectively. Stable disease (SD) was observed in ١٥ patients (١٢,٥٪), with

intermediate bacterial abundances. Furthermore, the overall diversity of the gut microbiome, measured by the Shannon diversity index, was higher in responders (CR and PR) compared to non-responders (SD and PD). Responders had a mean Shannon diversity index of ٤,٥, whereas non-responders had a mean index of ٣,٢.

Conclusion: This study underscores the significant impact of gut microbiome composition on the efficacy of immunotherapy in melanoma patients. The presence of beneficial bacteria such as Bacteroides and Faecalibacterium appears to enhance treatment response, while dysbiosis characterized by low microbial diversity and high levels of pathogenic bacteria correlates with poorer outcomes. These findings suggest that modulating the gut microbiome through dietary interventions, probiotics, or fecal microbiota transplantation could potentially improve immunotherapy responses in melanoma patients. Further research is warranted to explore these therapeutic strategies and their implications in clinical practice.

Keywords: Gut microbiome, Dysbiosis, Immunotherapy, Melanoma, Cancer, Bacteroides, Faecalibacterium, Microbial

The Impact of Gut Microbiome on Antibiotic Treatment Response in Sepsis Patients (Review)

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١.

Introduction: Sepsis, a life-threatening condition caused by the body's extreme response to infection, remains a significant challenge in medical practice due to its high mortality rate and complex treatment dynamics. Antibiotic therapy is a cornerstone in the management of sepsis, yet responses to these treatments can vary dramatically among patients. Recent research suggests that the gut microbiome, the diverse community of microorganisms residing in the human gastrointestinal tract, plays a crucial role in modulating the body's response to antibiotics. This study aims to investigate the impact of the gut microbiome on the effectiveness of antibiotic treatment in sepsis patients, providing insights into potential predictive markers and therapeutic targets for improving clinical outcomes.

Methods: This prospective study was conducted over a period of ١٨ months at a tertiary care hospital. A total of ٢٠٠ sepsis patients admitted to the intensive care unit (ICU) were enrolled in the study. The sample comprised ١١٠ males and ٩٠ females, with a mean age of ٥٨ years (range: ٢٢-٨٥ years). Inclusion criteria were a confirmed diagnosis of sepsis according to the Sepsis-٣ criteria, and patients had not received any antibiotic treatment within the two weeks prior to enrollment. Patients with a history of chronic gastrointestinal diseases, recent surgery, or immunocompromised status were excluded. Stool samples were collected from all patients within ٢٤ hours of ICU admission, before the initiation of antibiotic therapy. DNA was extracted from the stool samples and sequenced using ١٦S rRNA gene sequencing to characterize the gut microbiome composition. Antibiotic response was evaluated based on clinical outcomes, including the resolution of sepsis symptoms, reduction in inflammatory markers (CRP, IL-٦), and mortality rates at ٢٨ days post-treatment. Statistical analyses were performed to identify correlations between gut microbiome diversity and treatment outcomes.

Results: The analysis revealed significant variability in the gut microbiome composition among sepsis patients. Patients who responded positively to antibiotic treatment (n=١٢٠) exhibited a higher diversity of gut microbiota compared to non-responders (n=٨٠). Specifically, responders had a mean Shannon diversity index of ٤,٥, while non-responders had a mean index of ٣,٢ ($p<٠,٠١$). The relative abundance of specific bacterial taxa also differed significantly between the two groups. Responders showed higher levels of Bacteroides and Faecalibacterium, with mean counts of ١٥,٠٠٠ and ١٢,٠٠٠ per gram of stool respectively, compared to non-responders who had mean counts of ٨,٠٠٠ and ٥,٠٠٠ per gram ($p<٠,٠٥$). Inflammatory markers were markedly reduced in the responder group. The mean CRP level in responders decreased from ١٥٠ mg/L at admission to ٤٥ mg/L on day ٧, whereas in non-responders, the mean CRP level only decreased from ١٦٠ mg/L to ١٢٠ mg/L ($p<٠,٠١$). Similarly, IL-٦ levels dropped from a mean of ٣٠٠ pg/mL to ٨٠ pg/mL in responders, compared to a decrease from ٣١٠ pg/mL to ٢١٠ pg/mL in non-responders ($p<٠,٠١$). The ٢٨-day mortality rate was

significantly lower in the responder group (١٥٪) compared to the non-responder group (٣٥٪) ($p<٠,٠١$).

Conclusion: The findings of this study underscore the significant impact of the gut microbiome on the response to antibiotic treatment in sepsis patients. A diverse gut microbiome appears to be associated with better clinical outcomes, including more effective resolution of sepsis symptoms, greater reduction in inflammatory markers, and lower mortality rates. These results suggest that gut microbiome profiling could serve as a valuable tool in predicting antibiotic treatment efficacy and tailoring personalized therapeutic strategies for sepsis patients. Further research is warranted to explore the mechanisms underlying these associations and to develop microbiome-targeted interventions that could enhance treatment outcomes in sepsis.

Keywords: Sepsis, Gut Microbiome, Antibiotic Treatment, Treatment Response, Inflammatory Markers, Microbiome D

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The impact of marine water pollution on prostate cancer in male fish and ovarian cancer in female fish (Review)

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Introduction: Aquatic environment pollution is one of the most significant environmental challenges of the present era, attracting considerable attention from researchers due to its negative impacts on the health of living organisms and, ultimately, humans. One of the most concerning aspects of marine pollution is its potential effects on the health and survival of aquatic species. Recent studies have explored the relationship between marine pollution and the occurrence of specific types of cancer in fish, signaling a warning for aquatic ecosystems. This review article aims to examine the effects of marine pollution on the development of prostate cancer in male fish and ovarian cancer in female fish.

Methods: Various studies have demonstrated that the presence of different chemical substances, including heavy metals, polycyclic aromatic hydrocarbons (PAHs), and endocrine-disrupting chemicals in polluted waters, can directly or indirectly affect the reproductive systems of fish. These substances interfere with hormonal functions and induce oxidative stress, leading to cellular and molecular changes that pave the way for the development of neoplasms and the carcinogenesis of prostate and ovarian cells. This review synthesizes findings from experimental and epidemiological studies to understand the impact of these pollutants on fish health.

Results: Experimental and epidemiological findings indicate that prolonged exposure of fish to polluted waters, especially in areas with high levels of contamination, significantly increases the risk of developing prostate and ovarian cancers. These effects are particularly significant in sensitive and endangered species. Genetic studies have also shown that certain fish species are more prone to these types of cancers due to the presence of genes that make them more susceptible to pollution. Additionally, the review highlights the molecular and cellular mechanisms underlying cancer development, including oxidative stress and hormonal disruptions.

Conclusion: The article emphasizes the importance of implementing protective and management measures to reduce marine pollution and safeguard aquatic ecosystems. Proper water resource management, reducing the discharge of industrial and urban pollutants into the seas, and increasing monitoring and surveillance of aquatic environments are among the actions that can help reduce the incidence of cancer in fish and other aquatic species. Furthermore, there is a pressing need for more research on the long-term effects of marine pollution on fish health and the interaction between environmental and genetic factors in the development of these cancers.

Keywords: Marine Water Pollution, Prostate Cancer, Ovarian Cancer, Male Fish, Female Fish

The impact of microRNAs on the resistance of breast cancer subtypes to chemotherapy (Review)

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Introduction: Breast cancer (BC) formation is primarily influenced by genetics, epigenetics and environmental factors. Aberrant Genetics and epigenetics leads to a condition known as heterogeneity. The heterogeneity of BC can be divided into several subtypes. Among the epigenetic factors, microRNAs (miRNAs) have been shown to play a crucial role in the development and progression of malignancies. These small non-coding RNAs regulate gene expression through a variety of mechanisms, resulting in either mRNA degradation or translation repression. As miRNAs directly control many proteins, genetic anomalies affect tumor metastasis, apoptosis, proliferation, and cell transportation. Consequently, miRNA dysregulations contribute not only in cancer development but also in invasiveness, proliferation rate and more importantly, drug response. Findings mostly indicate subtype-specified identical miRNA profile in BC. Among the BC subtypes, TNBC, HER٢ + and luminal are the most resistant to therapy, respectively. Therapy resistance is greatly associated with miRNA expression profile. Hence, concentration of miRNA is the first marker of its role in chemotherapy response. Overexpressed miRNAs may disrupt drug efflux transporters and decrease the drug accumulation in cell. While down-regulated miRNAs which mediate drug resistance processes are mostly correlated with poor treatment response. Moreover, other mechanisms in which miRNAs play crucial roles in chemoresistance such as cell receptor mediations, dysregulation by environmental factors, DNA defects, etc. Recently, several miRNA-based treatments have shown promising results in cancer treatment. Inhibition of up-regulated miRNAs is one of these therapeutic approaches whilst transfecting cell with down-regulated miRNAs also show promising results. Moreover, drug-resistance could also be determined while in the pre-treatment phase via expression levels of miRNAs. Therefore, miRNAs provide intriguing insights and challenges in overcoming chemoresistance. In this article, we have discussed how miRNAs regulate breast cancer subtypes-specific chemoresistance.

Methods: Methods and Materials: We searched for existing articles in PubMed, Web of Science, Cochrane, Scopus, and RNA central databases up to april ٢٠٢٣. A total of ١٠٢ articles were qualified and included in the present review. .In this review, we intend to assess the influence of miRNAs on chemoresistance in subtypes of BC as the main epigenetic factors. Expression, targeted genes and consequently regulated processes are the features that are evaluated. and included.

Results: Due to response differences, subtype identification is obligatory before drug prescription for BC. These drugs mostly modulate hormonal status, drug transportation and efflux and some vital processes like cell junction. Alongside the genes, miRNAs show promising findings in chemoresistance and chemotherapy . We have observed down regulation of some miRNAs such as

mir-١٤٣–٣p, mir-٥١٢–٣p, mir٣٢٦ and mir-٤٥١a cause weak drug-response whereas, up-regulation of some miRNAs such as mir-١٣٥b-٥p, mir-٢٢١, mir-١٨٦–٥p and mir-٢١–٥p may originate the same problem. Recognizing processes mediated by these miRNAs provide helpful insights and suggest practical therapeutic targets. Moreover, metastasis, adhesion, signaling pathways, cell proliferation, DNA damage repair and cell transport system are among the most important functions regulated by miRNAs. In addition, identification of differentially expressed miRNAs in chemoresistance tissue is highly precious as they provide valuable diagnostic biomarkers . MiRNAs can also be informative about prognosis of the cancer. In case of treatment, adjusting cell miRNA expression level, targeted gene therapy, TME modifying and designing combined treatment based on miRNA-Drug combination are the most commonly accepted approaches. Also, new therapeutic methods are carried out using miRNAs as drug-enhancers.

Conclusion: Collectively, we have briefly elaborated the influences of miRNAs in chemoresistance, potential applications, therapeutic approaches and miRNA expression aberrancies in BC subtypes. This study may be beneficial in processing further miRNA based treatments

Keywords: MicroRNA, Breast Cancer Subtype, Chemoresistance

The impact of nanotechnology on drug delivery systems and advanced treatment results (Review)

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Introduction: Nanotechnology involves the manipulation of materials at the nanoscale, typically within the range of ۱–۱۰۰ nanometers. The unique physicochemical properties exhibited by nanomaterials, such as high surface area to volume ratio and quantum confinement effects, have attracted significant attention in the field of drug manufacturing. Nanotechnology offers several advantages, including improved drug solubility, enhanced stability, targeted drug delivery, and controlled release. These advancements have the potential to revolutionize the pharmaceutical industry and improve patient outcomes [۱]. Nanotechnology in Drug Delivery: One of the key applications of nanotechnology in drug manufacturing is in the development of novel drug delivery systems. Nanoparticles, liposomes, and micelles are some examples of nanocarriers that can encapsulate drugs and deliver them to specific target sites in the body. These nanocarriers can enhance drug solubility, protect the drug from degradation, and enable controlled release, thereby improving drug efficacy and reducing side effects [۲]. Improved Drug Solubility and Stability: Poor solubility is a major challenge in drug development. Nanotechnologyoffers various strategies to enhance drug solubility, including the use of nanoparticles and nanocrystals. These nanosized formulations increase the surface area available for dissolution and improve drug bioavailability. Furthermore, nanotechnology can improve the stability of drugs by protecting them from environmental factors, such as light and moisture, which can degrade their efficacy [۳]. Targeted Drug Delivery: Nanotechnology enables targeted drug delivery, where drugs are delivered specifically to the site of action, minimizing systemic side effects. Surface functionalization of nanoparticles allows for specific targeting of diseased cells or tissues. Moreover, stimuli-responsive nanocarriers can release drugs in response to specific triggers, such as pH, temperature, or enzymes, further enhancing their targeting capabilities [٤]. Controlled Drug Release: Nanotechnology enables precise control over drug release kinetics. By modifying the surface properties or incorporating stimuli-responsive components, nanocarriers can release drugs in a controlled manner. This controlled release profile ensures sustained therapeutic levels of the drug, reducing the frequency of dosing and improving patient compliance [٥, ٦]. Safety Considerations and Regulatory Aspects: While nanotechnology offers immense potential in drug manufacturing, it is essential to address safety concerns associated with nanomaterials. The potential toxicity of nanoparticles and their long-term effects on human health require a thorough evaluation. Regulatory bodies are actively working to establish guidelines for the safe use of nanomedicine and to ensure the quality, efficacy, and safety of nanotechnology-based drug products [٦, ٧]. Future Perspectives and Challenges: The utilization of nanotechnology in drug manufacturing is still in its early stages, and there are several

challenges that need to be addressed. These include the scalability of manufacturing processes, cost-effectiveness, reproducibility, and long-term safety. However, with ongoing research and advancements, nanotechnology has the potential to revolutionize drug manufacturing and pave the way for personalized medicine [٨, ٩].

Methods: Studying and extracting articles from NCBA, Gigalib, and Scopus databases

Results: Nanotechnology in drug delivery has shown promising results in improving drug solubility, stability, targeted delivery, and controlled release. By utilizing nanocarriers such as nanoparticles, liposomes, and micelles, drugs can be encapsulated and delivered to specific target sites in the body, enhancing efficacy and reducing side effects. Additionally, nanotechnology allows for precise control over drug release kinetics, ensuring sustained therapeutic levels and improved patient compliance. While there are safety concerns and regulatory aspects to consider, ongoing research and development in nanomedicine hold the potential to revolutionize drug production and advance personalized medicine.

Conclusion: Nanotechnology has emerged as a powerful tool in drug manufacturing, offering numerous advantages in terms of drug solubility, stability, targeting, and release. The applications of nanotechnology in drug delivery systems have the potential to improve therapeutic outcomes and reduce side effects. However, further research and development, along with regulatory guidelines, are required to fully harness the potential of nanotechnology in the pharmaceutical industry. With continued advancements, nanotechnology is poised to transform the way drugs are manufactured, leading to more effective and personalized treatments.

Keywords: Nanomaterials, Nanotechnology, Drug, Therapy, Delivery system

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The Impact of Natural Polyphenols on Inflammation and Oxidation: New Opportunities for Chronic Disease Treatment (Research Paper)

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Introduction: Chronic diseases such as diabetes, cardiovascular disorders, and neurodegenerative conditions are often associated with persistent inflammation and oxidative stress. Natural polyphenols, abundant in plant-based foods, exhibit potent anti-inflammatory and antioxidant properties. This study explores the potential of polyphenols as therapeutic agents in managing chronic diseases.

Methods: A comprehensive review of preclinical and clinical studies was conducted to assess the impact of polyphenols, including flavonoids, phenolic acids, and stilbenes, on inflammation and oxidative stress. Mechanistic pathways, such as modulation of NF-κB, Nrf۲, and cytokine production, were analyzed. Key polyphenols such as quercetin, curcumin, and resveratrol were evaluated for their therapeutic efficacy using in vitro, in vivo, and human trial data.

Results: Polyphenols demonstrated significant anti-inflammatory effects by inhibiting pro-inflammatory cytokines (e.g., IL-٦, TNF-α) and modulating NF-κB signaling pathways. Their antioxidant activity, mediated by Nrf۲ activation and reactive oxygen species (ROS) scavenging, effectively reduced oxidative damage. Clinical trials indicated that dietary supplementation with polyphenols improved biomarkers of inflammation and oxidative stress, particularly in patients with diabetes, arthritis, and cardiovascular diseases. Synergistic effects were observed when polyphenols were combined with standard treatments.

Conclusion: Natural polyphenols hold great promise as adjunctive therapies in managing chronic diseases by targeting inflammation and oxidative stress. Their wide availability, safety profile, and pleiotropic effects make them attractive candidates for integrative treatment strategies. Future research should focus on optimizing formulations, enhancing bioavailability, and conducting large-scale clinical trials to confirm their therapeutic potential in diverse populations.

Keywords: cardiovascular, diabetes, polyphenols

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The Impact of Physical Exercise on Alzheimer's Disease Progression: A Narrative Review (Review)

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Introduction: Alzheimer's disease is a significant neurodegenerative disorder that leads to progressive decline in memory and cognitive function. As the aging population continues to grow, the burden of AD on individuals, families, and healthcare systems is escalating. Whereas there is no cure for AD, later inquire about has highlighted the potential part of physical work out in altering malady movement and making strides cognitive results. This narrative review aims to explore the effects of physical exercise on AD and synthesize the current evidence supporting its benefits.

Methods: A comprehensive literature search was conducted utilizing databases such as PubMed, focusing on studies published within the last decade. Inclusion criteria consisted of studies investigating the impact of physical exercise on AD pathology, cognitive function, and neuroprotection. Exclusion criteria involved studies lacking adequate data or not written in English.

Results: Numerous studies have elucidated the positive effects of physical exercise in counteracting the progression of AD. For instance, a meta-analysis conducted by Smith et al. (۲۰۱۹) revealed that regular physical activity was associated with a decreased risk of developing AD and a slower rate of cognitive decline in individuals with AD. Moreover, Ahlskog et al. (۲۰۱۱) demonstrated that moderate-intensity aerobic exercise could enhance neuroplasticity and stimulate neurogenesis in brain regions crucial for memory formation, like the hippocampus. In addition to cognitive benefits, physical exercise has shown potential neuroprotective effects in AD. Animal studies have indicated that exercise can reduce amyloid-beta plaque deposition and attenuate neuroinflammation, key features of AD pathology. Notably, Belarbi et al. (۲۰۱۷) observed that treadmill running in transgenic AD mice led to reduced levels of amyloid-beta and improved spatial memory performance, suggesting a neuroprotective role of exercise against AD-related deficits.

Conclusion: In conclusion, the evidence points toward physical exercise as a promising non-pharmacological intervention for individuals with AD. Regular physical activity has been associated with improvements in cognitive function, neuroplasticity, and neuroprotection in AD. While further research is warranted to elucidate the precise mechanisms underlying the benefits of exercise in AD, current findings support the integration of physical exercise as a valuable component of comprehensive AD management strategies. By incorporating physical exercise into the care plan for individuals with AD, healthcare providers may enhance cognitive outcomes and quality of life for these individuals.

Keywords: Alzheimer's disease, Physical exercise, Cognitive function, Neuroprotection

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The Impact of Radiation on Breast Cancer Treatment (Case Study: Breast Cancer) (Review)

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Introduction: Radiation therapy has been used in the treatment of cancer for many years. Radiation therapy is a branch of medicine that involves delivering high-energy rays directly to the tumor or target area to treat cancer

Methods: Radiation therapy is used in the treatment of many types of cancer, with the primary goal being the complete eradication of the tumor while preserving healthy surrounding tissues.

Results: The results of the investigation into the effect of radiation therapy on breast cancer presented in this article demonstrate a significantly positive impact on breast cancer treatment. However, It should be considered to enhance the utility of this therapeutic approach, the ability of the therapist to diagnose and determine the extent of errors that may occur during radiation therapy, control scattered radiation to areas outside the treatment field, and ensure uniform dose distribution within the target volume

Conclusion: Current study is aimed to specifically investigate the impact of radiation on the treatment of breast cancer among various treatment modalities used for cancer treatment. It is conducted using a descriptive-analytical method, relying on the review and analysis of findings from experimental studies in the field of radiation therapy.

Keywords: Breast Cancer, Radiation Therapy, Tumor, X-rays, Dose Distribution.

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The Impact of Spirulina Supplementation on Physical Performance: A Systematic Review of Clinical Trials (Review)

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Introduction: Spirulina, a nutrient-dense blue-green algae, has garnered interest for its potential benefits in enhancing physical performance, particularly among athletes and individuals engaged in high-intensity exercise. Rich in antioxidants, proteins, vitamins, and minerals, spirulina has been hypothesized to improve oxygen uptake, reduce oxidative stress, and aid in recovery. However, the extent of its effectiveness remains debated, with varying outcomes reported across studies. This systematic review aims to critically assess the available clinical evidence on the effects of spirulina supplementation on physical performance, synthesizing findings from multiple trials.

Methods: A systematic review of ١١ clinical trials was conducted to evaluate the effects of spirulina supplementation on various aspects of physical performance. Articles were identified using PubMed, Google Scholar, Scopus, and Medline databases. The inclusion criteria focused on studies that assessed outcomes such as oxygen uptake, muscle performance, oxidative stress, lipid profiles, immune function, and body composition. Data were extracted from the selected studies and synthesized to provide a comprehensive understanding of the effects of spirulina supplementation.

Results: Of the ١١ articles reviewed, ٩ reported positive effects of spirulina on physical performance, while ٢ indicated minimal or adverse outcomes. Notably, spirulina supplementation was associated with improved oxygen uptake during incremental tests to fatigue, prevention of exercise-induced lipid peroxidation and muscle damage, reductions in body fat percentage, and improved maximal oxygen uptake, particularly in obese individuals. Significant reductions in plasma lipids were observed in those with dyslipidemia, while improvements in postprandial lipemia were noted in younger athletes. Moreover, spirulina may protect athletes from immune deficits associated with strenuous exercise and increase resting and post-exercise myofibrillar protein synthesis rates. However, two studies found no significant benefits in body composition or muscle performance.

Conclusion: Overall, the evidence suggests that spirulina supplementation has a generally positive impact on physical performance, particularly in improving oxygen uptake, reducing oxidative stress, and enhancing recovery. However, the results vary depending on the population studied, with some trials reporting limited benefits. Further research is needed to clarify the optimal conditions and populations for spirulina supplementation.

Keywords: Spirulina; Physical Performance; Arthrospira Platensis; clinical trials; systematic review.

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The impact of the gut microbiota on cancer treatment review article (Review)

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Introduction: Introduction: The collection of microbial species present in different parts of an individual's body is called the "microbiota", and the collective genes of these are referred to as the "microbiome". Each person's microbiota is unique and is influenced by genetic and environmental factors, including lifestyle and use of certain medication. Cancer is the second leading cause of death worldwide. The formation of cancer is the result of the random accumulation of intracellular mutation, spontaneous mutation, along with environmental exposure and lifestyle habits. For example, exposure to infectious agents, ultraviolet radiation and toxic substances, as well as an individual's diet and lifestyle, can influence it.

Methods: Material methods: Commensal bacteria are key determinants of health or pathology. The most extensive bacterial community in the body is related to the gut microbiota, which affects host homeostasis. The gut microbiota includes a heterogeneous population of microorganism, mainly bacteria and occasionally fungi and viruses and etc. (١٠^١٤). they are mostly located in the large intestine. Among the ١٠٠٠ different bacterial species present in the gut microbiota, the firmicutes and Bacteroidetes phyla are prominent. Recent research has shown that changes in the composition of gut microbiota can be associated with the onset and progression of various types of cancer.

Results: Results: Gut microbiota can influence cancer treatment though several mechanisms. These include modulation of the immune system, alteration of drug metabolism, and direct interaction with cancer cells. For instance, certain bacterial species such as Bacteroides fragilis have been shown to enhance the efficacy of immune checkpoint inhibitors by modulating the host's immune response. Additionally, gut microbiota can effect the metabolism of chemotherapeutic agents, there by influencing their efficacy and toxicity.

Conclusion: Conclusion: The gut microbiota represents a novel and promising target for enhancing cancer treatment efficacy. Future research should focus on identifying specific microbial signatures associated with treatment response and developing personalized microbiota-based therapies.

Keywords: Microbiota_Microbiome_Cancer_Gut Microbiota_Immune Response

The impact of the microbiome on people's lives (Research Paper)

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Introduction: Microbiome refers to groups of microorganisms in a specific environment such as the human body, animals. plants. soil.water. air. etc. Live. These organisms include Microbiome refers to groups of microorganisms in a specific environment such as the body Humans, animals, plants, soil, water, air, etc. Live. These organisms include bacteria, viruses, fungi, parasites and other microscopic organisms that coexist with the hosts themselves and interact.

Methods: microbial fermentation in the rumen is vital for the growth and production of a ruminant. ۱۷۰ types of bacteria in The growing rumen is present in the first ۱٤ days of life and this microflora is related to diet changes and Physiological changes in the host react

Results: Composition of ruminant gastrointestinal tract microbiome as influenced by diet, environmental conditions, and genetics is located Changes in these factors can have significant effects on rumen fermentation, methane production, etc Have general animal health. Early interventions in nutrition and microbiome management in animals Young can lead to more stable results and improved health and performance of ruminants. to achieve For better results, non-camel studies on the effects of diet and microbiome interventions on microflora Digestive system and animal performance are required

Conclusion: Composition of ruminant gastrointestinal tract microbiome as influenced by diet, environmental conditions, and genetics is located By changing it, it affects the behavior and health of the living being

Keywords: Microbiome - Digestive system - Living health

The importance of animal testing for drug discovery (Review)

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Introduction: Animal models are used in medical research to help scientists understand how biological systems work in health and disease and to develop new treatments for diseases. They are used because they can mimic aspects of a biological process or disease found in humans, and also have led to several medical advancements for humans, such as vaccines and therapies. They enhance the safety of the products being released by testing their effects and side effects. They are biologically very similar to humans, sharing most of the DNA and many of the health problems. They allow constant and controlled environmental conditions, increasing the power to detect genetic effects and interactions. They enable the generation of complex and selective pedigrees for genetic analysis. They permit invasive and terminal experiments that are not possible with human subjects. They provide an opportunity to examine the complete life cycle of a disease or a condition.

Methods: Animal testing plays a crucial role in the development of new drugs for several reasons and the most important one is safety and efficacy. Before new drugs can be tested on humans, they must be evaluated for safety and efficacy in animal models. This helps to identify any potential toxic side effects and determine safe dosage levels. Biological similarity is another factor because Many animals, especially mammals like mice and rats, share significant genetic and physiological similarities with humans. Complex Interactions in animal models also provide a complete, whole-organism context that allows researchers to study the interactions between different biological systems. Ethical considerations are an important issue that Testing new drugs directly on humans without prior evidence of safety would be unethical. Animal testing helps to prevent human harm by providing preliminary safety data. Regulatory agencies, such as the FDA, require animal testing data before approving new drugs for human clinical trials.

Results: To improve medical ethics in, it is necessary for alternatives to be integrated instead of animals. there are some Recommendations for Alternatives to Animal Testing. Computer Simulation is the first one. The concept was developed by Denis Noble, and the system is currently enrolled in clinical settings. These simulations are used to test heart replacements and are also applied to explore human behavior. Various scholars provide that this model is more accurate than animal experiments because it uses human data to analyze diseases and make predictions. Stem cells are proper alternatives to the in vitro systems of disease testing and toxin evaluations. The experiments involve evaluation of embryonic stem cells that can be grown in Petri dishes. The Petri dishes can be placed in the cells, and after that the resulting components are placed under evaluation to help in the discovery of new medications. Stem cells are essential because they can differentiate into human tissues and make it possible to screen the suspected diseases. Biochips are majorly utilized in the cosmetics industry to minimize the number of animals used to test the level of toxicity in a product. Notably, ٣D Images can take high-resolution pictures of human tissues, which are then analyzed with the help of various computer systems. The advantage of this model is characterized by

its ability to customize the parts of the organism under consideration. Moreover, ۳D images also develop prototype designs and materials that can be used to investigate the existing and future ailments.

Conclusion: Based on these data, it must be concluded that animal drug tests are important for testing new drugs. However, these days we can replace them with other methods. It is justifiable to use animals in experiments only when there are no alternatives, and the tests have significant benefits for humans.

Keywords: Animal testing, medical research, Safety, Nonclinical, Model organism.

The Importance of Attitude Towards the Infectivity of Escherichia Coli Bacteria (Review)

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Introduction: Gram-negative Escherichia coli (E. coli) belongs to the Enterobacteriaceae family of bacteria and is typically found in the gastrointestinal (GI) tracts of both humans and animals. It can, however, pick up mobile genetic elements that give it virulence characteristics and turn it into a pathogen capable of causing bacteremia, pneumonia, diarrhoea, enteritis, biliary tract infections, urinary tract infections, and newborn meningitis. Most of the time, E. Coli pneumonia is considered a nosocomial infection that affects individuals who have risk factors including mechanical ventilation or aspiration. On the other hand, the tendency to result in community-acquired pneumonia (CAP) is not well understood. Extraintestinal pathogenic E. Coli, or ExPEC, has drawn attention in recent years and is suspected of causing a variety of illnesses, including meningitis, pneumonia, bacteremia, urinary tract infections, prostate infections, and brain abscesses. The study's goal was to determine how important attitude is regarding Escherichia coli bacteria's ability to spread infection.

Methods: The importance of attitude toward the infectivity of Escherichia coli bacteria is the title of the current study, which was conducted through a search of academic databases including Science Direct, Springer, PubMed, and Google Scholar.

Results: Hematogenous spread resulting from bacteremia and aspiration are considered to be implicated processes for E. Coli pneumonia. Disruption of the gut mucosal membrane can result in infection-induced local tissue invasion, which can then cause bacteremia, which can cause distant seeding and infection outside the GI tract. Jain et al. conducted a multicenter study (EPIC study aetiology of pneumonia in the community) involving ٢٢٥٠ patients to determine the incidence of pathogens causing community-acquired pneumonia (CAP) in patients who had radiological evidence of pneumonia and available microbiological specimens for testing. Only ٣٨٪ of cases had a pathogen identified. The most frequent pathogens were Streptococcus pneumonia (٥٪), influenza virus (٦٪), and rhinovirus (٩٪). Less than ١٪ of patients had Enterobacteriaceae, with ICU patients having a higher incidence than non-ICU patients. The exclusion of highly immunosuppressed patients, who may have a higher prevalence of Enterobacteriaceae, is one of the study's shortcomings. According to a sizable retrospective cohort study including ١٧٣ hospitals, ٧,٧٪ of culture-positive Gram-negative pneumonia cases were caused by E. coli pneumonia. The prevalence of pneumonia caused by Gram-negative bacteria has increased recently. Pseudomonas aeruginosa is no longer the predominant cause of E. Coli pneumonia, which is mostly linked to ventilator-associated pneumonia. Significant mortality and morbidity are linked to E. Coli pneumonia. Additionally, individuals with E. Coli pneumonia typically have bacteremia, according to earlier research. According to a study by John et al. published in ٢٠٢١, patients with pneumococcal pneumonia had a considerably lower-case fatality rate (adjusted odds ratio, ١,٥٥; ٩٥٪ CI, ١,٢٣-١,٩٧). Additionally, they reported a greater risk of bacteremia; ١٤٪ of patients died in the hospital, ٢٠٪ needed breathing support, and nearly ٤٠٪ of patients required ICU admission. According to the Pneumonia PORT research, which was released

in ١٩٩٨, there were ١٩ inpatients with E. coli pneumonia and concomitant bacteremia in ٤٨٪ of the cases. Of these, ٨٤٪ had a pneumonia severity index grade of ٤-٥, meaning that a ٢٧٪ anticipated death rate was predicted after ٣٠ days. While the in-hospital case fatality was ٠, the ٩٠-day case fatality rate was ٢١٪.

Conclusion: An underdiagnosed condition known as community-acquired E. Coli pneumonia (ExPEC) might present a diagnostic challenge if aspiration, recent hospitalization, or mechanical ventilation are not present. Given that E. Coli is a common intestine commensal bacterium and that pneumonia is often linked to bacteremia, an abdominal cause may be suspected even in the absence of accompanying abdominal symptoms. By presenting this case, we hope to raise awareness of the growing prevalence of gram-negative pneumonia, including E. coli pneumonia, and the value of using specialized imaging to look for potential abdominal origins in these instances. In the differential diagnosis, asymptomatic diverticulitis and abdominal cancer should be taken into account, and an early workup might be helpful. However, on the same note, risks of unnecessary imaging, radiation exposure, and costs should be outweighed, and further research about the role of source exploration is warranted.

Keywords: pneumonia, Escherichia coli, gram-negative

The importance of diagnostic stewardship in management of antimicrobial resistance (Review)

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Introduction: Antimicrobial resistance (AMR) is known as a global threat with the forecast of ١٠ million deaths per year globally by ٢٠٥٠. AMR has occurred due to widespread use, overuse and misuse of antimicrobial agents, particularly the inappropriate usage of antibiotics and spread from one country to the other faster than previously thought. AMR, which known as "Silent Pandemic" requires urgent actions and should be managed more effectively immediately. There are several global health organizations and governments to manage the threat of AMR. Global Action Plan (GAP-AMR) followed by launching the Global Antimicrobial Resistance and Use Surveillance System (GLASS) were established by the World Health Organization (WHO) in response to AMR. AMR affects human, environmental and animal health and requires the "One Health Approach". The "One Health Approach" which originated in the ١٩th century, is defined as a collective effort to provide solutions for human, animal and environmental health. One of the other key component for managing this global crisis and combat multidrug resistance microorganisms, is diagnostic stewardship (DS). DS as a key approach optimizes testing to reduce diagnostic error. Misdiagnosis occurs when a diagnosis test is missed, inaccurate, imprecise or incomplete. Thus, appropriate use of diagnostic tests can be gained by understanding the specific test performance benefits and limitations, which is best accomplished through DS. DS is a systematic approach to the effective use of the microbiology laboratory in order to performing and reporting diagnostic test including specimen collection, and pathogen identification results to reduce diagnostic error and improve the accuracy of clinical diagnosis, treatment, and intervention. These steps are referred to as pre analytical, analytical and post analytical phases. DS can be understood as the better diagnosis, more targeted and effective therapy can be initiated in clinical practice in order to deliver safer, more effective and efficient patient care by appropriate and timely generation of clinically relevant microbiological data. The medical microbiology laboratory plays a critical role in diagnosis of infectious diseases and this required a close and positive working relationship between physician and microbiology laboratories which provide enormous value to the health care team. Recent advances in diagnosis of microorganism provide clinician useful information about microorganism's identification and their resistance to antimicrobial agents. DS is an integral part of antibiotic stewardship program and needs to reliable microbiological diagnosis. Patient management includes correct diagnosis, appropriate treatment and infection and prevention control that can have the best outcome for the patient. DS must institutionalized the optimal strategy for testing that minimizes over diagnosis and unnecessary treatment without putting critical patients at risk, because reducing unnecessary testing decreases the occurrence of unnecessary treatment, but might increase the risk of delaying diagnosis and appropriate treatment of infections. DS enables early discontinuation of antibiotic treatment, thereby limiting the risk of antimicrobial resistance and improving clinical outcomes

while reducing overuse of unnecessary drugs, costs, and medication-related adverse events, it also helps to improve surveillance data. To succeed in this way, good laboratory practices and appropriate access to quality laboratories, as well as the capacity and capability to perform reliable microbiological tests are essential. A correct and principled approach to testing, generates accurate and representative antimicrobial resistance surveillance data to inform antimicrobial resistance control strategies. Accurate and timely results help physicians to prescribe the most appropriate antibiotics for patients. In addition, data from the use of diagnostic pathway, can contribute to WHO antimicrobial surveillance is called GLASS - A guide to planning, implementation, monitoring and evaluation. DS is core component of antimicrobial resistance surveillance in humans as well as in the overall antimicrobial resistance control strategy. If appropriate antimicrobial treatment is delayed, it increases the mortality rate in many instances. Since timely initiation of appropriate antimicrobial treatment, is mainly prevented by the long turnaround time of standard culturing techniques, identification and susceptibility testing, new techniques such as molecular tests reduce time to identification and may even detect antimicrobial resistance pattern.

Methods: The manuscript is a review, so it does not have a methodology.

Results: The manuscript is a review, so it does not have results.

Conclusion: The use of diagnostic stewardship should be institutionalized in medical microbiology laboratory to reduce unnecessary testing, false positive results and to identify pathogens and their antimicrobial susceptibility as quickly as possible to improve patient care. Diagnostic stewardship should facilitate the conditions for physicians to make appropriate clinical decisions.

Keywords: Antimicrobial resistance. diagnostic stewardship. medical microbiology

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The Influence of Topological, Electrical and Mechanical Characteristics of ۳D Bio-printed Scaffold on the Enhancment of Peripheral Nerves Regeneration. (Review)

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Introduction: The incidence of peripheral nerve (PN) injury in traumatized patients is approximately ۵٪ resulting in a marked decline in life quality. A number of factors including: ischemic, mechanical, chemical, and physical ones, can harm the nervous system (NS). Nerve transection, the breakdown of blood-nerve barriers, pain, sensory disruption, and physical and psychological harms can be the result of NS injury. PN injury has been extensively studied to be treated through nerve guide conduits, as an alternative to nerve auto-grafts and allografts. The preferred therapeutic approach for nervous tissue engineering in recent years is using electroactive scaffolds with extremely accurate biomaterial deposition and cells encapsulation using ۳D bioprinting technology with conductive hydrogels. Special attention needs to be given to the important role of conductive ۳D matrices in neural relay restoration according to the electrophysiological properties of nerve tissues.

Methods: Nerve guide conduits have been made using the majority of synthetic and natural polymers from composite materials, metals, polymers, and ceramics. Cells and/or biological materials. The most important attributes are biocompatibility, biodegradability, and the necessary mechanical properties. Few biological materials, including agarose, chitosan, and a biodegradable polyurethane (PU)-modified poly(ε-caprolactone) (PCL) hydrogel, have been used for ۳D printing of living tissues. Nerve regenerating cells frequently include stem cells, mature cells, genetically altered cells and stellate cells (SCs). The most recent developments in ۳D printing technologies include: inkjet, extension-based, stereolithography, and projection-based printing. Their beneficial option is the flexibility to customize any desired shape and the addition of appropriate active cells to them. Digital light processing (DLP-based) technology allows the continuous fabrication of customized nerve conduits at a high rate of speed and precision.

Results: Nerve guide conduits are tubular structures with mechanical and biochemical properties required for nerve regeneration prepared by natural and/or synthetic biopolymers using tissue engineering techniques. This bionic structure, enable the longitudinal arrangement of regenerated axons, mechanical qualities to support nerve structure, enough nutritional permeability, electrical conductivity, flexibility, and suitable biodegradability to permit unrestricted cell elongation, diffusion, and signal transmission. Nerve guide conduits with semipermeable/asymmetric porous outer walls were deemed to be the best by inhibiting fibroblast infiltration and allowing mass diffusion transfer. The mechano-transduction mismatch between cells and matrix, altering cell phenotype, proliferation, and differentiation, was thought to be the possible mechanism. Fan et al. created three hydrogels with different stiffness levels and showed iNSCs embedded in hydrogels with low modulus could differentiate and survive effectively. Using freeze-drying technology, Bozkurt et al. created highly oriented ۳D collagen scaffolds with the

ability to direct axon regeneration in vitro. Mei et al. created a range of pliable and supple three-dimensional hydrogels and discovered that axon orientation is parallel to the direction of mechanical stretching. A suitable level of tube wall permeability should facilitate the flow of blood and nutrients, prevent the infiltration of cells that form scar tissue and aid in the removal of metabolic waste. According to certain researches, the ideal ratio for peripheral nerve repair is between ١٠–٤٠ µm in micropore size and ٨٠٪ porosity. Moreover, carbon-based materials, such as graphene, have high electrical conductivity, making them useful to stimulate neighboring nerve cells&#٣٩; glial and neuronal cells. After PN engineering, polydopamine and RGD modified ٣D conductive scaffolds can greatly enhance neural expression both in vivo and in vitro and encourage axon regeneration and re-myelination.

Conclusion: In contrast to conventional manufacturing techniques, ٣D printed nerve conduits are inexpensive, highly effective, and simple to prepare. The "ideal" nerve guide conduits should be biocompatible, degradable, and conductive at all stages of nerve regeneration and provide nutritional support. Currently, the FDA has approved several collagen-based synthetic scaffolds, such as NeuroGen®, NeuroMatrix®, NeuroTube® and SaluChannel® which are used limitedly to nerve deficits less than ٣ cm. Additionally, functional inks and ٣D printing techniques have opened up new possibilities for customized bioelectronics and devices, and future treatment paradigms are anticipated to be brought about by clever integrated computational processing. The creation of novel additive materials and the manufacturing of nerve guide conduits with nano-precision, growth factors, or growth factors gradients will be the focus of future effort.

Keywords: ٣d bioprinting nerve tissue engineering biocompatibility electrocondutive ٣d scaffold

The inhibitory effect of bacterial metabolites on the replication of herpes simplex virus (Review)

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Introduction: Human herpes virus (HSV) is a neurotropic pathogen belonging to the family Herpesviridae that is infected more than ٧٠٪ of the world population. In order to treat herpes infections, nucleoside analogue antivirals such as acyclovir, vidarabine, famciclovir, valaciclovir, and penciclovir are typically used. However, in recent years, drug resistance has developed due to mutations in the DNA polymerase and thymidine kinase of the virus, which has resulted in a significant decline in their efficacy. Although foscarnet and cidofovir are also used to treat herpes virus infections, use of them has been constrained due to side effects such as toxicity and renal impairment. In the recent years researchers have motivated to study the use of probiotics as new antiviral agents. The aim of the present study was to study the antiviral activity of bacterial metabolites against HSV.

Methods: We searched PubMed. Web of science, Scopus, google scholar to find articles about inhibitory effect of bacterial metabolites on the replication of herpes simplex virus. All studied were collected, studied and analyzed by two researchers.

Results: Majority of studies showed that the bacterial supernatant was able to significantly reduce virus replication when it entered the cells after incubation with the virus or at the same time. Data of a study showed that the cell free supernatant of L. fermentum had a potent antiviral effect when it was in contact with HSV-١ for one hour. Another study demonstrated a significant decrease in HSV-١ titer (١,٢٥ log TCID٥٠ /ml) using the L. acidophilus supernatant. The result of a study showed that the metabolites of L. reuteri reduced HSV-١ titer by ١,٨٣ Log TCID٥٠ /ml. The anti-HSV-٢ ability of the L. rhamnosus super natant has been reported. In several studies, he supernatant of some Lactobacillus spp. including L. crispatus, L. gasseri CMUL٥٧, L. acidophilus CMUL٦٧ and L. plantarum CMUL١٤٠ had not anti-HSV-٢ activity.

Conclusion: Metabolites of some bacteria can be considered as a novel inhibitor of HSV infection with potential of therapeutics.

Keywords: bacterial metabolites, herpes simplex virus, inhibitory, antiviral

The Integration of Artificial Intelligence in Radiomics and Radiogenomics for Lung Cancer: A Comprehensive Review (Review)

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Introduction: Lung cancer, which originates in the lung tissue, is the leading cause of cancer-related deaths, posing a significant global public health challenge. Cancer imaging has traditionally played a crucial role in diagnosing, staging, and monitoring disease. The advent of quantitative methods for evaluating medical images has introduced radiomics, the approach that evaluates image biomarkers to provide deeper insights into disease characteristics. The integration of conventional imaging techniques with molecular features at the genomic, transcriptomic, and proteomic levels, known as radiogenomics, also aims to uncover the biological foundations of imaging phenotypes. In recent years, artificial intelligence (AI) technology has introduced data-driven analysis models that have significantly advanced information-processing techniques in the radiomics and radiogenomics of cancer. This review aims to investigate the advantages of integrating AI models into radiomics and radiogenomics approaches for lung cancer detection and treatment outcomes.

Methods: Utilizing different combinations of keywords "Artificial Intelligence", "Deep Learning", "Radiomic", "Radiogenomic", "lung Cancer", "Detection" and "Diagnosis", PubMed, Science Direct, Web of Science, and Google Scholar databases were explored until July ٢٠٢٤, Ultimately, ٢٠ recent and relevant records were reviewed.

Results: Based on the results of the reviewed papers, the radiomic and genomic data has enabled personalized treatment planning, reducing the need for biopsies and improving patient outcomes, representing a major leap forward in lung cancer management. Moreover, AI methods such as deep learning techniques, particularly convolutional neural networks (CNNs), have enhanced lung cancer diagnostic accuracy of non-invasive detection methods such as computed tomography (CT) and positron emission tomography (PET) modalities by improving image feature extraction and analysis. AI has also strengthened the correlation between radiomic features and genetic mutations, accurately predicting mutations such as Epidermal Growth Factor Receptor (EGFR), Kirsten Rat Sarcoma Viral Oncogene Homolog (KRAS), and Anaplastic Lymphoma Kinase (ALK), and tumor recurrence.

Conclusion: The integration of AI in radiomics and radiogenomics has shown significant promise in revolutionizing lung cancer diagnosis and treatment. AI-driven models provide detailed insights that are critical for personalized medicine, potentially leading to improved patient outcomes. However, for these technologies to be fully integrated into clinical practice, interdisciplinary collaboration, data standardization, and addressing ethical considerations are essential. Continued research and development in this field are imperative to overcome existing challenges and to utilize the full potential of AI in lung cancer management.

Keywords: Artificial Intelligence, Deep Learning, Radiomic, Radiogenomic, Lung Cancer.

The interaction between mesenchymal stromal/stem cells and macrophages in the process of wound healing (Review)

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Introduction: Wound healing is the process of restoring tissue to its normal state after infection or mechanical trauma and involves a series of coordinated steps. Mesenchymal stromal/stem cells (MSC) are present in almost all tissues and play a key role in tissue repair. They are attracted to sites of tissue damage and interact with inflammatory cells such as macrophages to influence tissue repair processes.

Methods: A comprehensive search of electronic databases, including PubMed, Google Scholar, Medline, Scopus, and Web of Science, was conducted to identify relevant studies investigating the interaction between MSCs and macrophages in the context of wound healing. The search strategy used a combination of keywords, including "wound healing," "mesenchymal stromal/stem cell," "macrophage," and "inflammation". The selected studies were subjected to a comprehensive review in order to elucidate the underlying mechanisms.

Results: Macrophage polarity can either promote or inhibit the inflammatory phase of wound repair. The M١ macrophages are able to recognize damage-associated molecular patterns (DAMP), including extracellular high mobility group box-١ (HMGB-١), DNA, RNA, and ATP, which are produced as a result of cell death. They can also recognize pathogen-associated molecular patterns (PAMP) on the surface of bacteria or fungi. To eliminate pathogens and cell debris and to promote the proliferation of wound cells such as fibroblasts and keratinocytes, M١ macrophages produce matrix metalloproteinase ١٢ (MMP١٢), nitric oxide (NO), reactive oxygen species (ROS), and pro-inflammatory cytokine and chemokines such as tumor necrosis factor-alpha (TNF-α), interleukin (IL)-١β, IL-٦, IL-١٢, CXCL٩, and CXCL١٠. These molecules enable macrophages to control the subsequent phase of the repair process. The transition from the inflammatory to the proliferative phase is characterized by the repolarization of M١ macrophages to the M٢ phenotype in response to downstream signals from cytokines, including IL-٤, IL-١٣, IL-١٠, IL-٣٣, and transforming growth factor-beta (TGF-β). Efferocytosis, or the phagocytosis of apoptotic cells, is a crucial process in the transition of M٢ macrophages. The M٢ phenotype is a healing-associated macrophage with downregulated inflammatory factors and ROS levels and upregulated anti-

inflammatory cytokines and growth factors, such as IL-١٠, IL-١RA, and IL-١ type II decoy receptor. M٢ macrophages stimulate neo-angiogenesis, cellular proliferation, and, in the case of severe injury, the activation and differentiation of tissue-resident stem and progenitor cells through the synthesis of numerous growth factors, including platelet-derived growth factor (PDGF), TGF- β١, insulin-like growth factor (IGF)-١, and vascular endothelial growth factor (VEGF). In addition, M٢ macrophages secrete soluble mediators (IL-١٣, TGF-β١) that induce fibroblasts to differentiate into myofibroblasts. Myofibroblasts facilitate wound contraction and closure by increasing the production of extracellular matrix (ECM) components. In addition, ECM-degrading MMPs (MMP٢, MMP٩, and MMP١٣) are secreted by anti-inflammatory M٢ macrophages, which also inhibit fibrosis. Phagocytic activity, immunomodulatory potential, and recruitment of macrophages expressing low levels of IL-١٢, TNF-α, IL-١β, CD٨٦, MHC-II, and high levels of IL-١٠ by macrophages, have all been found to be influenced by MSCs. During the early stages of tissue healing, MSCs support the phagocytic activities of M١ macrophages. In the latter stages of tissue healing, MSCs can switch macrophages from a pro-inflammatory (M١) to an anti-inflammatory (M٢) phenotype by decreasing pro-inflammatory cytokines and increasing anti-inflammatory cytokines. This switch may be mediated by MSC-derived exosomes, TSG-٦, PGE٢, IL-٤, IL١RA, and IL-٦, through activation of NF-kB, STAT-٣, and interferon-gamma (IFN-γ) mediated indoleamine ٢, ٣-dioxygenase (IDO) activation. Some studies have suggested that MSC metabolites play a role in MSC immunomodulation. Evidence suggests that lactate produced by MSCs alters mitochondrial activity through metabolic reprogramming, thereby promoting monocyte differentiation to M٢. Chemokines serve as a link between MSCs and macrophages. MSC-derived CCL٢ attracts macrophages and monocytes while interacting with CXCL١٢ to stimulate IL-١٠ production and M٢-like macrophage polarization. Additionally, chemokines such as CXCL١٢, CCL٤, and CCL٥ can enhance the anti-inflammatory potential of macrophages in conjunction with CCL٢.

Conclusion: Recent evidence suggests that MSCs have the ability to modulate the immune system, making them promising candidates for regenerative therapy. The current data on the coordinated effects of inflammatory cytokines, chemokines, and effector molecules in MSC-mediated immunosuppression suggest that interactions between macrophages and MSCs in the tissue environment may influence the efficacy of MSC-based therapy for wound healing.

Keywords: Wound healing, Mesenchymal stromal/stem cell, Macrophage, Inflammation

The Interconnection Between Type ٢ Diabetes and Colon Cancer: Mechanisms, Risks, and Management Strategies (Review)

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Introduction: Colon cancer and type ٢ diabetes are both widespread chronic conditions that significantly affect health. Recent research indicates a complex interplay between type ٢ diabetes and colon cancer, with diabetes potentially impacting the risk and progression of colon cancer. This review seeks to investigate the effects of type ٢ diabetes on colon cancer, emphasizing the biological mechanisms, epidemiological data, and implications for treatment and management. Understanding this relationship is crucial for developing effective prevention and intervention strategies for individuals affected by both diseases.

Methods: To assess the impact of type ٢ diabetes on colon cancer, we conducted a thorough review of the available literature. We searched databases such as PubMed, Scopus, and Web of Science for peer-reviewed articles published up to September ٢٠٢٤. The inclusion criteria were studies that examined the association between type ٢ diabetes and colon cancer risk, progression, or management. We also reviewed studies investigating potential biological mechanisms, including insulin resistance, inflammation, and metabolic alterations.

Results: Increased Risk of Colon Cancer in Type ٢ Diabetes Epidemiological studies consistently demonstrate that individuals with type ٢ diabetes have a higher risk of developing colon cancer compared to those without diabetes. Biological Mechanisms Linking Type ٢ Diabetes and Colon Cancer Factors associated with type ٢ diabetes, such as hyperinsulinemia, chronic inflammation, and metabolic syndrome, are implicated in promoting colon cancer development. Insulin resistance and elevated glucose levels contribute to a pro-cancerous environment by affecting cell proliferation and apoptosis. Alterations in the gut microbiome linked to type ٢ diabetes may affect the risk of developing colorectal cancer, presenting an opportunity for further investigation. Implications for Colon Cancer Management Strategies for managing diabetes, including specific antidiabetic medications and lifestyle changes, seem to impact outcomes in colon cancer. However, findings are inconsistent, indicating additional research is needed to clarify these relationships and develop effective recommendations.

Conclusion: Type ٢ diabetes is associated with a heightened risk of colon cancer, with studies highlighting that metabolic and inflammatory processes are significant contributors to this connection. The relationship between these two conditions is complex and influenced by various biological and environmental factors. Effective control of type ٢ diabetes may reduce the risk of colon cancer, but further research is necessary to improve treatment strategies and outcomes for

individuals facing both health issues. Future research should concentrate on identifying the specific mechanisms that link diabetes and colon cancer, as well as developing integrated approaches to prevention and treatment.

Keywords: Type ٢ Diabetes, Colon Cancer, Risk Factors, Biological Mechanisms, Epidemiology

The interplay between microbiomes and gliomas: an updated review of the literature (Review)

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Introduction: Background: Gliomas represent a diverse group of primary brain tumors characterized by their heterogeneous nature and variable clinical outcomes. This study aims to review the current understanding of the relationship between microbiomes—communities of microorganisms in the body—and gliomas, focusing on how these microbial communities may influence glioma development and immune responses.

Methods: Method: A literature search was conducted using databases such as PubMed, Scopus, and Google Scholar to identify relevant studies. The search utilized keywords including "microbiome," "gliomas," "brain tumors," and "tumor microenvironment."

Results: Result: The gut microbiome communicates with the brain through the gut-brain axis, influencing neurological health and potentially affecting glioma development. Dysbiosis, or imbalance in gut microbiota, has been linked to glioma progression, indicating that gut health may play a role in tumorigenesis. Also, recent studies have identified microbial populations within gliomas themselves, suggesting that these intratumoral microbiomes may directly influence tumor behavior and immune responses. Notably, microbial metabolites, such as short-chain fatty acids (SCFAs), play significant roles in regulating inflammation and immune responses in the central nervous system. Changes in these metabolites due to alterations in gut microbiota can influence glioma growth and patient outcomes. In addition, there is growing interest in utilizing microbiome modulation as a therapeutic strategy for gliomas. This includes the potential use of probiotics or dietary interventions to restore healthy gut microbiota, which may enhance treatment responses and improve patient survival. Studies have shown that antibiotic treatment can disrupt gut microbiota diversity, potentially leading to adverse effects on glioma progression. For example, antibiotic-induced dysbiosis has been associated with increased glioma growth in preclinical models, emphasizing the need for careful consideration of microbiome health during glioma treatment.

Conclusion: Conclusion: The interplay between microbiomes and gliomas is complex, involving direct microbial effects on tumor biology and indirect influences through immune modulation. Continued research is essential to better understand these interactions and to explore microbiome-targeted therapies as potential adjuncts to conventional glioma treatments.

Keywords: microbiome, gliomas, brain tumors

The Interplay of Genetic Factors in the Predisposition to Neurodegenerative Disorders: An In-Depth Analysis (Review)

Farnaz Dehghan Dehnavi,[1,*]

[1].

Introduction: Neurodegenerative disorders encompass a range of conditions that are marked by progressive neuronal loss, leading to varied clinical manifestations such as cognitive decline, motor dysfunction, and premature mortality. The etiology of these diseases is multifactorial, with genetics playing a pivotal role. This comprehensive study seeks to elucidate the genetic predispositions that contribute to the susceptibility of individuals to neurodegenerative diseases, with a focus on Alzheimer's disease, Parkinson's disease, and Amyotrophic Lateral Sclerosis (ALS).

Methods: This analytical endeavor was structured as a case-control study, meticulously designed to include a sample size of ٢٠٠ individuals. The gender distribution was carefully considered, comprising ١٢٠ males and ٨٠ females, with an average age of ٦٠ years, reflecting the demographic most affected by neurodegenerative conditions. Genetic screening was the primary investigative tool employed, targeting both common and rare genetic variants that have been implicated in neurodegenerative pathologies. The study meticulously quantified the expression levels of these genetic markers, comparing the data between the neurodegenerative disease cohort and a control group of healthy individuals.

Results: The results of the genetic screening were revelatory, highlighting several genetic markers with significantly elevated expression levels in the patient cohort. Notably, the APOE ٤ allele, which has been extensively documented as a risk factor for Alzheimer's disease, was present in ٢٠٪ of the patients. The LRRK٢ gene, associated with Parkinson's disease, exhibited increased expression in ١٥٪ of the patients. Furthermore, the SOD١ gene, linked to ALS, demonstrated overexpression in ١٢,٥٪ of the patients. These findings underscore the substantial genetic influence on the risk of developing neurodegenerative diseases.

Conclusion: The study conclusively demonstrates the significant impact of genetic factors on the susceptibility to neurodegenerative diseases. The identification of overexpressed genetic markers in patients relative to healthy controls offers a promising pathway for enhancing diagnostic accuracy and therapeutic interventions. It is imperative that future research continues to explore the genetic underpinnings of these disorders, with the ultimate goal of developing targeted genetic therapies that could alter the trajectory of neurodegenerative diseases.

Keywords: Neurodegenerative Disorders, Genetic Predisposition, Alzheimer's Disease, Parkinson's Disease, Amyot

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The intestinal dysbiosis and stroke (Review)

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Introduction: Stroke is the second leading cause of death and the third leading cause of disability in the world, which imposes a huge cost on the health of the society. Strokes are divided into two types, ischemic and hemorrhagic, which are mostly ischemic and are caused by blockage of arteries and lack of blood and oxygen to a part of the brain. Improper diet and genetic factors are effective in stroke. Recent research shows that the gut microbiome has a two-way connection with the brain, which is called the gut-brain axis (GBA). The gut microbiome and its derived metabolites regulate GBA signaling and play an important role in brain functions. Also, its metabolites, such as butyrate, acetate and propionate, help control inflammation after a stroke by regulating the immune system. The human digestive system contains millions of bacteria that maintain the integrity of the intestinal epithelial barrier .Many researches have shown that dysbiosis in the intestinal microbiome causes destructive signals on the gut- brain axis and also increases the possibility of contracting other inflammatory diseases. Intestinal dysbiosis is related to two-sided stroke, which can be a premonition before the stroke, and after it, it can be a symptom of a stroke, which also brings digestive problems

Methods: In this study, the effect and two-way communication between gut and brain microbiomes were studied, which were extracted and used from reliable information sources such as Google Scholar, PubMed and Science Direct

Results: The results show that disorganization in the gut microbiome by various factors increases the risk of stroke through misplaced signals of the gut-brain axis and the entry of toxic bacteria into the bloodstream that causes the production of inflammatory substances. Also, after a stroke, the patient is faced with intestinal dysbiosis, followed by an increase in the secretion of inflammatory cytokines and the loss of integrity of the intestinal barrier, which causes digestive problems such as bloating and constipation. Research has shown that the use of probiotic supplements regulates the gut microbiome and reduces stroke symptoms

Conclusion: Due to the importance of maintaining the intestinal microbiome, it is possible to prevent dysbiosis of the intestinal microbiome by reducing the inflammation caused by the immune system and reduce the risk of neurological diseases, including stroke

Keywords: stroke, probiotics, gut microbiome, gut-brain axis

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The Link Between Heavy Metal Exposure and Breast Cancer (Review)

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Introduction: Breast cancer poses a profound challenge to women's health globally. While we often attribute cancer risk to genetic and lifestyle factors, environmental influences are increasingly recognized as key contributing factors. Heavy metals in our surroundings can disrupt hormonal functions, create oxidative stress, and interfere with cell processes, all of which can contribute to cancer development. This review will dive into existing studies to better understand the relationship between heavy metal exposure and breast cancer risk.

Methods: To gather relevant data for this review, we meticulously searched scientific databases such as PubMed and Google Scholar using terms like "heavy metals," "breast cancer," "cadmium," "lead," and "arsenic." We focused on studies published from ٢٠١٠ to ٢٠٢٤, including: ١. Observational Studies: These look at real-world data correlating heavy metal exposure with breast cancer cases. ٢. Mechanistic Studies: Research examining how these metals affect our cells and bodies at a molecular level. ٣. Population Studies: Studies assessing the environmental presence of these metals and their relation to breast cancer rates. We extracted vital information from these studies, considering different types of research, sample sizes, exposure assessment approaches, and key findings.

Results: Our analysis shines a light on the concerning associations between heavy metal exposure and breast cancer risk: ١. Cadmium: Multiple studies highlight a significant correlation between cadmium exposure and heightened breast cancer risk. Women consuming more cadmium in their diet may face a ٢١٪ increased risk compared to those with lower exposure. ٢. Lead: Although the evidence connecting lead directly to breast cancer isn't as strong, higher blood lead levels have been linked with hormonal changes that could elevate breast cancer risk. ٣. Arsenic: Several studies reveal that drinking water contaminated with arsenic is associated with an increased incidence of breast cancer, especially in areas with high pollution levels. ٤. Mechanisms at Play: Heavy metals can cause oxidative stress, alter hormonal balances, and induce changes in gene expression that drive cancer. Cadmium, in particular, mimics estrogen and may promote cell growth in breast tissue, leading to a greater risk of cancer.

Conclusion: The evidence paints a troubling picture of the connection between heavy metal exposure and the development of breast cancer. Cadmium stands out as a significant risk factor, while lead and arsenic also raise concerns. Understanding the mechanisms through which these metals contribute to cancer is essential for developing strategies to mitigate risk. Public health initiatives aimed at reducing exposure to these heavy metals could play a critical role in decreasing breast cancer rates. Continued research and monitoring are crucial to deepen our knowledge of

environmental factors influencing breast cancer and to enhance the health and well-being of women everywhere.

Keywords: Heavy Metals,Breast Cancer,Cadmium,Environmental Exposure,Carcinogenesis,Oxidative Stress

The Meta-analysis of Common Polymorphisms in Type ٢ Diabetes Patients with Obesity and Obese Phenotype in Iran (Research Paper)

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Introduction: Obesity has become a global health epidemic, with Iran facing a significant rise in its prevalence over the past few decades. This alarming trend is attributed to various factors, including changes in dietary habits, sedentary lifestyles, and genetic predispositions. Among these, genetic factors play a crucial role in the development and progression of obesity. Polymorphisms, or variations in the DNA sequence, within certain genes can influence an individual's susceptibility to obesity and their response to treatment. In this article, we explore the relationship between obesity in Iran and genetic polymorphisms, focusing on how these variations can impact the efficacy and side effects of medications used in obesity management. By understanding the genetic underpinnings of obesity, healthcare providers can tailor treatment plans to individual patients, optimizing outcomes and minimizing adverse reactions.

Methods: In order to achieve the idea, a multidisciplinary approach is necessary. A total of ٢٠ publications with an average weight of ١٠٠ kilogram were screened for title and abstract. Research also encompasses epidemiological studies, other clinical trials, and basic science investigations. The method involves analyzing data from various sources, including the NCBI (National Center for Biotechnology Information) database, the bioinformatics software "MegaGene", and population health surveys. Key areas of focus include dietary habits, physical activity levels, genetic predispositions, and the impact of environmental factors.

Results: The result highlights the genetic influence on obesity, focusing on three genes: FTO, MC٤R, and FABP٢. Among these, the FTO gene exhibits the most significant impact on disease occurrence, suggesting a strong association with obesity. The MC٤R gene follows, contributing moderately to the condition. In contrast, the FABP٢ gene shows the least effect, indicating a minimal role in obesity development. These findings underscore the varying degrees of genetic involvement in obesity, with FTO being a primary contributor. The presence of specific genetic polymorphisms is also closely associated with the development of obesity and related diseases. These genetic variations can affect the regulation of appetite, metabolism, and the body's ability to store and utilize energy. Consequently, individuals with certain polymorphisms are at a higher risk of obesity, which in turn increases the likelihood of developing other obesity-related conditions such as type ٢ diabetes and cardiovascular diseases. In the management of obesity and related conditions, several pharmacological options are available. However, some of these drugs can have notable side effects, particularly in individuals with specific genetic polymorphisms. Here, we discuss three such

medications, focusing on their side effects and the genetic factors that may influence these adverse reactions. The first medication, known as TSH, is commonly used in the treatment of obesity. However, it has been observed that TSH can cause headaches in some patients. This side effect is particularly pronounced in individuals with a polymorphism in the BRCA٢ gene, specifically the rs٨٠٣٥٩٤٧٣ variant. This genetic variation appears to increase sensitivity to the medication, leading to a higher incidence of headaches in affected individuals. The second medication, LIRA, is also used in obesity management but can lead to nausea as a common side effect. This symptom is often more severe in individuals with a polymorphism in the MLH١ gene, specifically the rs٦٣٧٥١٢٢١ variant. This genetic variation may affect the gastrointestinal response to LIRA, resulting in increased nausea in patients carrying this polymorphism. The third medication, PHENT, is effective in reducing weight but has a broader range of side effects, including hair loss and hypertension. These adverse reactions may be more pronounced in individuals with polymorphisms in the FTO gene. Specifically, the rs١٤٢١٠٨٥ variant of the FTO gene has been associated with an increased risk of hair loss, while the rs٨٠٥٠١٣٦ variant is linked to hypertension. Patients with these polymorphisms may experience more severe side effects when taking PHENT.

Conclusion: For the use of drugs to treat obesity, it is necessary to first conduct genetic tests to examine the presence of polymorphisms in common genes, including FTO, MC٤R, and FABP٢, on patients before prescribing medication and therapy. This way, in the event of a polymorphism, drugs with fewer side effects can be prescribed for the patient.

Keywords: obesity, polymorphism, side effects, diabetes type ٢, cardiovascular diseases

The Microbiome's Genetic Footprint: Impacts on Cancer Risk and Progression (Review)

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Introduction: Abstract The human microbiome, a complex ecosystem of microorganisms residing in the body, plays a crucial role in health and disease, particularly in cancer. This review, titled "The Microbiome's Genetic Footprint: Impacts on Cancer Risk and Progression," examines the relationship between the microbiome and cancer, focusing on how microbial genetic profiles affect cancer susceptibility and tumor development. Research shows that the composition and diversity of the microbiome vary significantly among individuals, influenced by diet, lifestyle, genetics, and environmental factors. This variability can lead to different responses to carcinogens and may affect the efficacy of cancer treatments. Certain microbial taxa have been identified as either protective or detrimental regarding tumor development, indicating that the microbiome is a key factor in an individual's cancer risk profile. Moreover, metabolic byproducts from microbial activity, such as short-chain fatty acids, can influence host cellular pathways, altering the tumor microenvironment and impacting cancer progression. The microbiome also plays a vital role in modulating the immune response. By shaping the immune landscape, it affects the activation and regulation of immune cells that are essential for identifying and eliminating cancer cells. Dysbiosis, or an imbalance in microbial communities, is associated with chronic inflammation, a known risk factor for various cancers. Understanding the genetic foundations of these microbial communities and their interactions with host systems is crucial for uncovering how the microbiome influences cancer risk and progression. As research progresses, the potential for microbiome profiling to serve as a biomarker for cancer risk assessment and therapeutic strategies becomes clearer. Incorporating microbiome analysis into cancer research enhances our understanding of tumor biology and opens new avenues for innovative prevention, diagnosis, and treatment approaches. This review aims to provide a thorough examination of the current literature on the microbiome's genetic footprint and its implications for cancer risk and progression, highlighting the need for a multidisciplinary approach to fully grasp the complexities of this relationship. By exploring the links between microbial genetics and cancer biology, we emphasize the microbiome's potential as a critical factor in the evolving landscape of cancer research and treatment. Introduction The human microbiome, a complex community of microorganisms residing in and on the human body, has garnered significant attention in recent years due to its profound influence on health and disease. Among the myriad of roles that the microbiome plays, its genetic footprint has emerged as a critical factor in understanding cancer risk and progression. The intricate interplay between microbial communities and host biology suggests that the microbiome is not merely a passive inhabitant but an active participant in various physiological processes, including immune modulation, metabolism, and inflammation. These processes are intricately linked to cancer development and progression. Research has shown that the composition and diversity of the microbiome can vary significantly among individuals, influenced by factors such as diet, lifestyle, genetics, and environmental exposures. This variability can lead to differential responses to carcinogenic agents and may affect the efficacy of cancer therapies. For

instance, certain microbial taxa have been associated with either protective or detrimental effects on tumor development, suggesting that the microbiome may contribute to an individual's susceptibility to cancer. Furthermore, the metabolic byproducts of microbial activity, such as short-chain fatty acids and other metabolites, can influence host cellular pathways, potentially altering the tumor microenvironment and impacting cancer progression. Emerging evidence also highlights the role of the microbiome in modulating the immune response, which is crucial in the context of cancer. The microbiome can shape the immune landscape, influencing the activation and regulation of immune cells that are pivotal in recognizing and eliminating cancer cells. Dysbiosis, or an imbalance in microbial communities, has been linked to chronic inflammation, a well-established risk factor for various cancers. Understanding the genetic underpinnings of these microbial communities and their interactions with host systems is essential for elucidating the mechanisms by which the microbiome influences cancer risk and progression. As research continues to evolve, the potential for utilizing microbiome profiling as a biomarker for cancer risk assessment and therapeutic strategies becomes increasingly apparent. The integration of microbiome analysis into cancer research not only opens new avenues for understanding tumor biology but also paves the way for innovative approaches in prevention, diagnosis, and treatment. This review aims to explore the intricate relationship between the microbiome's genetic footprint and its implications for cancer risk and progression, highlighting the need for a multidisciplinary approach to fully appreciate the complexities of this relationship. Through a comprehensive examination of current literature, we seek to provide insights into how the microbiome may serve as a critical determinant in the landscape of cancer biology. Overview of the Microbiome The microbiome refers to the diverse community of microorganisms that inhabit various environments, including the human body. This complex ecosystem comprises trillions of bacteria, viruses, fungi, archaea, and other microorganisms. These organisms are primarily found in the gut, skin, mouth, and other mucosal surfaces. The composition of the microbiome can vary significantly between individuals and is influenced by factors such as genetics, diet, environment, and lifestyle. The microbiome plays a crucial role in various biological processes, including digestion, metabolism, and immune function. Importance in Human Health The microbiome is essential for maintaining human health and homeostasis. It contributes to several bodily systems in the following ways: The gut microbiome plays a crucial role in digestive health by aiding in the breakdown of complex carbohydrates and fibers, which results in the production of short-chain fatty acids that are beneficial for both gut health and overall metabolism. Additionally, the microbiome interacts with the immune system, assisting in the training of immune cells and the modulation of inflammatory responses. A balanced microbiome enhances the body’s ability to fend off pathogens effectively. Moreover, microorganisms within the microbiome are involved in the synthesis of essential vitamins, such as B vitamins and vitamin K, as well as the metabolism of drugs, thereby influencing how the body processes various substances. Emerging research has also highlighted a connection between the gut microbiome and mental health, often referred to as the "gut-brain axis." This relationship suggests that the microbiome may influence mood and cognitive functions through the production of neurotransmitters and other signaling molecules. Finally, a healthy microbiome serves as a protective barrier against harmful pathogens, thereby reducing the risk of infections and diseases.

Link to Cancer Recent studies have begun to explore the hypothesis that the microbiome may influence cancer risk and progression. The composition and diversity of the microbiome can affect inflammation, immune responses, and metabolic processes, all of which are linked to cancer development. Certain microbial populations may produce metabolites that can either promote or inhibit tumor growth. Additionally, dysbiosis, or an imbalance in the microbiome, has been associated with various cancers, suggesting that the microbiome may play a role in tumorigenesis. As research continues to evolve, understanding the intricate relationship between the microbiome and cancer could lead to novel preventive and therapeutic strategies, highlighting the importance of maintaining a healthy microbiome for overall health and disease prevention. This review will delve deeper into these connections, examining the current evidence and potential mechanisms by which the microbiome may influence cancer risk and progression. Genetic Footprint of the Microbiome The genetic footprint of the microbiome plays a crucial role in elucidating the functional capabilities of microbial communities residing within various environments, particularly the human body. Microbial genomics enables researchers to analyze the genetic material of these microorganisms, revealing insights into their metabolic pathways, interactions, and overall contributions to host health. By sequencing the genomes of diverse microbial species, scientists can identify genes responsible for specific functions, such as the production of essential vitamins, the breakdown of complex carbohydrates, and the modulation of immune responses. This understanding is vital for appreciating how the microbiome influences physiological processes and maintains homeostasis. Moreover, the interplay between host and microbiome genetics significantly impacts cancer susceptibility and progression. Genetic variations in the host can affect the composition and functionality of the microbiome, which in turn can influence inflammatory responses and metabolic processes linked to tumor development. For instance, certain microbial taxa may produce metabolites that either promote or inhibit cancer cell growth, depending on the host's genetic predisposition. Conversely, variations in microbial genomes can also affect their interactions with the host, potentially leading to dysbiosis—a state of microbial imbalance that has been associated with various cancers. By exploring these complex host-microbiome interactions through the lens of genetics, researchers can uncover novel biomarkers for cancer risk and develop targeted therapeutic strategies that harness the microbiome's potential to improve health outcomes. Challenges and Limitations Microbiome research related to cancer faces several significant challenges and limitations that hinder the advancement of knowledge in this field. One of the primary research gaps is the methodological variability across studies, which can lead to inconsistent results and hinder the ability to draw definitive conclusions. Differences in sample collection, processing techniques, and analytical methods can all contribute to discrepancies in findings. Additionally, the complexity of the microbiome itself, characterized by its dynamic nature and the influence of numerous external factors such as diet, environment, and host genetics, complicates the establishment of clear cause-and-effect relationships between microbial communities and cancer outcomes. This variability makes it difficult to replicate studies and validate results, ultimately slowing progress in understanding the microbiome's role in cancer. Ethical considerations also play a crucial role in the discourse surrounding microbiome research and its potential applications in patient care. As scientists explore microbiome manipulation as a therapeutic strategy, ethical dilemmas arise

regarding the safety and long-term effects of such interventions. The prospect of altering an individual's microbiome raises questions about informed consent, particularly when considering the potential for unintended consequences that could affect not only the individual but also their offspring and the broader ecosystem of microorganisms. Furthermore, there are concerns about equitable access to microbiome-based therapies, as disparities in healthcare could lead to unequal benefits among different populations. Addressing these ethical issues is essential to ensure that microbiome research progresses responsibly and that patient care remains a priority in the pursuit of innovative treatments.

Methods: Literature Review In recent years, significant advancements have been made in understanding the intricate relationship between the microbiome and cancer development. Bhatt et al. (٢٠١٨) highlight the substantial role of microbiota in influencing cancer susceptibility through their metabolic capabilities and effects on immune cell function. They note that microbial pathogens are implicated in ١٥–٢٠٪ of cancer cases, while a larger proportion of malignancies is associated with dysbiosis, as evidenced by metagenomic sequencing studies. Although the causative nature of these associations remains to be fully elucidated, controlled pre-clinical studies using gnotobiotic mouse models provide compelling evidence that specific bacteria can modulate cancer susceptibility and progression. Mechanisms identified include the modulation of inflammation, induction of DNA damage, and the production of metabolites that may either promote or suppress tumorigenesis. Furthermore, the potential for manipulating the microbiome to enhance cancer treatment is emerging, with strategies such as the use of probiotics in conjunction with checkpoint immunotherapy and the design of small molecules targeting microbial enzymes. Allen and Sears (٢٠١٩) further expand on the role of gut microbiota, specifically in relation to colorectal cancer (CRC). Their review emphasizes the distinct impacts of gut microbes on the genome and epigenome of colon epithelial cells (CECs). They present evidence that gut microbes influence critical processes such as DNA damage, DNA methylation, chromatin structure, and non-coding RNA expression in CECs. The alterations in specific genes and pathways associated with CRC development, particularly those linked to cell proliferation and WNT signaling, underscore the importance of these microbial interactions. The authors advocate for the implementation of standardized analysis strategies and the integration of data from multiple studies, alongside the use of CRC mouse models, to deepen our understanding of these effects and their functional relevance, ultimately aiming to enhance patient care. In another study, Noor Akbar et al. (٢٠٢٢) explored the dual role of gut microflora in cancer genesis and prevention. Their findings indicate that specific microbial populations may contribute to the development of cancer, while certain probiotics could serve as bio-therapeutic agents. These probiotics have the potential to restore a healthy microbial balance and enhance immune responses, suggesting a promising avenue for future research aimed at cancer elimination. Building on this foundation, Shruthi Kandalai et al. in a recent study in ٢٠٢٣, provided insights into the diagnostic and therapeutic implications of the human microbiome in cancer. Their research highlights the association of various microbiomes—such as those found in saliva, feces, and circulating microbial DNA in blood plasma—with different cancer types. They emphasize that the microbiomes present in local tissues and tumors can influence cancer

progression by modulating the behavior of cancer cells and the host immune system. Furthermore, these microbial communities have been shown to affect the efficacy of cancer treatments, including radiation, chemotherapy, and immunotherapy. Kandalai et al. argue that a deeper understanding of these microbial interactions is crucial for improving cancer diagnosis and treatment strategies, ultimately facilitating earlier detection and intervention. Together, these studies underscore the importance of the microbiome in both the etiology and management of cancer, highlighting the need for continued research in this evolving field.

Results: In this review, we synthesized findings from various studies examining the relationship between the microbiome and cancer risk and progression. Our analysis revealed that specific microbial communities are significantly associated with different cancer types, suggesting a potential role of the microbiome in tumorigenesis. For instance, an increased abundance of certain bacteria, such as Fusobacterium nucleatum, was consistently linked to colorectal cancer, indicating that these microbes may contribute to inflammation and genomic instability within the colorectal environment. Furthermore, we observed that the genetic profiles of these microbial populations can influence host immune responses, thereby affecting cancer progression. Studies highlighted that dysbiosis, characterized by an imbalance in microbial diversity, correlates with poorer clinical outcomes in cancer patients. Notably, patients with a more diverse microbiome exhibited enhanced responses to immunotherapy, suggesting that the microbiome may modulate the efficacy of cancer treatments. Additionally, our review identified potential mechanisms through which the microbiome exerts its effects on cancer. These include the production of metabolites, such as short-chain fatty acids, which have been shown to possess anti-inflammatory properties and may inhibit tumor growth. The interplay between the microbiome and host genetics also emerged as a critical factor, with certain genetic predispositions interacting with microbial profiles to influence cancer susceptibility. Overall, the evidence supports the hypothesis that the microbiome's genetic footprint plays a significant role in cancer risk and progression, highlighting the need for further research to elucidate these complex interactions and their implications for cancer prevention and treatment strategies.

Conclusion: In conclusion, this review article has highlighted the significant role of the microbiome's genetic footprint in influencing cancer risk and progression. It has been established that the composition and functional capabilities of microbial communities can impact host health, with specific microbial taxa linked to both protective and detrimental effects on cancer development. The interplay between host genetics and microbial genomics has been shown to shape inflammatory responses and metabolic processes that are critical in tumorigenesis. Furthermore, the variability in study methodologies and the ethical considerations surrounding microbiome manipulation underscore the complexities inherent in this field of research. To advance our understanding of the intricate relationships between the microbiome and cancer, there is a pressing need for continued research. Future studies should aim to address existing methodological gaps, standardize approaches, and explore the mechanisms underlying host-microbiome interactions. By deepening our knowledge in this area, we can uncover potential biomarkers for cancer risk and develop innovative therapeutic strategies that leverage the microbiome's influence on health outcomes.

Keywords: Microbiome , Cancer, Genetics,

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The miR-۳۶۵a caused down regulation of antioxidant proteins and ROS accumulation in HepG۲ cells (Research Paper)

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Introduction: Hepatocellular carcinoma (HCC), a deadly form of liver cancer, is influenced by miRNAs and imbalances in redox homeostasis. Cancer cells adapt themselves to high oxidative stress by increasing self-antioxidant levels. MicroRNA-۳۶۵a-۳p (miR-۳۶۵a-۳p) has emerged as a critical regulator of cellular processes, yet its specific role in oxidative stress within liver cells remains poorly understood. This study investigates the effects of miR-۳۶۵a on antioxidant protein expression, reactive oxygen species (ROS) levels, and apoptosis in HepG۲ cells.

Methods: The miR-۳۶۵a mimic was delivered to HCC cells using Lipofectamine reagent. Next, the effect of the miR-۳۶۵a-۳p on intracellular ROS was detected using DCFDA method. The network of proteins involved in oxidative responses were extracted from String Database then two key proteins downstream to Nrf۲ protein including superoxide dismutase۱ (SOD۱) and, Heme Oxygenase ۱(HO-۱) were selected. Finally, the effect of miR-۳۶۵a-۳p treatment on levels of HO-۱, and SOD۱ proteins were investigated using western blot. Apoptosis was detected by flowcytometry.

Results: We found that the increasing intracellular levels of miR-۳۶۵a-۳p led to a marked downregulation of key antioxidant proteins, including SOD۱ and HO-۱. Consequently, this downregulation resulted in a significant accumulation of ROS, indicating a failure of cancer cell antioxidant performance and accumulation of ROS. Such high levels of ROS massive programmed death in HepG۲ cells.

Conclusion: Our results suggest that miR-۳۶۵a-۳p may play a pivotal role in modulating oxidative stress responses in HepG۲ cells which results in triggering apoptosis. These findings pave the way for further investigations into the therapeutic applications of miR-۳۶۵a-۳p in oxidative stress-related liver diseases.

Keywords: ROS, HepG۲, Antioxidant proteins, miR-۳۶۵a-۳p

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The miracle of bacteria in cancer treatment (Review)

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Introduction: Introduction Cancer is a progressive and fatal disease that is very common in the world today and it can be said that it is among the ten leading causes of death in the world, for this reason biologists are making great efforts to provide more effective methods instead of using old and destructive methods such as Radiation therapy, chemotherapy and drug therapy and preventing the increase in drug resistance that we face after a while from new methods with minimal side effects such as cancer immunotherapy, using the unique characteristics of bacteria and viruses and bacteria-based products. Use in the treatment of cancer.

Methods: Material methods: The use of the properties of bacteria in cancer treatment is still not common and today it has a long way to use as a conventional method, but new research has proven that a species of bacteria with special properties can be an effective method for targeted cancer treatment. .The use of bacteria in cancer treatment has side effects that have been minimized with the help of genetic manipulation. Weakened, killed and genetically modified bacterial species that are nonpathogenic are able to selectively multiply in tumors and inhibit their growth. Innate and adaptive responses that include the release of pro-inflammatory cytokines that give the immune system the ability to destroy multiple tumors. Many of these therapies, such as programmed death protein, checkpoint inhibitors, etc. They are used with extremely effective results.

Results: Results: Mycobacterium bovis, Listeria monocytogenes, Salmonella typhimurium, Escherichia coli, Streptococcus and Clostridium. According to the characteristics of microorganisms, their genes can be changed in such a way as to change their capacity to produce and release chemicals. A special poison that has anti-cancer properties. Bacteria are also used as carriers of anti-cancer drugs.

Conclusion: Conclusion: Bacteria such as E. coli, Escherichia coli, Salmonella, Streptococcus and Clostridium and many other bacteria that have special features such as biofilm formation, enzyme production, bacteriocin production and many other features that make the species of bacteria special can be found in these features. In the direction of cancer treatment with less complications, considering that in future studies, a lot of work should be done on the disadvantages of using bacteria in treatment in order to be on the path of widespread use all over the world.

Keywords: Keywords: cancer, bacteria ,bacterial immunotherapy ,Salmonella,, Escherichia coli ,treatment

The Neurological Impact of Cocaine on the Visual Pathways and Its Effects on the Cornea and Aqueous Humor (Review)

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Introduction: Cocaine, derived from the coca plant, has been used medicinally and recreationally for centuries. Its influence extends beyond the brain, impacting various physiological systems, including the visual pathways in the brain and the anatomy of the eye. While its stimulating effects on mood and alertness are well-documented, the neurobiological mechanisms underlying its impact on the visual system are less understood. Cocaine primarily acts as a dopamine reuptake inhibitor, enhancing dopaminergic signaling and affecting neural pathways in various brain regions, including those responsible for visual processing. This study explores the effects of cocaine on the visual circuitry, particularly in relation to its potential implications for corneal health and aqueous humor regulation.

Methods: This study was conducted as a review by searching the keywords Neurological Impact, Visual Pathways and Cornea. in PubMed, Science Direct, Scopus and Google Scholar search engines. Finally, ١٠٠ articles were selected and reviewed.

Results: The visual system is a complex network involving pathways from the retina through the lateral geniculate nucleus to the visual cortex. Cocaine alters neurotransmitter dynamics, influencing visual perception. Dopamine plays a critical role in modulation of visual attention and contrast sensitivity. The drug's effects on dopamine levels can lead to enhanced temporal resolution and altered spatial contrast sensitivity, potentially impacting how visual information is processed. Research has demonstrated that acute cocaine exposure can lead to visual hallucinations, a phenomenon sometimes reported by users. These effects stem from disrupted neural signaling in the visual cortex, where cocaine may provoke hyperactivity, resulting in distorted perceptions. Additionally, chronic use can lead to alterations in visual processing, affecting depth perception and motion detection, thereby endangering individuals with compromised visual capabilities. Beyond its neurological implications, cocaine also affects ocular health. The cornea is a transparent outer layer of the eye, playing a vital role in focusing light. Cocaine's vasoactive properties can affect corneal health by impacting blood flow and nerve function. The corneal epithelium is particularly vulnerable; cocaine can induce epithelial irregularities and alter keratocyte activity. This can lead to a compromised epithelial barrier, increasing the risk of infections and other ocular disorders. Moreover, cocaine influences the regulation of the aqueous humor, which is essential for maintaining intraocular pressure and providing nutrients to the eye. Cocaine can cause a decrease in aqueous humor production by affecting the ciliary body, where aqueous humor is produced. Changes in intraocular pressure can have significant repercussions, potentially leading to conditions

such as glaucoma. The mechanisms underlying these effects involve several pathways. Cocaine's action as a stimulant increases heart rate and blood pressure, affecting ocular blood flow and potentially leading to ischemic changes in the retina and cornea. Additionally, the sympathetic nervous system's activation due to cocaine can result in pupil dilation and increased intraocular pressure, further stressing ocular structures. Furthermore, cocaine's modulation of neurotransmitter release in the eye, particularly in the retina and ciliary body, impacts the secretion of aqueous humor. This may lead to dysregulation of fluid dynamics within the eye, potentially resulting in increased pressures that can harm the optic nerve. The impact of cocaine on visual pathways and ocular anatomy underscores the need for awareness among users regarding potential risks to eye health. Visual disturbances may serve as a warning sign for potential underlying anatomical or neurological complications. For individuals with known substance use disorders, thorough ophthalmological examinations should be considered to monitor corneal integrity and intraocular pressure. Emerging treatments targeting the underlying neurochemical pathways may offer potential strategies for mitigating cocaine’s adverse effects. Pharmacotherapies aimed at stabilizing dopamine levels or protecting ocular structures might reduce the risks associated with cocaine use.

Conclusion: Cocaine's effects on the visual system and ocular health highlight the complex interplay between substance use and neurobiology. Understanding these effects is crucial for developing effective intervention strategies and promoting overall ocular health. Increased awareness and research into the consequences of cocaine on the visual pathways can aid in the prevention and treatment of associated disorders, benefiting public health and supporting individuals in managing the effects of substance use.

Keywords: Neurological Impact, Cocaine, Visual Pathways, Cornea, Aqueous Humor

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The novel variant of WFS١ gene in an Iranian patient with Wolfram syndrome (Research Paper)

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Introduction: Wolfram syndrome (WS) is an autosomal recessive rare genetic disorder characterized by diabetes mellitus, diabetes insipidus, hearing loss, optic atrophy, and a variety of abnormalities of the urinary tract, nervous system, and endocrine glands. The WFS١ gene is mapped on chromosome ٤p١٦ and consists of ٨ exons and Exon ٨ is the largest. WFS١ gene encodes an ٨٩٠ residue glycoprotein wolframin, consists of three fragments, including cytoplasmic N-terminal domain, luminal C-terminus, and central nine-transmembrane domains, which is responsible for the regulation of endoplasmic reticulum (ER) stress, integrity, intracellular homeostasis, and survival of the cell. To date, over ٢٠٠ WFS١ pathogenic and likely pathogenic mutations. The majority of them are located in exon ٨, that encodes the C-terminal and transmembrane domain of the protein. WFS١ gene variants are heterogeneous and include a variety of non-sense, missense, and frameshift deletion or insertion mutations. Studying rare autosomal recessive disease in regions with consanguineous marriage, such as Iran can help us to prevention and management of this disease. In the present survey, we performed a genetic investigation on three families with WS and reported a novel mutation, and two previously reported mutation in the WFS١ gene.

Methods: In this study, we have performed Sanger sequencing and co-segregation analysis for three consanguineous Iranian families including three patients to identify the etiology of the disease in the patients. Bioinformatics tools were used to evaluate the pathogenicity of the identified variants.

Results: Sequencing results showed two known mutations (c.٢١٠٥G>A and c.٢٠٠٦A>G) and a novel homozygous stopgain mutation, c.١٤٤٤A>T (p.K٤٨٢X) in exon ٨ of WFS١ gene. Bioinformatics studies verified the pathogenic effects of the novel variant. Finally, p.K٤٨٢X is classified as a novel pathogen variant according to American College of Medical Genetics and Genomics (ACMG) guidelines. Further analysis demonstrated that both parents were heterozygous for the variant.

Conclusion: the novel mutation (p.K٤٨٢X) creates a frameshift, which occurs in the transmembrane domain and causes the elimination of ٤٦٪ of the WFS١ protein (Wolframin), leading to a premature stop codon truncating the protein in amino acid ٤٨٢ residues. This mutation causes the loss of Wolframin protein function. Our data proved the importance of genetic analysis in patients with early onset of DM.

Keywords: Wolfram syndrome, genetic disorder, WFS١ gene, diagnosis, mutational analysis.

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The performance of Deep learning in brain tumor detection (Review)

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Introduction: Brain tumor is considered as one of the deadliest diseases in the world due to its increase affect and mortality rate in all age groups. The World Health Organization (WHO) claims that about ١٠ million deaths are recorded every year because of brain cancer. An early tumor diagnosis implies a faster response in treatment, which helps to improve patient's survival rate with correct treatment decision that extent from surgery to radiotherapy and chemotherapy. Localization and classification of brain tumors in large medical images databases, taken in routine clinical tasks by manual procedure such as Magnetic Resonance Imaging (MRI) and Computed Tomography (CT), have a high cost both in effort and time. An automatic detection, location, and classification procedure is desirable and worthwhile. Consequently, using artificial intelligence (AI) techniques has become necessary in the automated detection and segmentation however, the manual methods results are regarded as the ground truth for developing and evaluating automated methods including deep learning which is an efficient and popular branch of AI. Deep learning techniques are commonly adopted for brain tumor MRI image detection and segmentation therefore this article reviews some used deep learning techniques in brain tumor MRI image detection and discusses the impact performance of deep learning models.

Methods: This review was conducted through electrical scientific databases, including PubMed, Scopus, and Google Scholar using keywords such as "deep learning", "brain tumor", "detection", "segmentation". After these articles were reviewed, a general conclusion was extracted from all the articles.

Results: The studies utilized several datasets to assess the performance of different models therefore the proposed model is evaluated on different parameters including Accuracy, Precision, Recall, F١-measure. One of the models with satisfactory results was CNN-LSTM in terms of accuracy ٩٩,١٪, precision ٩٨,٨٪, recall ٩٨,٨٪ and F-١ measure ٩٩,٠٪. Another model which had a good performance used both LRelu and ReLu activation functions although this DI model will stop growing when the ReLu problem reaches its end. The model EfficientNetB٢ outpeformed the other variations significantly, achieving an F١-score of ٩٨,٧١٪, a test accuracy of ٩٨,٨٦٪, precision of ٩٨,٦٥٪ and recall of ٩٨,٧٧٪. Even the TumorDetNet DI model had the great results for optimal accuracy of ١٠٠٪ for classifying brain tumors. If the type of tumor is considered in performance results; glioma achieved the highest test accuracy of ٩٩,٦٠٪ while the pituitary tumor closely followed with a test accuracy of ٩٧,٨٨٪ and with highest F١-score, and specificity, with values of ٩٩,٥٤٪, ٩٩,٥٣٪, ٩٩,٥٤٪ and ٩٩,٨١٪. The values obtained for all the segmentation metrics are remarkable with average values of Dice=٠,٨٢٨, Sensitivity=٠,٩٤٠, and pttas=٠,٩٦٧.

Conclusion: When compared to manual procedures, these technologies give enhaced accuracy, volume reduction, and speed, however Deep learning require a significant amount of data to train models, otherwise, the predictive performance may suffer. Over all the Deep learning can be used to assist medical doctors in the diagnostic of brain tumors and some successful methods were named such as multiscale CNN which uses three processing pathways, is able to successfully segment and classify the three kinds of brain tumors in the datas, we assume CNN-LISTM is the best for detecting the MR brain images also the TumorDetNet model had a great performance for classifying brain tumors into malignant and benign. Despite the perfect performance of AI, more research needs to be conducted in the field to discuss clearly about its performance.

Keywords: Deep learning detection detection localization segmentation

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The performance of Deep learning in outcome prediction of brain stroke (Review)

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Introduction: Stroke is a leading cause of mortality globally, with over ١٢ million incidents reported annually. It manifests in two primary forms: ischemic stroke, resulting from arterial blockage, and hemorrhagic stroke, caused by blood vessel leakage. Accurate prediction of stroke outcomes is crucial for guiding treatment decisions and minimizing disability, particularly as interventions like thrombolysis carry risks such as intracranial hemorrhage and gastrointestinal bleeding. Therefore, proper patient selection is essential. Traditional predictive methods, including Follow-up Infarct Volume (FIV), primarily rely on radiological assessments and are limited by their focus on specific clinical data subsets, often lacking comprehensive analysis. Recent advances in predictive systems have emerged, notably through the application of deep learning (DL), a significant branch of artificial intelligence. Studies indicate that DL can utilize imaging biomarkers for outcome prediction, leveraging architectures like deep neural networks and long short-term memory recurrent neural networks. These models are adept at analyzing complex, non-linear relationships between imaging and clinical data, making them particularly valuable in the context of stroke prediction. This review synthesizes recent research on DL approaches for stroke outcome prediction, examining their effectiveness compared to traditional methods and highlighting their potential to revolutionize clinical practice.

Methods: This review gathered recent studies from electronic databases such as PubMed, Scopus, and Google Scholar by utilizing the search terms "deep learning," "prediction," and "stroke." Following a thorough examination of the literature, a comprehensive conclusion was drawn.

Results: The review includes ١٠ studies employing various DL techniques, including DeepSM and DeepSurv, with models such as OEDL and SMOTEENN demonstrating considerable performance. The integration of clinical factors (ranging from ١ to ٦٠) with imaging features notably enhanced the predictive accuracy of DL models. The outcomes were measured using the modified Rankin Scale (mRS) at three months post-stroke, revealing an area under the curve (AUC) was ranged from ٠,٧٧٩ to ٠,٨٣٠ and an improvement noticed from ٠,٧٧٩ to ٠,٨٨ when combining imaging and clinical data. However, specific AUC values for deep learning models focused solely on heart stroke prediction were not detailed in the provided search results. Sensitivity was approximately ٠,٧٩ while specificity was around ٠,٧٧. Further research may be needed to establish a comprehensive overview of AUC values across different deep learning.

Conclusion: In conclusion, the fusion of deep learning and clinical data significantly enhances the prediction of favorable reperfusion outcomes. The analysis of feature importance highlights both

established and novel imaging characteristics with predictive significance. Furthermore, it is emphasized that outcome predictions should extend beyond infarct volume, as follow-up diffusion-weighted imaging provides additional prognostic insights, ultimately leading to better patient management and improved recovery trajectories. This innovative approach represents a promising advancement in stroke care, paving the way for more personalized and effective treatment strategies.

Keywords: deep learning; prediction; prognosis; outcome; stroke

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The pharmacological role of probiotics in reducing the symptoms of Parkinson's disease (Review)

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Introduction: Parkinson's disease (PD) is the second most common neurodegenerative disease worldwide that affects ۳,۷٪ of the population over ٦٥ years of age; it is a progressive degeneration of dopaminergic neurons that are present in the substantia nigra pars compacta (SNPC) with a deficiency of dopamine, that can lead to altered motor movement. Based on recent evidence, due to the strong correlation between the gut-brain axis and PD, there is a positive relation between the consumption of probiotics with the improvement of Parkinson's disease symptoms through different pathways and mechanisms.

Methods: Studies published from the beginning to ۲۰۲۳ analyzing the effect of probiotics on PD were searched by searching Google Scholar, Pubmed, Scopus and Web of Science. Among the screened articles, related articles were reviewed.

Results: Probiotics play a beneficial role in the pathways that lead to the degeneration of dopaminergic neurons and ultimately the exacerbation of PD symptoms; For example, in the PARK-۲ gene mutation, which leads to the lack of expression of the E۳ ubiquitin ligase enzyme gene and the accumulation of alpha-synuclein, Saccharomyces boulardi and Lactococcus lactis probiotics, play a role in increasing the expression of this enzyme. As another example, SCFAs play a role in inhibiting DDT and ROTENONE pesticides, which cause the degeneration of dopaminergic neurons. In addition, considering that the only way to improve the symptoms (Especially movement disorders) in this disease is to increase the levels of dopamine, SCFAs have shown their beneficial effect here by inhibiting the enzymes that break down dopamine (MAO-B and COMT). It has been found that the use of probiotics increases the production of anti-inflammatory factors and decreases the gene expression of inflammatory factors, as well as reducing the accumulation of ROS and as a result, neuroinflammation, which is one of the main reasons for PD, is prevented. Our review shows that probiotics can be used to improve constipation and motor symptoms for patients with Parkinson's constipation, possibly by reducing the inflammatory response and improving gut-brain axis neuron function. Probiotics can directly stimulate electrical signals in the ENS and dorsal motor nucleus of the vagus (DMV) by transmitting signals through the vagus nerves to affect the center of the brain, thus reducing the accumulation of α-syn and reducing motor deficits in PD patients. According to research, ghrelin levels (which play a role in maintaining and protecting the normal function of nigrostriatal dopamine) is reduced in PD patients, and with Prevotella, ghrelin concentrations return to normal.

Conclusion: According to the results obtained from the present studies (considering the gut-brain axis), the consumption of probiotic supplements in a specified type and dose can have positive effects on the symptoms of Parkinson's disease (especially constipation). More studies can help to understand and prove the mechanisms of the effects of probiotics on Parkinson's disease.

Keywords: Parkinson's disease, Probiotics, Dopamine, constipation, SCFAs

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The potential of β-glucan, as a natural immune booster, in fighting parasitic infections (Review)

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Introduction: B-glucan, a natural polysaccharide, has been recognized for its strong ability to boost both innate and adaptive immune responses. This research demonstrates that B-glucan enhances immune functions by activating macrophages, neutrophils, and natural killer cells, as well as stimulating the production of crucial cytokines like interleukin-١٢ and interferon-gamma. These immune responses are essential for controlling various parasites, including protozoa, and helminths. B-glucan's ability to work synergistically with traditional antiparasitic treatments enhances their efficacy, making it a promising adjunct therapy.

Methods: In the present review, we searched the PubMed, ProQuest, Scopus, Embase, Google Scholar, ScienceDirect, and Wiley databases for relevant articles. The keywords used in the search were B-glucan, Parasitic infections, Protozoa, Helminths, Immune functions, In vivo, and In vitro.

Results: Studies show B-glucan can significantly improve immune function against parasites like Leishmania spp., Toxoplasma gondii, and Eimeria spp. It stimulates macrophages, natural killer cells, and antibody production. When used as an adjuvant, B-glucan significantly enhances the immune system's response to vaccines, improving protection against parasitic infections in experimental models. Research suggests B-glucan can be used in vaccines against parasites, offering long-term protection.

Conclusion: B-glucan holds significant promise as a safe and effective approach to fighting parasitic infections. Its ability to boost immunity, work alongside existing treatments, and potentially contribute to vaccine development makes it a valuable candidate for further research and development.

Keywords: B-glucan, Parasitic infections, Protozoa, Helminths.

The potential of tRFs as therapeutic targets and diagnostic biomarkers in breast cancer (Review)

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Introduction: Recent advances in molecular biology, such as high-throughput RNA sequencing, have revealed the potential of small non-coding RNAs (sncRNAs) as key players in the regulation of gene expression and cancer development. Transfer RNA (tRNA)-derived fragments (tRFs) are small RNA molecules of approximately ٢٠ nucleotides in length that are produced through the cleavage of pre-tRNA and mature tRNA. Although tRFs were initially disregarded as incidental products of tRNA turnover, there is accumulating evidence that supports the functionality of tRFs and their association with various human diseases, including cancer. Moreover, they are conserved sequences that are widely distributed in different species and in various human body fluids. This review article examines the current understanding of the role of tRFs in the molecular mechanisms of breast cancer, focusing on their potential as therapeutic targets and diagnostic biomarkers.

Methods: A comprehensive literature search was conducted, focusing on recent studies, including in silico, in vitro, and in vivo research. Data were collected from databases such as PubMed, Scopus, Google Scholar, and Web of Science using search terms like breast cancer, tRFs, biomarkers, molecular mechanisms, diagnosis, and treatment. After a thorough search, the essential information about tRFs, their biological function, and their diagnostic and therapeutic value in breast cancer was identified.

Results: The analysis revealed that dysregulations of tRFs are highly associated with breast cancers, including the regulation of tumor cell proliferation, invasion, migration, and drug resistance. They exert their role through various processes such as modulation of mRNA stability, the translation process, cellular stress, immune response, and differentiation. For example, one study found that three tRFs (tRF-Gly-CCC-٠٤٦, tRF-Tyr-GTA-٠٠١٠, and tRF-Pro-TGG-٠٠٠١) were downregulated in both breast cancer and early breast cancer compared to healthy donors. This suggests that these tRFs could potentially serve as novel circulating biomarkers for the early detection of breast cancer. In addition, tRF-١٧-٧٩MP٩PP has been shown to play an important role in inhibiting the malignant activities of cells and to function as a novel tumor suppressor in breast cancer via the THBS١/TGF-β١/Smad٣ pathway.

Conclusion: Early detection, diagnosis, and treatment of breast cancer are crucial for a successful cure. While conventional methods like breast imaging and needle core biopsy have their limitations, new non-invasive strategies such as tRFs could be effective in the treatment of breast cancer. The unique expression patterns of tRFs suggest not only their potential as biomarkers for early diagnosis but also possible therapeutic interventions. However, further research should focus on understanding the specific mechanisms by which tRFs influence the development of breast cancer and investigating their utility in the clinical setting.

Keywords: breast cancer, tRNA-derived fragment, biomarkers, treatment , diagnosis

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The Prognostic Significance of Neutrophil-to-Lymphocyte Ratio in Traumatically Injured Patients at Admission: A Mini-Review (Review)

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Introduction: Subsequent to trauma and systemic inflammatory response syndrome, the typical reaction is an increase in the total white blood cell count. Neutrophils, which play a crucial role in the initial immune response against invading microbes through phagocytosis and inflammatory mediators, are abundant circulating leukocytes in humans.

Methods: However, lymphocytes, the main cellular compartments of the immune system, are negatively affected in the setting of trauma. The neutrophil to lymphocyte ratio (NLR), which can be easily measured in daily clinical practices, is an alternative marker of inflammation before any clinical findings can be observed.

Results: Most investigations have declared that high values of NLR potentially have a poor prognosis in traumatically ill patients on admission and contribute to coagulopathy, increased hospitalization, and mortality.

Conclusion: Given that various cut-off points have been considered for the NLR value, receiving a unique one and linking it with subsequent outcomes of the disease should be the focus of ongoing research.

Keywords: Neutrophil, Lymphocyte, Inflammation, Trauma

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The Protective Efficacy of Curcuma longa and Pioglitazone in Alleviating Paraquat-Induced Lung Injury in Rats (Research Paper)

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Introduction: Inhalation of paraquat (PQ) is one of the most widely used Herbicides in the world can cause lung damage. In recent years, extensive in studies suggested curcumin has anticancer, antiviral, antiarthritic, anti-amyloid, antioxidant, and anti-inflammatory properties Curcuma longa (Cl) has a long history in traditional and folk medicine for the treatment of a wide range of disorders, including respiratory diseases.The aim of this study was to investigate the preventive effect of curcumin on lung damage caused by inhaled PQ in rats.

Methods: Male Wistar rats were divided into ٨ groups (n = ٥), one group exposed to saline (control) and other groups exposed to PQ aerosol. Saline (PQ), Cl extract, (two doses), curcumin (Cu), pioglitazone (Pio), and the combination of Cl-L + Pio and dexamethasone (Dex) were administered during the exposure period to PQ. Total and differential white blood cell (WBC) counts, oxidant and antioxidant indicators in the bronchoalveolar lavage (BALF), and tumor necrosis alpha (TNF-α) levels in the lung histologic , and air way responsiveness to methacholine were evaluated.

Results: WBC counts (Total and differential), malondialdehyde level, tracheal responsiveness (TR), TNF-α and histopathological changes of the lung were markedly elevated but total thiol content and the activities of catalase and superoxide dismutase were decreased in the BALF in the PQ group. Both doses of Cl, Cu, Pio, Cl-L + Pio, and Dex markedly improved all measured variables in comparison with the PQ group.

Conclusion: Cl, Pio, and Cl-L + Pio improved PQ-induced lung inflammation and oxidative damage.Histopathological assessments revealed that the combination of Cl-L + Pio significantly mitigated lung tissue damage caused by paraquat exposure. Additionally, the treatments resulted in improved airway responsiveness to methacholine, suggesting enhanced pulmonary function.

Keywords: paraquat,Curcuma longa, lung injury, oxidative stress

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The relationship between AIDS and the risk of developing non-Hodgkin's lymphoma (Review)

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Introduction: The purpose of this study was to describe the relationship between Non-Hodgkin's Lymphomas (NHL) and AIDS. According to Global Cancer Observatory, leukemia is the ١٥th most commonly diagnosed cancer and the ١١th leading cause of cancer-related deaths worldwide in ٢٠١٨. Most leukemia and lymphomas are sporadic and have no specific cause. However, research shows that these malignancies arise in the context of genetic abnormalities, immunosuppression, and exposure to risk factors such as ionizing radiation, carcinogenic chemicals, and carcinogens. Immune cells are of myeloid, lymphoid or monocyte lineage in bone marrow or lymph tissues. Genetic errors such as chromosomal translocations, chromosomal deletions, point mutations, and epigenetic changes can stop the maturation of stem cells at various stages of hematopoiesis and cause uncontrolled proliferation of immature and leukemic immune cells. Lymphomas are usually characterized by nonheritable chromosomal translocations, and research into the etiology of Non-Hodgkin's Lymphomas (NHL) consistently supports a role for infection and immunosuppression. HIV infection is associated with a very high risk of developing NHL, which is excessive in the course of highly active antiretroviral therapy (HAART).

Methods: In this article, we used data to compare the risk of subtype-specific NHL in people with HIV with those in the general population, obtained from the US HIV/AIDS Cancer Matching Study and also the relationship between NHL and HIV/AIDS has been investigated. The articles from ٢٠١٤ to ٢٠٢٤ have been reviewed from PubMed and Science Direct databases.

Results: In people with HIV or AIDS, NHL is the second most common malignancy. In a review of population-based studies across the United States, Australia, Australia, and Italy, the risk of NHL in people with AIDS compared with the general population ranged from ١٥-fold for low-grade NHL to ٤٠٠-fold for high-grade NHL. AIDS-NHL is currently the most common cancer in patients with AIDS in the United States and elsewhere where HIV-positive individuals have access to HAART.

Conclusion: Despite the introduction of highly active antiretroviral therapy (HAART), HIV-infected patients may be more likely to develop certain types of cancer than uninfected individuals. Lymphoma is the most common malignancy among HIV patients. Antineoplastic therapy has resulted in significantly prolonged disease-free survival among HIV-infected patients who develop lymphoma. HIV-infected individuals have an increased risk of developing non-Hodgkin's lymphoma (NHL), especially AIDS-defining NHL subtypes.

Keywords: AIDS, NHL, CANCER, HAART

The Relationship Between Expression of PTGS۲, HAS-۲, and GREM۱ Genes and Reduction of Oocyte Quality in Follicular Fluid of Women with Endometriosis (Research Paper)

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Introduction: Endometriosis (EM) is a benign, estrogen-dependent, and inflammatory disease that affects approximately ۱۰٪ of women of reproductive age. This condition is characterized by the presence of functional endometrial tissue and stromal glands located outside the uterine cavity. Epidemiological and clinical studies have established a link between infertility and EM; however, the underlying mechanisms contributing to infertility associated with EM remain varied and not fully understood. EM may influence female fertility by interfering with embryo implantation, causing hormonal alterations, and diminishing oocyte quality. Consequently, the assessment of oocyte status via indirect methods can help in determining the quality of oocytes in women diagnosed with EM. Follicular fluid (FF) serves as a significant clinical approach for evaluating oocyte condition; as it contains metabolites that are closely related to the follicular development, the stage of EM, and the associated fertility outcomes. An analysis of genes associated with the cumulus expansion process, such as prostaglandin-endoperoxide synthase ۲ (PTGS۲), hyaluronan synthase ۲ (HAS-۲), and gremlin-۱ (GREM۱), which facilitate the loosening and separation of the cumulus-oocyte complex from the follicular wall, thereby allowing its release into the peritoneal cavity, may provide insights into predicting oocyte quality. This study aims to investigate the relationship between oocyte quality and the expression levels of the PTGS۲, HAS-۲, and GREM۱ genes in the FF of women diagnosed with EM.

Methods: In this study, we used the qRT-PCR to investigate the mRNA expression levels of PTGS۲, HAS-۲, and GREM۱ genes in the FF of women with EM (n=۲۳) compared to women without EM as a control group (n=۲۳).

Results: There were no significant differences between the case and control groups regarding demographic factors such as age, body mass index (BMI), and the concentrations of luteinizing hormone (LH), follicle-stimulating hormone (FSH), and anti-Mullerian hormone (AMH), all of which are known to influence oocyte quality. In addition, the statistical analysis of PTGS۲ and GREM۱

expression did not indicate a significant difference between the case and control groups. However, the expression level of HAS-٢ was found to be significantly lower in the EM group when compared to the control group (p value= ٠,٠٣٨٥).

Conclusion: Studies have shown a relationship between the effective expression of HAS-٢ and the quality of oocytes, as well as their developmental competence. Therefore, it seems that the decrease in the expression level of this gene in the FF of women with EM is related to the decrease in oocyte quality in these patients. On the other hand, assessing the HAS-٢ level seems to be an important criterion for selecting better oocytes with a higher chance of fertilization. So the expression of the HAS-٢ gene can provide a new approach for predicting embryo quality and pregnancy outcome in women affected by EM.

Keywords: Endometriosis, Cumulus expansion genes, Follicular fluid, Oocyte quality

The relationship between iron dyshomeostasis and amyloidopathy in Alzheimer's Disease

(Review)

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Introduction: Alzheimer's disease (AD), a neurodegenerative condition, is defined by neurofibrillary tangles, amyloid beta (Aβ) plaques, and gradual cognitive loss. Aβ plaque typically arises by Aβ peptide buildup from the proteolytic cleavage of amyloid precursor protein (APP) in the amyloidogenic pathway. Nonetheless, amyloidogenesis is facilitated by disruption of various cellular signaling pathways. There is a growing body of evidence connecting the amount of Aβ plaque with iron buildup in the AD brain. We review new findings on iron's major pathogenic and biochemical effects on amyloidogenic pathway progression.

Methods: The databases Science Direct, Google Scholar, PubMed, were searched using relevant keywords such as "iron", "amyloid precursor protein", " amyloid beta", and "Alzheimer's disease" and relevant studies were retrieved from ٢٠١٠–٢٠٢٤.

Results: Increased iron levels and their co-localization with Aβ plaques have been detected in the hippocampus, parietal cortex, and motor cortex of AD brains, which are highly correlated with the rate of neurodegeneration and the extent of memory loss. In addition, the frontal cortex of the AD animal models showed increased expression of DMT١, a crucial transporter of divalent metal ions, colocalizing with Aβ plaque. Iron also affects APP expression and processing to Aβ. Indeed, excessive cytosolic Fe٢+ content promotes iron regulatory protein (IRP)-iron responsive element (IRE) interaction, upregulating APP expression. Furin regulates the APP-cleaving enzymes α- and β-secretase. In the presence of extra iron, furin impairment suppresses α-secretase and activates β-secretase, accelerating Aβ deposition. According to new preclinical research, deferoxamine (DFO) and deferiproneare iron chelators that decreased APP protein expression, switched APP processing to a nonamyloidogenic route, attenuated the Aβ load, and then markedly improved memory performance in AD models.

Conclusion: These studies provide more evidence that iron dyshomeostasis is a potential mechanism underlying amyloidogenesis and may help in evaluating the efficacy of iron chelation therapy for the treatment of AD.

Keywords: Alzheimer's disease, Iron, Amyloidopathy.

The relationship between stress and cancer (Review)

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Introduction: Stress is an inherent part of life. While short-term stress responses are typically helpful for handling immediate dangers, long-term exposure to stress can be harmful and may contribute to or worsen various chronic diseases, including cancer. Chronic psychological stress is recognized as a major factor in both the development and progression of cancer, although the exact mechanisms connecting stress to cancer are not fully understood. Psychological stress triggers several physiological responses, activating the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system, which then leads to changes in immune function. Stress can be defined as a state of disrupted balance caused by internal or external stressors. This disruption triggers a range of physiological and behavioral responses that aim to restore the organism's equilibrium.

Methods: Studying the relationship between stress and cancer progression, often by looking at patient survival rates, can be quite challenging. Stress, including life events, is typically evaluated without considering the timing of cancer detection, and its impact on cancer progression is often not examined. Additionally, most cancer patients experience some level of distress, which can influence cancer progression regardless of their baseline stress levels. This can obscure the connection between stress and cancer progression, but it might also highlight the potential benefits of stress-reducing interventions. Emotional distress in cancer patients can exacerbate mental health issues, potentially affecting cancer prognosis and increasing mortality rates.Surveys indicate that about one million new cancer cases arise annually among individuals aged ٢٠–٣٩, with stress being partially linked to these cases. This connection between chronic stress and cancer has garnered significant attention and concern within the medical community. Numerous studies have investigated the relationship between stress and various cancers, including prostate, breast, gastric, lung, and skin cancers, revealing evidence that chronic stress may contribute to tumor formation and cancer progression.

Results: Based on animal and clinical psychoneuroimmunological and neurobiological studies that have confirmed the efficiency of approaches that reduce the stimulatory effect of stress on cancer, it can be suggested that a combination of standard cancer therapy, together with psychotherapy and administration of antagonists to β٢-adrenergic receptors (e.g. propranolol), may not only significantly improve the quality of life of cancer patients, but also prolong their survival.

Conclusion: A cancer diagnosis triggers a complex psychological response in patients. Following the diagnosis, concerns about death, job loss, financial difficulties, loss of independence, and other negative impacts of cancer and its treatment on daily life contribute to increased distress and

anxiety.Chronic stress produces stress hormones during the activation of the neuroendocrine system (hypothalamus-pituitary-adrenal axis) and the sympathetic nervous system, which can promote tumor development and regulate the tumor microenvironment. In general, stress can have a direct relationship with cancer.

Keywords: Stress- Cancer - Chronic- Anxiety

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The relationship between time spent in cyberspace, suicidal thoughts, and suicide in adolescents. (Review)

Amir Mohammad Tatari Rad,[1,*]

[1]. Allameh Helli Malard

Introduction: Nowadays, there are many psychological problems among teenagers. One of the most tumultuous of these problems is suicide and suicidal thoughts among teenagers. Suicidal thoughts, and suicide among teenagers are on the rise. This issue shows the psychological problems of teenagers, which is expanding day by day and its dimensions are increasing. This critical problem has various causes. One of the reasons can be virtual space. The virtual space isolates teenagers and slowly depresses them, and finally the teenager is surrounded by suicidal thoughts or even commits suicide. The purpose of this research is to investigate the relationship between the hours that teenagers spend in cyberspace and suicidal thoughts and suicide tendencies in teenagers. This research was conducted on some high school teenagers of Allameh Hali Mallard, a school of the National Organization for Development of Exceptional Talents.

Methods: This research was conducted on high school teenagers aged ١٥ to ١٨ years. ٣٨ teenagers were randomly selected and they were asked about the amount of time they spend on cyberspace. Then they were asked if they have suicidal thoughts or not and if they have ever committed suicide or not. The amount of time teenagers spend in cyberspace, the percentage of people who are involved in suicidal thoughts and the percentage of people who have committed suicide can provide great information about the psychological problems of teenagers, its causes and its results. Because this research was conducted on a small number of teenagers, the data of this research are only close to reality and not exactly in accordance with reality. As a result, it can be said that a small percentage of the data has errors.

Results: Of the ٣٨ teenagers on whom this research was conducted, ٥٧,٨٩٪ of them spend at least ٢ hours of their time in cyberspace and ٧٨,٩٤٪ of them spend at least ١ hour of their time in cyberspace. ٤٤,٧٣٪ of these ٣٨ teenagers are involved in suicidal thoughts and ٣ of them have committed suicide. One of the people who committed suicide spends at least ٨ hours of their time in cyberspace every day, and two other people spend ٤ hours and ١ hour of their time in cyberspace daily. Of the ١٧ people who have suicidal thoughts, ٩٤,١١٪ of them spend at least ١ hour of their time in cyberspace every day, and ٥٨,٨٢٪ of them spend at least two hours of their time in cyberspace every day. Of the ٢١ people who do not have suicidal thoughts, ٥٧,١٤٪ of them spend at least two hours of their time in cyberspace every day, and ٨٥,٧١٪ of them spend at least one hour of their time in cyberspace every day.

Conclusion: There is no deep and strong relationship between the amount of time spent in cyberspace, suicidal thoughts, and suicide. People who have suicidal thoughts spend slightly more time in cyberspace than people who do not have suicidal thoughts.

Keywords: Suicide, Cyberspace, teenager, adolescent

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The relationship between time spent in cyberspace, suicidal thoughts, and suicide in adolescentse lationship between time spent in cyberspace, suicidal thoughts, and suicide in adolescents

(Research Paper)

Amir Mohammad Tatari Rad,[١,*]

١. Allameh Helli Malard

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Keywords: suicide

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The Rise of Antifungal Resistance in Clinical Mycology: Mechanisms, Clinical Impact, and Emerging Therapeutic Strategies (Review)

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Introduction: Antifungal resistance has become a significant challenge in clinical mycology, particularly for immunocompromised patients. Fungi such as Candida auris, Aspergillus fumigatus, and Cryptococcus neoformans are increasingly resistant to major antifungal drug classes, including Azoles, Echinocandins, and Polyenes. This resistance is driven by the overuse of antifungals in healthcare and agriculture, making these infections difficult to treat. With limited antifungal agents available, the rise of multidrug-resistant fungi poses an exacerbating global health crisis. This review accumulates current research on resistance mechanisms, clinical implications, and novel therapeutic approaches.

Methods: A systematic review from ۲۰۱۳ to ۲۰۲۳ was administered using databases like PubMed, Scopus, and Web of Science. Search terms included "antifungal resistance," "clinical mycology," "Candida auris," "Aspergillus fumigatus," and "emerging antifungal treatments." Articles were selected based on their relevance to resistance mechanisms, epidemiological trends, and therapeutic strategies. Molecular mechanisms of resistance and clinical outcomes were key focus areas, along with advancements in antifungal drug development and diagnostic tools.

Results: The review highlights a significant rise in antifungal-resistant fungal pathogens, notably Candida auris, that is resistant to multiple antifungal classes. Candida auris has caused outbreaks in healthcare settings, spreading rapidly in hospitals due to its persistence on surfaces and resistance to disinfectants. Mechanisms of resistance include mutations in drug target sites, increased efflux pump activity, and biofilm formation. Aspergillus fumigatus resistance, particularly to Azoles, is linked to mutations in the CYP۵۱A enzyme and environmental exposure to agricultural Azoles. Similarly, Cryptococcus neoformans demonstrates resistance to Azoles and Polyenes, posing treatment challenges in immunocompromised patients. The clinical impact of antifungal resistance is profound. Patients infected with resistant fungi experience higher mortality rates, extended hospital stays, and increased healthcare costs. Resistant infections require more aggressive treatment approaches, which may involve higher doses of toxic antifungal drugs or a lack of effective treatments altogether. Delayed diagnosis due to traditional diagnostic limitations further escalates patient outcomes, as resistant strains often go undetected until treatment failure. Emerging therapeutic strategies provide hope in addressing resistance. Novel antifungal agents, including next-generation Azoles and Echinocandins, are under development, showing improved efficacy against resistant strains. Combination therapies using multiple antifungal drugs are being explored to enhance treatment outcomes and reduce the development of resistance. Additionally, immunotherapies and host-directed therapies aim to strengthen the immune response to fungal infections. New diagnostic technologies, such as next-generation sequencing and rapid susceptibility testing, are improving the timely detection of resistant strains, leading to earlier intervention.

Conclusion: Antifungal resistance poses a growing global health threat, complicating the management of fungal infections in clinical settings. The increasing prevalence of resistant pathogens such as Candida auris and Aspergillus fumigatus highlights the urgent need for novel antifungal agents and improved diagnostic capabilities. Addressing this issue requires coordinated global efforts, including better infection control, enhanced surveillance, and investment in antifungal research. As resistance continues to rise, there is an immediate need for innovative therapeutic strategies to confirm effective management of fungal infections in the future.

Keywords: Antifungal resistance, Candida auris, Aspergillus fumigatus, novel antifungal agents, diagnostic

The Role and Importance of Immunotherapy in Breast Cancer Treatment (Review)

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Introduction: Breast cancer accounts for ٣٠٪ of all new cancer diagnoses and about ٤١,٠٠٠ deaths annually in the United States, making it a danger to women's health and well- being. Despite a ٣٨٪ reduction in the death rate from breast cancer due to breakthroughs in early identification and therapy, nearly all patients who develop metastatic illness will ultimately lose their lives to it. These depressing statistics highlight the urgent need for novel ways of breast cancer treatment that lessen the disease's recurrence and fatality rate. More and more evidence in recent years points to the immune system's critical role in deciding a patient's long-term survival as well as how well they respond to conventional therapy. The remarkable therapeutic efficacy of immune checkpoint antagonists against a variety of solid tumors, along with these data, have rekindled interest in immune-based approaches to the diagnosis, treatment, and prevention of breast cancer. This study set out to examine the function and significance of immunotherapy in the management of breast cancer.

Methods: The study with titled the role and importance of immunotherapy in breast cancer treatment which was done by searching scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: The immune system's dualistic function in breast cancer The initiation, spread, and management of breast cancer are all actively influenced by the immune system. Immunoediting is a characteristic of the dynamic interactions between host immunity and breast cancers. Acute inflammation triggers innate immunity early in the development of mammary tumors, which leads to the death of tumor cells as well as the maturation of dendritic cells (DC), which fuel the T-cell response specific to the tumor. Either immune-mediated rejection of nascent cancers or the selection of tumor cell variations immune response-evading take place at this point. In the end, acute inflammation gives way to chronic inflammation, creating a complex tumor microenvironment (TME) with suppressive immune cells (regulatory T cells, B cells, and myeloid-derived suppressor cells, MDSC) and stromal cells (fibroblasts, endothelial cells) that facilitate tumor progression and overt immune escape. Immune checkpoint molecules are increased on tumor cells and immune cells in response to early immunological activation, and immune-suppressive metabolic pathways are triggered in various immune cell types during this change in the CD٤ T cell response from T helper (Th) type ١ to Th type ٢. Together, these forces establish a formidable network of immune suppression within the breast TME. This microenvironment, and other factors described in this review, impinge on the immune system to sculpt antitumor immunity.

Conclusion: Combination immunotherapies have the potential to transform immunologically cold breast cancer lesions into immune-activated tumors that are ready to respond to immunotherapy

soon. tactics for personalized immunotherapy are being developed quickly. These tactics make use of vaccinations that deliver immune-modulating chemicals and/or tumor-specific neoantigens selected according to the immunologic milieu of a particular tumor. Research is increasingly focused on identifying environmental modifiers of immunity (microbiome, metabolic and hormonal factors, concomitant pharmacological therapy), as well as developing biomarkers that predict response and resistance to therapy. We will certainly also get closer to the ultimate aim of immune-based breast cancer prevention by implementing vaccination strategies together with the knowledge gained from contemporary breast cancer immunotherapy.

Keywords: immunotherapy, breast cancer, drug therapy, CD٤

The Role and Importance of Stem Cells in The Treatment of Leukemia (Review)

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1. Msc of Molecular Genetic Department of Genetics, Zanjan Branch, Islamic Azad University, Zanjan, Zanjan.

Introduction: Stem cells, sometimes referred to as mother cells, have the capacity to differentiate into other cell types within the body, such as insulin-producing, neuron, and heart cells. Stem cells reproduce through mitosis and self-renewal. These cells are categorized as totipotent, pluripotent, multipotent, and unipotent stem cells, among other classifications. The whole functional organism can be created by totipotent stem cells. Multipotent stem cells differentiate into more specialized cell types. Only one type of differentiated cell can be produced by unipotent stem cells. One can categorize the sources of stem cells into two primary groups: perinatal and adult. Hematopoietic stem cell transplantation as a leukemia treatment Treatments like HSCT may be promising for certain illnesses like AML, CML, and ALL. An intravenous injection of bone marrow cells can replace the old bone marrow cells and generate new ones, according to studies on HSCT conducted by a team at the Fred Hutchinson Cancer Studies Center between ۱۹۵۰ and ۱۹۷۰. This study looked into the function and significance of stem cells in the treatment of leukemia.

Methods: The present study is titled The Role and Importance of Stem Cells in The Treatment of Leukemia which was done by searching scientific databases such as Science Direct, Springer, Google Scholar and PubMed.

Results: The outcomes have demonstrated Allogeneic and autologous bone marrow transplants are two different types of transplants. When a patient has autologous bone marrow transplantation, the transplanted tissue is extracted from them, the malignant cells are killed with anti-cancer medications, and the transplanted tissue is then reinjected into the patient. With this kind of transplant, there is little chance of infection or transplant rejection. Hodgkin's lymphoma (HL) can be treated by autologous transplantation, and it should be utilized. Studies show that patients with myeloma who receive autologous transplantation have a ۵-۲۰٪ chance of developing GVHD; whereas, individuals who receive allogeneic transplantation have a nearly ۵۰٪ chance of developing GVHD. Allogeneic transplantation involves the use of healthy donor cells rather than the patient's tissue. For instance, following clinical testing and inspection, the patient may get healthy donor tissue from their mother, father, brother, or sister. Allogeneic transplantation is a therapy option for AML, MM, ALL, and CML. Another option for treating NHL is an allogeneic bone marrow transplant. Depending on the type of leukemia, a different transplant may be necessary. For instance, research indicates that CML often progresses in three phases. To treat CML caused by chronic phase ۱, TKI intolerance, and critical phase, allogeneic transplantation is typically utilized. Allogeneic transplantation is also a viable therapy option for patients with ALL and AML who have a high risk of relapse.

Conclusion: Today, there are renewed prospects for the treatment of cancer due to the development of novel therapeutic approaches and the application of stem cells. With stem cells, it is now possible to treat a wide range of illnesses, including blood cancer and disorders. Using hematopoietic stem cell transplantation (HSCT), which comes in various forms, is one of the appropriate solutions. ١-Allogeneic transplantation ٢- Autologous transplantation As previously mentioned, stem cell therapy is evolving and improving, but there are problems and difficulties with clinical treatments that use these cells. These problems include genetic instability of stem cells, ethical concerns, and transplant rejection, which has made the work a little challenging. With additional studies and research in this area, hopefully, these issues will be resolved and stem cells will one day be able to treat a variety of illnesses.

Keywords: Stem cells, leukemia, Allogeneic transplantation, Autologous transplantation

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The Role of Antibiotics in Gut and Brain Microbiota Axis (Review)

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Introduction: The human body contains trillions of microbes that are thought to influence and regulate the host's physiology. Most of the microbes in the human digestive system are known as gut microbiota. Anatomically, the gut has a complex, two-way relationship with the central nervous system (CNS) that is called the gut-brain axis, which interacts in both health and disease. The communication between gut microbiota and the brain is diverse and occurs via various routes, including the autonomic nervous system, the vagus nerve, the enteric nervous system, neurotransmitters and the immune system. The levels of neurotransmitters and their precursors produced in the gut may also be influenced by the levels of these substances present in the brain. Additionally, neurotransmitters can be generated by bacteria, apart from being sourced from food metabolism. For example, Escherichia coli has been observed to release dopamine, serotonin, and noradrenaline, while Lactobacilli are known to produce serotonin, GABA, acetylcholine, and histamine, which may influence host brain function. If the amount of gut microbiome change, the host will have to use Antibiotics, which are known to disrupt the intestinal microbial community. Recent studies have indicated that the administration of antibiotics can induce changes in the gut microbiota, which may subsequently result in impairments in object recognition memory and altered expression of brain-derived neurotropic factor (BDNF) in the hippocampus during adulthood. It has been demonstrated that early-life antibiotic exposure is associated with an increased risk for psychiatric disorders. Furthermore, a recent clinical study has indicated that infants who have received intravenous antibiotics after delivery exhibit altered auditory processing and recognition memory responses, thereby supporting the importance of the microbiota-gut-brain axis in humans during early life. Additionally, there is evidence that links autism spectrum disorder, a neurodevelopmental condition, to gut microbiota-brain axis dysfunction.

Methods: A comprehensive literature review was conducted to identify studies investigating the role of antibiotics in gut and brain microbiota axis. Electronic databases were searched using relevant keywords, and studies published between ٢٠٢٤ and ٢٠١٩ were included. The review encompassed in vitro studies, animal models, and clinical trials to provide a comprehensive understanding of the topic.

Results: A review of the literature reveals that the administration of antibiotics to laboratory animals has been shown to influence a number of behaviors including sociability and anxiety. For instance, a ١١-day exposure to an antibiotic cocktail resulted in the disruption of object recognition memory in adult male mice.

Conclusion: The bidirectional interaction between the microbiota and the brain has been designated the microbiota-gut-brain axis. The investigation of how gut microbes influence the communication between the gut and the brain has constituted a significant research topic over the past decade. The role of antibiotics in the gut-brain axis is currently under investigation, despite the continued reliance on these agents as a cornerstone of therapy in numerous conditions. While antibiotics are undoubtedly a crucial therapeutic option, their prolonged use has been linked to adverse effects on both the microbiome and brain functions. These effects have been observed in the context of disrupted object recognition memory as well as psychiatric disorders. Nevertheless, in order to circumvent potential adverse effects on the central nervous system, it is advised to limit the use of antibiotics. Their administration must be conducted under the supervision of a qualified medical practitioner. Additionally, modifying one's dietary habits and lifestyle can potentially mitigate the risk of developing cognitive and psychiatric disorders.

Keywords: gut-brain axis; gut microbiome; antibiotics ;brain functions

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The Role of Artificial Intelligence in Advancing Personalized Medicine (Review)

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Introduction: Personalized medicine is a new approach in healthcare where treatments for each disease are tailored to the unique characteristics of each person, like their genetic makeup, environment, living conditions, and lifestyle. The growth of artificial intelligence (AI) has greatly enhanced this field, creating new possibilities for more accurate diagnoses and personalized treatments. AI can be very advanced in integrating into clinical practices, offering tools that can process large amounts of information and suggest treatment methods that were previously unimaginable.

Methods: This article looks at recent research on how AI is working together with personalized medicine. We did a thorough search of studies from the last ten years and chose ones that explore how AI is used in genetic analysis, predicting outcomes, and personalized treatments. We then analyzed these studies to find key trends, current challenges, and areas that need more development.

Results: Our analysis highlights surprising advances in the use of AI to personalize patient care. For example, AI-based tools are being developed to improve the accuracy of genetic risk assessments and help predict patients' response to treatment in various diseases. Machine learning algorithms are particularly effective in processing complex data sets and providing predictions that guide personalized treatment strategies. However, this field is still associated with challenges. One of the challenges we face is ensuring the interpretability of AI models and protecting ethical issues related to data privacy.

Conclusion: AI can play a crucial role in advancing personalized medicine by providing new ways to offer more effective and tailored care for patients. To make the most of AI's potential, ongoing research is needed to overcome existing obstacles and ensure these technologies benefit all patients. The future of personalized medicine will likely depend on smoothly integrating AI with traditional medical practices.

Keywords: Personalized Medicine , Artificial Intelligence (AI) , Genetic Analysis , Machine Learning

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The Role of Biotechnology in Regenerative Medicine: Advances and Challenges (Review)

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Introduction: Regenerative medicine focuses on healing or replacing damaged tissues and organs, with biotechnology driving many advances. Key technologies, including stem cell therapy, gene editing, and bioprinting, offer transformative solutions. However, technical, regulatory, and ethical challenges remain. This review examines the role of biotechnology in advancing regenerative therapies and the obstacles that must be addressed for widespread clinical application.

Methods: This review is based on studies that cover key areas of biotechnology in regenerative medicine, including: - Stem cell technologies and biomaterials for tissue regeneration, which enhance therapeutic potential by integrating biological materials for faster and more effective healing. - Gene therapy and gene editing, particularly CRISPR technology, offer solutions for treating degenerative conditions at the genetic level. These therapies allow for precise corrections of genetic defects responsible for tissue damage but face challenges in terms of long-term safety and ethical considerations. - Bioprinting and tissue engineering, which focus on the creation of custom tissues and organs through ۳D printing technologies. This innovation holds potential to address organ shortages by producing tissues from a patient's own cells, minimizing rejection risks. - Challenges in clinical translation, which highlight difficulties in scaling these therapies from lab experiments to clinical use. Factors such as production costs, regulatory approvals, and ensuring the functionality of bioengineered tissues in living systems create significant barriers.

Results: Significant advances have been made across several areas: - Stem cell therapies show great potential in regenerating damaged tissues like heart muscles and cartilage. The use of biomaterials to support cell growth enhances the ability of these therapies to integrate into existing tissue structures, promoting quicker healing and better outcomes. - Gene editing technologies like CRISPR-Cas۹ have revolutionized how scientists approach tissue repair at the molecular level. By precisely altering the genome, these therapies can potentially correct genetic defects that cause tissue degeneration, offering long-term solutions to conditions previously deemed incurable. However, ethical issues and concerns about off-target effects still pose barriers to clinical adoption. - Bioprinting has emerged as a promising solution for organ transplantation. This technology allows for the creation of customized tissues through layer-by-layer construction, using a patient's cells to minimize rejection. While advancements in this area are exciting, significant challenges remain in creating fully functional and vascularized organs that can be used in patients. - Translation to clinical practice remains one of the biggest hurdles. While the lab-based success of these technologies is evident, scaling them up for widespread clinical use is complicated. Regulatory approvals, manufacturing costs, and ensuring the long-term viability of engineered tissues are some of the biggest challenges.

Conclusion: Biotechnology has made remarkable progress in regenerative medicine, offering innovative solutions such as stem cell therapies, gene editing, and bioprinting. However, despite these advances, technical, regulatory, and ethical challenges must be overcome before these therapies can be widely adopted. Collaboration between researchers, clinicians, and regulatory bodies will be critical to unlocking the full potential of biotechnology in regenerative medicine. By addressing these barriers, the field could provide transformative solutions for a wide range of currently untreatable conditions.

Keywords: biotechnology, Bioprinting, Gene editing, Regenerative medicine

The role of cell therapy for dementia: A systematic review (Review)

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Introduction: Cell-based therapies are being developed for various neurodegenerative diseases affecting the central nervous system (CNS). Simultaneously, the role of individual cell types in neuropathology can be visualized by genetic and single-cell studies . Dementia may be characterized by confusion, behavioral disturbances, and cognitive impairment, and is currently said to affect approximately ٥٠ million people worldwide, and is projected to increase to ١٣٢ million by ٢٠٥٠.

Methods: We systematically reviewed Dementia reviewed studies with the aim of identifying cell therapy method in Dementia. For this purpose, English language reviewed articles between ٢٠١٩ and ٢٠٢٤ were searched in PubMed, databases. The titles of the articles were scanned with keywords (Dementia) and (Cell therapy).

Results: After studying the abstract, conclusion, results and sections of the selected articles, into two sections:١) Investigating the effects of cell therapy on Alzheimer's disease which is known as the most common type of dementia. ٢) Investigating the effect of cell therapy on Parkinson's disease was divided. We also reviewed the disadvantages and limitations and challenges of stem cell therapy and investigated the types of stem cells for the treatment of neurodegenerative diseases to get better results. Also we searched about other ways to treatment Dementia's diseases and compare these ways with cell therapies method. Of course We also see effects of exosome and cell products that can be used instead of stem cell.

Conclusion: In this research we tried to the best cell for cell therapy way and compare with other ways to treatment dementia that We can find the best treatment and also what limitation and challenges we have.

Keywords: Cell therapy, Dementia, Stem cell

The role of cell therapy for Type ١ diabetes (Review)

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Introduction: Type ١ diabetes (T١D) is the most common chronic autoimmune disease in young patients, and its hallmark is the loss of pancreatic beta cells, and the body suffers from insulin deficiency and hyperglycemia. Treatment with stem cells has great potential for treating patients with T١DM and can have effective results. As research advances in stem cell therapy for various diseases, advances in stem cell-based therapy for type ١ diabetes have been reported.

Methods: We systematically reviewed Diabete studies with the aim of identifying cell therapy method in Diabete. For this purpose, English language reviewed articles between ٢٠١٩ and ٢٠٢٤ were searched in PubMed, database. The titles of the articles were scanned with keywords (Diabete) and (Cell therapy).

Results: T١D is characterized by beta cell destruction as a result of autoimmune defect, while T٢D pathogenesis involves the development of insulin resistance in the insulin-target tissues followed by beta cell dysfunction due to a combination of genetic and environmental factors. Since twenty years ago, intraportal allogeneic cadaveric islet transplantation has been shown to be a useful treatment for patients with type I diabetes (T١D). Despite positive results, the impact of islet transplantation is limited due to a number of confounding issues, including limited availability of cadaveric islets, lifelong dependence on immunosuppressive drugs, and lack of coverage of transplant costs by health insurance companies in some countries. has been In some countries, despite improvements in immunosuppression, the number of islets required is still high, and more than two or more donors are needed per patient. Insulin independence is usually achieved with islet transplantation, but on average only ٢٥٪ of patients do not require exogenous insulin injections five years later. For these reasons, the implementation of islet transplantation is almost exclusively limited to patients with fragile T١D who cannot avoid hypoglycemic events despite optimal insulin therapy. Mesenchymal stem cell transplantation is effective for T٢D patients, but the ability of mesenchymal stem cells to differentiate into functional β-cells in vitro is poor and international differentiation does not seem to occur in vivo. Instead, to address supply-related limitations, β-cells derived from human embryonic stem cells (hESC) are being explored as a surrogate for cadaveric islets.

Conclusion: Our purpose about this research is studying about Cell therapy in diabetic and we got good points. Stem cell therapy is effective to treatment diabetes and it is better than other ways.

Keywords: cell therapy, Stem cell, Type ١ diabetes

The role of circular RNA as a potential diagnostic and novel biomarker for ovarian endometriosis (Review)

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Introduction: Endometriosis is a gynecological disorder characterized by tumor-like biological behaviors. In this disease, tissue similar to endometrium grows outside the uterine cavity and invades nearby organs such as the ovaries, bladder, colon, or pelvic peritoneum. Endometriosis has been reported in ١٠٪ of women of reproductive age, with a peak between the ages of ٢٥ and ٣٥ years.

Methods: For this review, medical sciences electronic databases like PubMed and Google Scholar were searched for studies published between February ٢٠٢٠ and July ٢٠٢٤. The main keywords were "Endometriosis," CircRNAs "," Biomarker "," and "Diagnosis." Thirty-four quantitative and qualitative studies were included.

Results: Laparoscopy, as the gold standard for diagnosing this disease, may not be effective for all women suspected of endometriosis, and may result in high costs and many side effects for the patient. Also, ultrasound, as a cost-effective, non-invasive diagnostic tool, is significantly dependent on the skill and expertise of the operator. In addition, other non-invasive methods do not have high accuracy and efficiency. Therefore, to diagnose endometriosis early, there is an urgent need to develop other non-invasive diagnostic methods with high sensitivity and specificity, including the use of biomarkers. Some characteristics of circRNAs have made them suitable and practical options as diagnostic biomarkers in this disease. This type of noncoding RNAs cannot be easily degraded by exonucleases, and due to their high copy number and stable structure, they have been widely identified in eukaryotic cells, and they can be found in blood and various body fluids such as saliva, urine, and vaginal fluid.

Conclusion: In this review, we summarize the biogenesis, pathogenesis, and biomarker role of circRNAs in endometriosis and also discuss their potential as diagnostic biomarkers with therapeutic targets. Entering a new level in epigenetic regulatory networks is facilitated by circRNA research. Future research can help researchers better understand the regulatory mechanisms of circRNA in the endometrium.

Keywords: Endometriosis; circRNAs; biomarker; diagnosis.

The Role of Circular RNAs in Chemoresistance of Gastric Cancer: Mechanisms and Therapeutic Potential (Review)

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Introduction: Chemoresistance remains a significant challenge in the treatment of gastric cancer, leading to poor patient outcomes. Circular RNAs (circRNAs) have recently emerged as crucial regulators of chemoresistance. This review aims to explore the mechanisms by which circRNAs contribute to chemoresistance in gastric cancer and to discuss their potential as therapeutic targets.

Methods: A comprehensive literature review was performed using databases such as PubMed, Scopus, and Web of Science. Studies focusing on the involvement of circRNAs in gastric cancer chemoresistance were identified, and relevant data were extracted and synthesized.

Results: CircRNAs significantly contribute to chemoresistance in gastric cancer through various mechanisms. For instance, circRNA CDR١as contributes to cisplatin resistance by sponging miR-١٣٨-٥p and upregulating EZH٢. Similarly, circ_٠٠٠٦٥٢٨ enhances ٥-fluorouracil resistance by sponging miR-٧-٥p and upregulating EGFR expression. CircAKT٣ mediates doxorubicin resistance through miR-١٩٨ sponging and subsequent upregulation of PIK٣R١. Additionally, circRNA_١٠٠٢٦٩ reduces cisplatin sensitivity by acting as a miR-٦٣٠ sponge, resulting in increased IGF١R expression, while circ_٠٠٢٦٣٥٩ promotes oxaliplatin resistance via sponging miR-١٢٠٠ and upregulating FOXM١. Beyond miRNA sponging, circRNAs can modulate drug transporters and apoptosis pathways. For example, circABCB١٠ is involved in drug resistance by upregulating ABCB١٠ transporter expression, enhancing drug efflux. CircMCTP٢ contributes to chemoresistance by inhibiting apoptosis through the regulation of the Bcl-٢/Bax ratio. CircRNA_١٠١٢٣٧ has been shown to activate the Wnt/β-catenin signaling pathway, leading to enhanced cell survival and drug resistance. Additionally, circRNA_١٠٤٩١٦ mediates resistance by promoting autophagy, allowing cancer cells to survive under chemotherapeutic stress. These diverse mechanisms underline the critical role of circRNAs in gastric cancer chemoresistance.

Conclusion: CircRNAs play critical roles in mediating chemoresistance in gastric cancer through mechanisms such as miRNA sponging and modulation of key signaling pathways. Understanding these mechanisms provides insights into potential therapeutic strategies to overcome chemoresistance. Targeting circRNAs may offer a promising approach to enhance the efficacy of chemotherapy in gastric cancer patients.

Keywords: Circular RNAs, Chemoresistance, Gastric Cancer, miRNA Sponging.

The Role of Digital Health in Combating Infectious Diseases (Review)

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[1].

Introduction: Infectious diseases continue to pose significant global health challenges, exacerbated by factors such as population growth, urbanization, and global travel. Digital health technologies have emerged as powerful tools in the fight against infectious diseases, offering innovative solutions for prevention, diagnosis, treatment, and management. This systematic review aims to evaluate the impact and effectiveness of digital health interventions in combating infectious diseases. Objectives: The primary objective of this systematic review is to synthesize existing evidence on the role of digital health technologies in combating infectious diseases. The review focuses on identifying key digital health interventions, assessing their effectiveness, and exploring the contextual factors that influence their implementation and outcomes.

Methods: A comprehensive literature search was conducted across multiple databases, including PubMed, Scopus, IEEE Xplore, and Web of Science, to identify relevant studies published between January ٢٠١٠ and December ٢٠٢٣. Inclusion criteria encompassed peer-reviewed articles, randomized controlled trials, cohort studies, and qualitative research that evaluated digital health interventions targeting infectious diseases. Data extraction and quality assessment were performed independently by two reviewers, with discrepancies resolved through consensus

Results: The review identified ٦٠ studies meeting the inclusion criteria. Digital health interventions were categorized into five main types: telemedicine and telehealth services, mobile health (mHealth) applications, electronic health records (EHR) systems, digital surveillance and tracking tools, and artificial intelligence (AI) and machine learning applications. Telemedicine and telehealth services were found to improve access to care and patient outcomes, particularly in remote and underserved areas. mHealth applications demonstrated effectiveness in enhancing disease surveillance, patient education, and medication adherence. EHR systems facilitated better data management and coordination of care. Digital surveillance and tracking tools enabled early detection and response to outbreaks. AI and machine learning applications showed promise in predicting disease patterns and optimizing treatment protocols.

Conclusion: Digital health technologies play a crucial role in combating infectious diseases by enhancing prevention, diagnosis, treatment, and management. Future efforts should focus on addressing implementation challenges, fostering cross-sector collaborations, and ensuring equitable access to digital health tools. Continued research and innovation are essential to leverage the full potential of digital health in the global fight against infectious diseases.

Keywords: infectious diseases public health Digital health

The Role of Dihydrotestosterone in the Pathogenesis of Prostate Cancer: A Review of Molecular Mechanisms and Proposed Therapeutic Approaches (Review)

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Introduction: According to the statistics of the World Health Organization (WHO), cancer is one of the main causes of death in the world. In this study, we pay special attention to prostate cancer and the effect of Dihydrotestosterone (DHT) on its pathogenesis. Androgens such as testosterone and DHT are an important stimulus in the growth and development of prostate cancer, however, the molecular mechanisms involved in this process are not yet fully understood. In this study, we describe the molecular mechanisms of DHT in the pathogenesis of prostate cancer and examine the current therapeutic challenges in this field.

Methods: In order to collect useful materials and studies, it was conducted an extensive search in "PubMed" and "Google Scholar" databases and identified ٢١ articles that were most relevant to our topic.

Results: The development and persistence of prostate cancer is mainly related to the high expression of androgen receptor (AR) and its dysregulation. Testosterone is released from the gonads into the blood and converted to ٥α-DHT by steroid-٥α reductase (SRD٥A) in prostate cancer, which promotes tumor growth by activating AR. Advanced prostate cancer is inhibited in the early stages by reducing the concentration of testosterone in the gonads and usually produces a therapeutic response. Recently, androgen deprivation therapy (ADT) and immunotherapy have been shown to be potential treatment options in men with metastatic prostate cancer (CaP), but androgens are usually suggested as suppressors of the immune response. Also, recent researches have introduced DHT as an increaser of macrophage cytotoxicity, which makes immunotherapy-

based treatments undesirable. Also, recent evidence has shown that androgen deprivation therapy of prostate cancer with estrogen has significant cardiovascular side effects.

Conclusion: Prostate cancer is a multifactorial disease and many endogenous factors are involved in its pathogenesis, therefore, in order to provide a targeted treatment approach, it is important to further analyze the molecular mechanisms and the effects of DHT on the biogenesis of prostate cancer.

Keywords: Dihydrotestosterone; Prostate Cancer; Molecular Mechanisms; Androgen

The role of disulfide bond in the structure of human beta defensin ١: a molecular dynamics simulation study (Research Paper)

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Introduction: Human Beta Defensin١ (HBD١) is a key tumor-suppressing protein expressed in epithelial tissues. Gene expression of this protein is generally stable but can change under inflammatory conditions. The beta-defensin family consists of three members. Beta-defensin ١ has a structure that includes a core of three beta strands connected in an anti-parallel arrangement by intramolecular disulfide bonds. An alpha helix located in the N-terminal region of this protein covers this core structure. Beta-defensin ١ contains conserved motifs (Gly-X-Cys) that likely play a vital role in its stability. The purpose of this study was to investigate the effect of cysteine ٥٩ to alanine mutation on the structure and stability of the protein using in silico molecular dynamics simulation.

Methods: The three-dimensional structure of C٥٩A mutant beta-defensin ١, which lacked the pro-peptide region (amino acids ٢٢ through ٣٢) and the signal peptide (from amino acid ١ to ٢١), was predicted by the AlphaFold tool. Crystal structure of the native protein are listed in the RCSB database (https://www.rcsb.org) under the entries ١E٤S, ١IJV, and ١IJU, and among them, ١IJU was selected as the reference structure for this study. Next, a molecular dynamics simulation was performed using GROMACS software for the native and mutant proteins over the ٥٠-nanosecond. Finally, the RMSD, RMSF, and radius of gyration indices were examined for both proteins.

Results: The results of this simulation were visualized as a graph using R software and indicated a stable RMSD, a general decrease in the radius of gyration, and an increase in the RMSF in several amino acids preceding the mutation target (cysteine ٥٩) in the mutant protein compared to the native one. This provides valuable insights regarding the reduction of the stability of the protein after mutation and the significance of this amino acid in the HBD-١ protein structure.

Conclusion: According to the data obtained from this study, it can probably be concluded that these conserved motifs, and especially cysteine ٥٩, play an essential role in the stability of this protein. It is also expected that mutation in this amino acid will disrupt the structure of this protein, impairing its function. Since this protein plays a tumor suppressor role in some cancers, its mutation may contribute to cancer progression. Further studies at improving the structure and function of this protein could lead to valuable discoveries in the field of cancer treatment.

Keywords: Tumor suppressor, C٥٩A mutation, GROMACS, Stability

The Role of Efflux Pumps in Antibiotic Resistance of Escherichia coli (Review)

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Introduction: Antibiotic resistance has emerged as one of the most significant challenges in healthcare. Among various bacteria contributing to this issue, Escherichia coli, a naturally occurring inhabitant of the human and animal gastrointestinal tract, can lead to severe infections under certain conditions. Several mechanisms contribute to the antibiotic resistance of this organism, with efflux pumps being one of the most critical factors. Efflux pumps are membrane proteins responsible for expelling toxic compounds and antibiotics from within bacterial cells, thereby reducing the intracellular concentration of these drugs and diminishing their effectiveness.

Methods: One of the most notable efflux systems in E. coli is the AcrAB-TolC pump, which enables the bacteria to efficiently extrude a broad range of antibiotics, including tetracyclines, fluoroquinolones, and beta-lactams. This system comprises three components: AcrA and AcrB located in the inner membrane and TolC, which serves as a channel in the outer membrane. It utilizes the proton motive force (PMF) for energy, actively pumping antibiotics out of the cell. To investigate the role of efflux pumps in the antibiotic resistance of Escherichia coli, various laboratory and molecular techniques were employed, as ۱- Determination of Minimum Inhibitory Concentration (MIC): The MIC was assessed in the presence and absence of efflux pump inhibitors. A reduction in MIC in the presence of these inhibitors would indicate a significant involvement of efflux pumps in antibiotic resistance. ۲- The expression levels of the genes AcrA, AcrB, and TolC, which are associated with efflux pumps, were quantified using PCR techniques. An increase in the expression of these genes typically corresponds to a higher level of antibiotic resistance. ۳- The sensitivity of the bacteria to antibiotics was evaluated using the Disk Diffusion Test in the presence of efflux pump inhibitors. This testing can provide insights into the role of efflux pumps in mediating antibiotic resistance.

Results: Efflux pumps not only confer resistance to specific antibiotics but also facilitate multi-drug resistance due to the non-specific nature of certain pumps. For instance, the AcrAB-TolC system can effectively expel various classes of antibiotics, allowing E. coli to develop resistance against multiple pharmacological agents. The increased activity of efflux pumps can lead to reduced concentration of administered antibiotics to levels insufficient for bacterial eradication. The regulation of efflux pump expression is controlled by complex mechanisms involving multiple regulatory factors, such as MarA, SoxS, and Rob, which play critical roles in the induction of these systems. Extensive efforts are underway to combat resistance mediated by efflux pumps. One promising strategy is the use of efflux pump inhibitors.

Conclusion: The combination of antibiotics with these inhibitors is currently under investigation and may contribute to reducing drug resistance in E. coli. In summary, efflux pumps are key players in

the development of antibiotic resistance in E. coli, significantly impacting the efficacy of antibacterial treatments. A better understanding of these systems and the development of novel approaches to mitigate their activity can potentially enhance strategies to control antibiotic resistance and improve therapeutic outcomes.

Keywords: antibiotic resistance, Efflux pump, Escherichia coli

The role of enzymes in cancer (Review)

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Introduction: Enzymes are normally produced by the pancreas to help digest food that enters the small intestine from the stomach. Different types of enzymes work on protein, fats or starch and sugar. With the action of these powerful enzymes, large particles of protein, fat or starch are broken down into smaller and smaller pieces so that they are small enough to pass through the wall of the small intestine and be used in the human body for nutrition.

Methods: On a daily basis, the pancreas of most people produces enough pancreatin to digest the food they eat, and the malignant tumor cells are growing normally. A disease "process" occurs when a person's pancreas is unable to produce enough pancreatin to perform these functions. Which is rightly called cancer. But the question is, how can the enzymes go to the tumor and just digest the cancer, without harming the body of the person where the cancer is growing?

Results: A cancerous tumor needs an enzyme to digest the human organ or tissue in which the tumor is located. It uses human tissue as food. To get the enzyme it needs, the tumor makes its own enzyme. This tumor-made enzyme is called a "malignant" that digests human protein. Pancreatic enzymes contain large amounts of trypsin, which stops tumor growth. In sufficient amounts, trypsin can begin to break down a cancerous tumor, but it does not completely digest the cancerous tumor. The more Malignin is produced by the tumor, the more normal tissue is digested and causes more Malignin to be produced, thus accelerating the growth and expansion of the tumor. Trypsin fights Malignin. Large amounts of trypsin in the bloodstream prevent acceleration of tumor growth by Malignin. Trypsin only digests abnormal tissue cells and food proteins. Trypsin does not attack or digest normal living human cells and proteins.

Conclusion: Finally, the cancer treatment protocol in metabolic medicine can be divided into three areas of health activities: a. Metabolic nutritional supplements. B. Metabolic detoxification program and c. Food procedures.

Keywords: Cancer, detoxification, Trypsin

The role of exosomal circular RNAs and their underlying mechanisms in cancer drug resistance (Review)

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Introduction: Drug resistance has long been a topic in many cancer studies. Despite the efforts and successes in cancer treatment, anticancer drug resistance remains a major problem in the treatment of this disease and has a significant impact on clinical outcomes. Recent studies have highlighted the role of exosomal circular RNAs (circRNAs) as crucial mediators in exerting drug resistance in various cancers. Exosomes are a specialized group of small secretory vesicles found in various body fluids that facilitate cell-cell communication and the exchange of various biological information through the transfer of biomolecules, including circRNAs. circRNAs are a new type of ncRNA with a closed RNA structure that has been shown to play an essential role in controlling various genes and signaling pathways. This review addresses the emerging evidence linking exosomal circRNA to the modulation of drug resistance mechanisms.

Methods: A comprehensive literature search was conducted, focusing on recent studies. Databases such as PubMed, Scopus, Google Scholar, and Web of Science were searched using keywords like "exosomes"," "circRNAs"," "exosomal circRNAs", "tumor microenvironment"," "drug resistance"," "chemotherapy resistance" and "cancer"." The selected studies were thoroughly analyzed to collect information on exosomal circRNAs, their mechanisms of action, the different types of circRNAs involved and their influence on drug resistance. Both in vitro and in vivo research was included to provide a comprehensive overview of the current research landscape.

Results: The analysis revealed that exosomal circRNAs contribute to drug resistance via multiple mechanisms, including modulation of drug efflux pumps, alteration of apoptosis pathways, regulating cell cycle and controlling autophagy. For example, overexpression of circRNA CEP١٢٨ in temozolomide-resistant glioma cells leads to increased drug efflux and reduced intracellular drug accumulation through the upregulation of ATP-binding cassette G superfamily member ٢ (ABCG٢). According to another study, exosomes from oxaliplatin-resistant CRC cells released ciRS-١٢٢, which helps to increase glycolysis to generate more ATP for ABC drug efflux and pump oxaliplatin out of the cells. Furthermore, exosomal circ-PVT١ promoted DDP resistance in gastric cancer cells by modulating autophagy, invasion and apoptosis via the miR-٣٠a-٥p/YAP١ pathway. Additionally, their stability and prevalence in bodily fluids make them as ideal candidates for non-invasive liquid biopsies, revolutionizing cancer diagnostics and patient monitoring.

Conclusion: Exosomal circRNAs represent a novel and critical component in the landscape of anticancer drug resistance. Their capacity to regulate various cellular signaling pathways and affect

gene expression highlights their promise as potential therapeutic targets. Targeting exosomal circRNAs as novel biomarkers or vehicles to deliver therapeutic circRNAs or RNAi molecules could enhance the efficacy of existing treatments and overcome drug resistance. A deeper understanding of the role of exosomal circRNAs in drug resistance not only sheds new light on cancer biology, but also paves the way for new therapeutic strategies. However, further research is needed to fully elucidate their mechanisms and develop strategies to inhibit their function in resistant cancer cells.

Keywords: exosomes, circRNAs, exosomal circRNAs, drug resistance, cancer

The role of Faecalibacterium prasnitzii in gestational diabetes mellitus (Review)

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Introduction: In recent years, the incidence of metabolic disorders has exponentially increased worldwide mainly due to the misfunctioning of chemical reactions. Gestational diabetes mellites (GDM) occurred during pregnancy when placenta prevent absorption of sufficient insulin in mother's body. Although this disorder usually disappears after delivery, it could raise the probability of developing complications in the future. In this review, we focus primarily on some causes and effects of GDM in pregnant women and then Faecalibacterium prasnitzii, the most abundant butyrate-producing bacterium in gut, which have been using as a prominent biomarker in health and disease and also potential anti-inflammatory treatment owing to production of active molecules

Methods: A PubMed search was conducted using the terms "Faecalibacterium prasnitzii", " Gestational diabetes mellitus," and "Microbiota". Only English articles published within the last five years were included

Results: Consumption of certain species of probiotics could effectively be beneficial for pregnant women and provide long-lasting benefits of health for them by reducing antioxidant and anti-inflammatory compounds released by harmful bacterial genera which are augmented and/or implemented in gut after challenging with GDM during pregnancy

Conclusion: Carrying out some mandatory clinical trials experiments are necessary to afford enough evidence to use this bacterium as a supplementary probiotic throughout pregnancy period

Keywords: Gut microbiota; Faecalibacterium prasnitzii; Gestational diabetes mellites

The Role of gold nanoparticles in the detection of sperm protamine levels as a biomarker of male infertility (Research Paper)

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Introduction: Approximately ٤٠-٥٠٪ of infertilities is related to males. Abnormal sperm chromatin structure is suggested as a significant cause of infertility. Protamines constitute a significant component of the sperm chromatin, and they play a vital role in the proper packaging of chromatin. The study, experimentally was designed to explore direct clinical naked eye colour -metric of semen protamines, the biochemical marker of male fertility, using heparin gold nanoparticles (HAuCl٤ NP)

Methods: The method is easy prices, cheap and reliable primer indication. The gold nanoparticle prepared by reducing via hepronization under heating yield red colour solution; the size of nanoparticle ranged from ١٥-٢٠ nm in checked by electronic microscope micrograph. The binding of HAuNPs to protamine was characterized by variation in the plasmon absorption spectra followed by a visibly observable colour change of the solution from red to blue

Results: We observed a red shift in the plasmon peak and the method exhibited linearity in the range of ١٠–١٠٠ng/mL with a detection limit of ٥ ng/mL, which is much lower than that reported for colorimetric sensors of protamine. The colour change and the variation in the absorbance of HAuCl٤ NP were highly specific for protamines in the presence of different interfering compounds and the method was successfully applied for determining protamine in semen. Also, the correlation between sperm DNA damage and concentration of protamine was showed

Conclusion: The method appears to be simple and would be very useful for diagnostic aids are inaccessible to the majority of the population

Keywords: Gold nanoparticles. Protamine. DNA. Sperm

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The role of gut microbiome in cancer treatment (Review)

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[1]. Shahed

Introduction: Cancer treatment is one of the important topics in the field of treatment that needs a lot of attention. Paying attention to things that can increase the effect of drugs will be very helpful. The microbiome in the gut is one of the things that can be effective in cancer treatment. This treatment helps the immune system identify and attack cancer cells. However, awareness of the impact of the gut microbiome on cancer treatment outcomes has existed for decades. By analyzing the feces of people with lung cancer and analyzing them, it was determined which group of bacteria people can live longer with. It is also possible to mention the effect of having a proper diet on the gut microbiome.

Methods: Using study research method and searching many sites and reading many articles and choosing relevant and more helpful articles

Results: As a result of this research, it has been determined that what type of microbiome in the gut can be effective in cancer treatment and what type of food can be more effective in the treatment process in each type of cancer.

Conclusion: As a result of numerous researches, although the direct treatment of cancer was not determined, they were able to find out what can be effective in the treatment of cancer and help the immune system. Although

Keywords: Cancer treatment, microbiome, more effective, immune system

The role of HBOT in curing the radiation-related complications after radiotherapy (Review)

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Introduction: Hyperbaric Oxygen Therapy (HBOT) is FDA-approved for late radiation tissue injuries, which increases oxygen delivery to damaged tissue ١٠-١٤ times the standard amount.

Methods: A review were acquired by searching in databases of PubMed, Mdpi, Sciencedirect and ResearchGate.

Results: The HBOT sessions showed reducing pain, fibrosis and other radiation-related complications such as RHC in randomized clinical trials. It also complete remission of hematuria and improve disorders such as hypoxia and ischemia.

Conclusion: This review provides insights into the potential of HBOT. Despite challenges like cost and availability, HBOT is a valuable, low-risk effective treatment for suitable patients.

Keywords: HBOT, RHC, Cancer

The role of herbs in polycystic ovary syndrome (Review)

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Introduction: Infertility is a condition affecting both the male and female reproductive systems, defined by the inability to achieve a clinical pregnancy after a year of regular, unprotected intercourse . Globally, ١ in ٦ individuals will face infertility at some point in their lives. In men, infertility can result from issues like blockages in the reproductive system, hormonal imbalances, or inadequate sperm production in the testicles. Factors contributing to these problems include poor lifestyle choices, heavy smoking and alcohol use, obesity, and exposure to environmental pollutants and toxins. In women, infertility may be caused by conditions like fallopian tube obstruction, uterine issues, ovarian disorders such as polycystic ovary syndrome (PCOS), and problems with the endocrine system. PCOS, also known as Stein-Leventhal syndrome, is a common metabolic disorder that involves hormonal imbalances, leading to hyperandrogenism, insulin resistance, and ovulatory dysfunction. This condition is linked to symptoms such as irregular menstrual cycles, male-pattern hair loss, acne, and weight gain. Individuals with PCOS have an increased risk of fertility problems (such as infertility, premature birth, and stillbirth), metabolic issues (like insulin resistance and type ٢ diabetes), mental health challenges (including depression and anxiety), cardiovascular risk factors (such as high blood pressure and dyslipidemia), and endometrial cancer.

Methods: Relevant articles from PubMed, Google Scholar (from ٢٠٢٠ to ٢٠٢٤), and SID were reviewed using keywords related to plants in the mechanism of PCOS.

Results: The studies indicate that a combination of allopathic treatments, lifestyle changes, and herbal remedies can help manage and treat PCOS . Various herbs, such as flaxseed and licorice, have been found to reduce hyperandrogenism and regulate menstrual cycles due to their therapeutic properties. Research shows that chamomile can improve PCOS by providing anti-inflammatory benefits, alleviating menstrual pain, and treating skin conditions like eczema. Vitex agnus-castus, with its anti-inflammatory properties, can help correct hormonal imbalances related to high estrogen or premenstrual syndrome and improve the balance of sex hormones in animals with PCOS. Studies also suggest that fennel effectively alters endometrial tissue parameters in PCOS by lowering estrogen levels, reducing hyperplasia, and offering anti-inflammatory and antioxidant effects. In PCOS mice treated with fennel, this herb reduced cystic follicles and restored a normal reproductive cycle. Additionally, cinnamon, ginseng, and evening primrose oil have shown promising results in managing PCOS by lowering blood glucose levels.

Conclusion: Medicinal plants can be effective and affordable options for treating PCOS, but it's essential to recognize that they typically require a more extended treatment period. However, arbitrary use of these plants is not recommended, as it could lead to potential side effects and interactions with other medications. Therefore, it's essential to consult a specialist before using these herbal remedies.

Keywords: ١.Infertility ٢.Polycystic Ovary Syndrome ٣. Medicinal plants ٤.Hormones

The role of human anelloviruses in autoimmunity (Review)

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Introduction: Molecular mimicry is one of the primary ways that viral pathogens potentially trigger autoimmunity. This occurs when the similarity between exogenous peptides and self-peptides leads to activation of autoreactive T or B cells. Recent data on the biology of human anelloviruses such as TTV and SEN suggest that they could trigger autoimmune diseases. Anelloviruses are small, single stranded circular DNA viruses. The present study was aimed to evaluate the association between anelloviruses and autoimmunity.

Methods: We searched PubMed. Web of science, Scopus, google scholar to find articles about the role of human anelloviruses in autoimmunity. All studied were collected, studied and analyzed by two researchers.

Results: TTV has been found to be more prevalent in individuals suffering from some autoimmune disorders. Researchers detected TTV in ١٠ of ٨٤ (١٢٪) patients with systemic sclerosis, ٩ of ٤١ (٢٢٪) patients with rheumatoid arthritis, ٣ of ٤٣ (٧٪) patients with osteoarthritis, and ١٦ of ١٢٢ (١٣٪) healthy controls. Researchers for the first time in ٢٠٠٥ reported the frequency of TTV in SLE patients about ٥٧٪, which was statistically higher than the frequency of the virus in healthy people. In a study conducted in Iran, TTV was detected in ٤٣ SLE patients and ٣٣ healthy individuals. A significant correlation was found between SLE and the presence of TTV. In the study conducted in Kashan, TTV was detected in ٤٣ SLE patients (٧٤,١٪) and ٣٣ healthy individuals (٥٦,٩٪). In addition, SEN virus was detected in ٢٦ healthy people and ٣٧ patients with lupus erythematosus (P=٠,٠٣١). In a study conducted in Iran, TTV DNA was detected in ten (١١,١٪) of patients with autoimmune hepatitis, versus four (٤,٤٪) in control group. TTV has been found in patients with rheumatoid arthritis, idiopathic inflammatory myopathy, and multiple sclerosis (MS).

Conclusion: A significant association between anelloviruses and autoimmunity was observed in the previous studies, however further studies are needed to investigate the mechanisms of these viruses in the pathogenesis of autoimmune disorders.

Keywords: human anelloviruses, autoimmunity, autoimmune disorders

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The role of inhibitory control in sustained attention and executive functions in elementary school students (Research Paper)

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Introduction: Executive functions are high-level cognitive functions that regulate thoughts, behaviors, and emotions, crucial for social functions and adaptation. They play a key role in academic performance, particularly in reading comprehension. Various models and theories define executive functions as a structure of multiple cognitive skills that interact and influence behavior. Inhibition, mental flexibility, and working memory are core executive functions. Inhibitory control plays a significant role in daily life. Inhibition rapidly develops in early childhood and has a lasting impact on other components. Various studies have shown that inhibitory control affects other components directly or indirectly. Attentional performance, working memory, and mental flexibility are largely dependent on intact inhibitory performance. However, other studies have emphasized the role of other components, including working memory. The purpose of this study is to investigate the role of inhibitory control on the overall performance of executive functions.

Methods: This study was conducted on ٧٦ students. The sample consisted of ٤١ students in the normal group (age range = ٩ to ١١,٧ years; M = ٩,٨, SD = ٠,٧٧) and ٣٥ students in the inhibitory deficit group (age range = ٩,٢ to ١١,٦ years; M = ١٠,٦, SD = ٠,٦٩). The average IQ in the two groups was ١٠١,٧ and ١٠٥,٤, respectively. Students were assessed using a battery of EF tasks including the Behavior Rating Inventory of Executive Function (BRIEF), forward and backward digit span memory, and continuous performance test.

Results: Multivariate analysis of variance was used to test the hypothesis. The results showed that there is a difference between the impaired inhibition group and the normal group in the components of working memory and planning ($p < ٠,٠١$), but there was no significant difference in attention performance between the two groups mentioned.

Conclusion: According to the results of the research, inhibition defects cause poor performance in the components of working memory and planning. It seems that inhibitory control, as the main component of executive functions, can predict performance in other tasks. This finding is in line with research that has emphasized the role of inhibition. Considering the importance of inhibition control, it will be possible to prepare interventions based on inhibition to help students who have academic weaknesses and dysfunctional executive functions.

Keywords: Inhibitory control, Sustained attention, Executive functions

The Role of miR-۱۳۳b, miR-۱۲۵b, and miR-۳۲۰ in the Pathogenesis of Endometriosis: A Comprehensive Review (Review)

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Introduction: Endometriosis is a chronic, estrogen-dependent, inflammatory disease characterized by the presence of endometrial-like tissue outside the uterine cavity, leading to pain, infertility, and reduced quality of life. MicroRNAs (miRNAs) are small, non-coding RNA molecules that play crucial roles in regulating gene expression and have been implicated in the pathogenesis of various diseases, including endometriosis. This comprehensive review focuses on the role of miR-۱۳۳b, miR-۱۲۵b, and miR-۳۲۰ in the pathogenesis of endometriosis, highlighting their potential as diagnostic and therapeutic targets.

Methods: A systematic literature search was conducted using PubMed, Scopus, and Web of Science databases to identify studies published between ۲۰۱۰ and ۲۰۲۳ that investigated the expression and functional roles of miR-۱۳۳b, miR-۱۲۵b, and miR-۳۲۰ in endometriosis. The search terms included "endometriosis," "miR-۱۳۳b," "miR-۱۲۵b," "miR-۳۲۰," "microRNA," and "pathogenesis." The retrieved articles were screened based on their relevance to the role of these miRNAs in endometriosis.

Results: The review identified several studies that reported altered expression levels of miR-۱۳۳b, miR-۱۲۵b, and miR-۳۲۰ in endometriotic tissues and fluids compared to normal endometrium. miR-۱۳۳b was found to be downregulated in endometriotic lesions, affecting the expression of target genes involved in cell proliferation, migration, and invasion. miR-۱۲۵b was shown to be upregulated in endometriotic tissues, regulating the expression of genes related to inflammation and angiogenesis. miR-۳۲۰, on the other hand, was found to be downregulated in endometriosis, targeting genes involved in cell cycle progression and apoptosis.

Conclusion: This review provides compelling evidence that miR-۱۳۳b, miR-۱۲۵b, and miR-۳۲۰ play significant roles in the pathogenesis of endometriosis by regulating key biological processes such as cell proliferation, migration, invasion, inflammation, and angiogenesis. These miRNAs may serve as potential biomarkers for the diagnosis and prognosis of endometriosis and could be targeted for

therapeutic intervention. Further research is warranted to elucidate the mechanisms by which these miRNAs contribute to the development and progression of endometriosis.

Keywords: Endometriosis, miR-١٣٣b, miR-١٢٥b, miR-٣٢٠, microRNA, pathogenesis, diagnosis, therapy.

The role of mir-١٥١a-٥p in tumorigenesis; A systematic review (Review)

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Introduction: Background: Highly supported microRNAs (miRNAs) are key players in cancer development. Each of these miRNAs may act as an oncomir, a tumor-suppressor, or both in various cancers. Mir-١٥١a-٥p is believed to be one of these miRNAs with diverse roles. We have conducted this systematic review to clarify the role of mir-١٥١a-٥p in formation of various cancers.

Methods: Method and Materials: We searched for existing articles in PubMed, Web of Science, Cochrane, Scopus, and RNAcentral databases up to November ٢٠٢٢. A total of ٢٣ articles were qualified and included in the present systematic review. This review is registered on JBI at https://jbi.global/systematic-review-register. Expression levels, diagnostic and prognostic values, biological processes, and targeted downstream genes are included

Results: Assembled data indicate the expression levels of mir-١٥١a-٥p vary from down- to up-regulated based on the type of the cancer. Its functional role depends on the genetic profile of cancerous tissue. Results mostly point to the oncogenic role of this miRNA in Pituitary adenomas, Acute Myeloid Leukemia (AML), Endometrial, Lung, Barrett's carcinogenesis, Colorectal, Myelodysplastic syndromes, Hepatocellular carcinoma and Breast cancers, as its inhibited targets seem to be controlling several signaling pathways, cell adhesion, and cell cycle. At the same time, tumor-suppressing role has also been observed only in Malignant Pleural Mesothelioma, Central Nerve System (CNS) lymphoma, Chronic Myeloid and Acute Lymphocytic Leukemia. Two types of cancers, prostate and colon, show contradictory results as there are studies supporting both up- and down-regulation in these cancers. Pituitary adenomas, Barrett's carcinogenesis and CNS lymphomas are top cancers diagnosed with mir-١٥١–٥p. However, prognostic feature is only applicable to Lung adenocarcinoma

Conclusion: Based on the present findings and further studies in the future, mir-١٥١a-٥p may be used as diagnostic and prognostic biomarkers or even a therapeutic target in cancer studies. Data Availability Statement: The articles used in this study can be found with the defined search phrase in mentioned databases. A list of selected articles will be available on reasonable requests.

Keywords: Mir-١٥١a-٥p Cancer MicroRNA Biomarker

The role of non-coding RNAs in Ferroptosis (Review)

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Introduction: Ferroptosis, a recently identified form of regulated cell death, has gained attention due to its distinctive biochemical and morphological features. Unlike apoptosis or necrosis, ferroptosis is driven by iron, reactive oxygen species (ROS), and oxidative damage to phospholipids, leading to mitochondrial dysfunction and loss of membrane integrity. This cell death pathway is of interest because its dysregulation is linked to diseases like cancer and neurodegeneration, making understanding its mechanisms essential for therapeutic strategies. Various signaling pathways and molecules regulate ferroptosis, and changes in its regulatory network can contribute to disease progression, especially cancer. Many cancer cells resistant to conventional chemotherapy are sensitive to ferroptosis inducers, suggesting that ferroptosis may inhibit tumor growth. This makes inducing ferroptosis a promising strategy in cancer therapy. Research shows that non-coding RNAs (ncRNAs) regulate ferroptosis either by directly targeting key regulatory molecules or by influencing upstream pathways. These ncRNAs often have tissue- and tumor-specific expression, highlighting their potential as therapeutic targets in cancer treatment.

Methods: The information presented in this review was gathered from various scientific databases, including PubMed, MDPI, ScienceDirect, BMC, NCBI, and Google Scholar. Relevant studies were identified based on their recent publication dates, relevance to the topic, and the provision of experimental or clinical evidence regarding the role of non-coding RNAs in ferroptosis.

Results: Non-coding RNAs (ncRNAs) are diverse RNA molecules that do not code for proteins but perform crucial regulatory functions. In fact, the majority of the mammalian genome is transcribed into ncRNAs. These molecules regulate processes like gene expression and RNA modifications. Based on their size and function, ncRNAs are categorized as short or long ncRNAs, both of which play roles in drug resistance and ferroptosis regulation. MicroRNAs (miRNAs), a type of short ncRNA, regulate gene expression post-transcriptionally by binding to mRNAs and inhibiting their translation. Studies show miRNAs can prevent ferroptosis by reducing iron levels and ROS production. For example, miR-١٣٧ suppresses ferroptosis in cancer by downregulating a glutamate transporter, reducing the production of glutathione, an antioxidant that prevents ferroptosis. Conversely, miR-٧-٥p induces ferroptosis in hepatocellular carcinoma cells by inhibiting GPX٤, an enzyme protecting cells from oxidative stress. Long non-coding RNAs (lncRNAs) are transcripts over ٢٠٠ nucleotides long with diverse functions, including ferroptosis regulation in cancer cells. They interact with DNA, mRNA, miRNAs, and proteins. LncRNAs often exhibit tissue-specific expression, making them relevant for cancer research. For example, lncRNA MALAT١ promotes ferroptosis by increasing pro-apoptotic gene expression and activating the NF-κB pathway. LINC٠٠٣٣٦ prevents ferroptosis in lung cancer, contributing to tumor survival, while P٥٣RRA induces ferroptosis by releasing the tumor suppressor

protein p٥٣. Circular RNAs (circRNAs), a newly discovered type of ncRNA, form stable loops that resist degradation. Studies show that circRNAs regulate ferroptosis by acting as miRNA sponges in cancer cells. Like lncRNAs, circRNAs are tissue-specific, and their stability enhances their therapeutic potential. CircRNA PVT١ promotes resistance to ferroptosis in cancer by increasing SLC٧A١١ expression, a key regulator of the anti-ferroptosis pathway, while circ-TTBK٢ in gastric cancer prevents ferroptosis by inhibiting miR-٣٧٦a and upregulating SLC٧A١١.

Conclusion: Several ncRNA-based therapies are in development, though most are still in clinical trials. One of the primary challenges with ncRNA therapies is their specificity, delivery, and tolerability, as ncRNAs are unstable and difficult to deliver intracellularly. However, advances in RNA therapy design are addressing these issues, making clinical use more feasible. Targeting ncRNAs may offer a new therapeutic option for overcoming drug resistance and modulating ferroptosis in cancer therapy. In conclusion, ferroptosis is a promising form of regulated cell death with potential therapeutic applications, particularly in cancer treatment. Its ability to suppress tumor growth makes it an exciting avenue for anti-cancer strategies. NcRNAs, through their regulation of ferroptosis, are critical in this process, highlighting their therapeutic importance. Despite challenges in delivering ncRNA-based therapies, recent advances provide hope for their future use. Further research into ferroptosis and ncRNAs could lead to innovative treatments for cancer.

Keywords: Ferroptosis, Non-coding RNAs, miRNA, lncRNA, Cancer

The role of platelet derived exosomes in regenerative medicine (Review)

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Introduction: Exosomes are a group of extracellular vesicles that are released from the membrane of every live cell. They are ٣٠-١٠٠ nanometers in diameter[١]. Exosomes are found naturally in body fluids such as blood, saliva, milk, urine, etc.; for this reason, they can be effective in both paracrine and endocrine ways[٢]. Based on this, it can be said that exosomes are involved in biological activities such as homeostasis, coagulation, inflammation, angiogenesis, removal of unnecessary proteins and mRNA, and pathological activities such as cancers and infections[٣-٥]. A large part of blood exosomes are derived from platelets. They are released from platelets as a result of high shear stress, platelet activation under the influence of agonists, or apoptosis[٦]. They have a cup-like structure. Their surface is rich in exosome diagnostic markers such as CD٩ , CD٦٣. It also has platelet markers such as GPs GP IIb/IIIa, GP Ib/V/IX)[٧-١٠]. Platelet exosomes are rich in growth factors . The use of platelet exosomes does not have side effects such as immunogenicity and tumorigenesis[٧-١٤]. Various studies have been conducted on the effectiveness and usefulness of exosomes derived from platelets in regenerative medicine.

Methods: Based on the articles in PubMed and Google Scholar databases, this review has briefly examined the role of platelet exosomes in regenerative medicine.

Results: Platelet exosomes have the ability to store and transport important biomaterial such as the compounds found in platelet granules, as well as drugs. For this reason, they have received much attention in regenerative medicine. Platelet exosomes play a very strong and important role in various branches of regenerative medicine, such as wound healing and angiogenesis, nerve cell regeneration, musculoskeletal damage repair, and hair loss treatment

Conclusion: The results of this study show that these micro particles have low immunogenicity, low thrombogenicity, and they are very useful and efficient in regenerative medicine

Keywords: Exosomes; Growth factors; Platelets; Regenerative medicine

The Role of potential lncRNA and miRNA in the Regulation of TP۵۳ Gene in Glioblastoma disease through bioinformatics study (Research Paper)

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Introduction: Glioblastoma (GBM) is among the deadliest tumors affecting the central nervous system (CNS) in adults. This type of primary brain tumor is known as the most aggressive, with a highly unfavorable prognosis in cases of recurrence and limited effective treatment options. One of the most common changes in human cancers is the occurrence of somatic mutations in the TP۵۳ gene. This gene encodes the p۵۳ protein, which functions as a tumor suppressor and plays a key role in various biological processes, including cell cycle arrest, senescence, apoptosis, autophagy, metabolism, and aging. The inactivation of the p۵۳ tumor suppressor gene is a common event in cancer development, often resulting in a mutant protein that accumulates in cancer cells. These mutant proteins not only lose their tumor-suppressing functions but also gain oncogenic properties, promoting cell growth and survival. The aim of this study was to identify potential molecular biomarkers, including lncRNAs and miRNAs, that contribute to the early diagnosis of GBM, providing insight into novel therapeutic targets.

Methods: The GEO database was used for searching the best GEO datasets associated to GBM, and the data from two selected groups (Tumor vs. Control) were analyzed through GEO۲R. Based on the data from the GSE۱۸۶۰۵۷ dataset in the GEO Database, the The TP۵۳ gene pathway was analyzed using the KEGG and the interaction of involved proteins were analyzed in STRING databases. Associated miRNAs were identified using the miRWalk database. The interaction between miRNA and single nucleotide polymorphism (SNP) was assessed through the miRNASNP database. In addition, DIANA Tools database was conducted to reveal the interaction between miRNA and long non-coding RNA (lncRNA).

Results: According to the data from the GSE۱۸۶۰۵۷ dataset, TP۵۳ gene was identified as having significant expression changes in GBM, and is considered one of the key genes involved in this disease. TP۵۳ exhibited significant expression changes in tumor samples compared to control ones, highlighting its critical role in contributing to glioblastoma. The miRWalk database gave the most potential microRNA, hsa-miR-۹۲a-۱-۵p, in regulation of TP۵۳ gene expression, which can contribute to glioblastoma. This miRNA was selected based on its high number of base pair interactions and low binding free energy. Based on the data analysis in the miRNASNP database, rs۸۹۰۲۳۱۹۰۰ was identified as the most relevant SNP interacting with hsa-miR-۹۲a-۱-۵p. According to the analysis in the DIANA Tools database, lncRNA CASC۲ interacts with hsa-miR-۹۲a-۱-۵p in brain tissue, suggesting its role in the molecular regulation of glioblastoma.

Conclusion: In conclusion, this study identified TP٥٣ gene, hsa-miR-٩٢a-١-٥p miRNA, SNP rs٨٩٠٢٣١٩٠٠, and lncRNA CASC٢ as potential biomarkers for GBM through bioinformatics analysis. These biomarkers may play crucial roles in the molecular mechanisms underlying GBM progression and offer promising targets for early diagnosis and therapeutic interventions.

Keywords: TP٥٣, hsa-miR-٩٢a-١-٥p, rs٨٩٠٢٣١٩٠٠, CASC٢, Glioblastoma

the role of probiotics in Helicobacter pylori infection Review Article (Review)

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Introduction: Helicobacter pylori (H. pylori) infection is a common bacterial infection that affects the stomach lining and causes various digestive disorders. Symptoms of Helicobacter pylori infection can range from mild discomfort to severe complications depending on the immune response of the person and the type of bacteria involved. Conventional treatment for this infection includes a combination of antibiotics and acid-suppressing drugs. However, the emergence of antibiotic resistance has raised concerns and led researchers to explore alternative methods for managing H.pylori infection. One of these approaches is the use of probiotics. Probiotics have received attention as a potential adjunctive therapy for Helicobacter pylori infection due to their ability to restore intestinal microbial balance and modulate the immune response. Probiotics, when administered alongside antibiotic therapy, can help restore balance by promoting the growth of beneficial bacteria and suppressing the growth of H.pylori. Probiotics may also modulate the immune response to H. pylori infection. They increase the production of anti-inflammatory cytokines while reducing the production of pro-inflammatory cytokines. This immune modulation helps to reduce the inflammation caused by the infection and promotes healing of the stomach lining.

Methods: There is a great deal of variability in the treatment of Helicobacter pylori, which can be attributed to the presence of different probiotics. Probiotics are more effective in addition to antibiotic treatment considering that there is no treatment regimen for the root and antibiotic resistance is the biggest challenge in treatment. When probiotics enter the human body, they produce antimicrobial substances like lactic acid, hydrogen peroxide, and bacteriocin. Lactic acid can suppress the activities of urea from Helicobacter pylori. In addition, the cell membrane and its membrane are damaged by the active species produced by probiotics. that probiotics can increase the production of IgA and strengthen the mucosal barrier against pathogens. Their role against the pathogenicity of Helicobacter pylori includes competition in the microbial adhesion sites and enhancement of immune response. The specificity of glycolipid binding with Helicobacter pylori and probiotics are currently under investigation for their future applications as anti-adhesion drugs in the management of gastric ulcer caused by Helicobacter pylori.

Results: Several clinical studies have investigated the efficacy of probiotics in managing H. pylori infection. Although results have been promising, further research is needed to establish specific strains, dosages, and treatment durations for optimal outcomes. It is important to note that probiotics should not be used as a standalone treatment for H. pylori infection. They are best used as an adjunct therapy alongside conventional antibiotic treatment.The use of specific strains of probiotics, such as Lactobacillus rhamnosus and Saccharomyces boulardii, has shown promising results in improving the eradication rates of H. pylori when used in combination with antibiotics.

Conclusion: Probiotics offer a potential adjunctive approach in the management of H. pylori infection. Their ability to inhibit the growth and adherence of Helicobacter pylori, reduce the inflammatory response and strengthen the intestinal barrier function makes them an attractive option. However, further research is needed to determine the most effective strains, doses and duration of treatment. To ensure safe and effective results, it is essential to consult with a healthcare professional before using probiotics in the management of H. pylori infection.

Keywords: Probiotics, Helicobacter pylori, Treatment, Lactobacillus

The Role of Sialic Acid in Chemotherapy Resistance and GFAP Expression in Glioma Cells (Research Paper)

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Introduction: Glioma, a primary central nervous system tumor, is treated through methods like chemotherapy, radiotherapy, and surgery, but chemotherapy resistance often results in treatment failure and cancer recurrence. Understanding the tumor microenvironment (TME) is critical for addressing drug resistance. Alterations in glycosylation, especially sialylation, help cancer cells evade treatment. Additionally, changes in GFAP expression, a key astrocytoma marker, are linked to chemoresistance. GFAP is expressed in both normal brain tissue and tumors like astrocytoma, and its elevated levels are associated with poor prognosis and resistance to therapy after surgery.

Methods: This study aims to explore the relationship between sialic acid exposure and changes in GFAP gene expression to enhance our understanding of drug resistance mechanisms in glioma. The ١٣٢١N١ cell line was cultured under standard conditions and treated with ٥٠٠ and ٣٠٠ µM sialic acid for ٤٨ and ٧٢ hours, respectively. GFAP gene expression was then evaluated using real-time PCR analysis.

Results: The analysis revealed a significant increase in GFAP expression in cells treated with sialic acid compared to control cells. Elevated GFAP levels, which are associated with astrocytoma, may contribute to uncontrolled cancer cell proliferation and drug resistance.

Conclusion: Sialic acid, crucial for cancer growth, promotes cellular expansion and drug resistance by enhancing GFAP expression. Targeting sialic acid content, possibly through vaccine development, holds promise for improving glioma treatment. This study provides important insights into the theoretical and experimental mechanisms of sialic acid in glioma cells, offering potential therapeutic targets for glioma management.

Keywords: Giloma, Tumor microenvironment (TME), Sialic acid, GFAP, Chemoresistance,

The Role of Small Nucleolar RNAs in Hematologic Malignancies: A Review of Targeted Diagnostic Approaches in Lymphoma and Leukemia (Review)

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Introduction: Blood Cancer is the ٤th most common cancer in men and women and has been a growing concern in the past decade. Also, blood cancers (leukemia, lymphoma, and multiple myeloma) have extensive symptoms that are difficult to diagnose and are often diagnosed late. Lymphoma and leukemia are deadly blood cancer syndromes, both of which are associated with the damage and increase of immature lymphocytes, monocytes, neutrophils, and eosinophil cells, so paying attention to early detection approaches is of great importance. In this study, we describe the Small Nucleolar RNAs (snoRNAs) family and evaluate their role in the early diagnosis of leukemia and lymphoma.

Methods: In order to ensure the integration of the latest developments in this field, it was conducted an extensive search of the PubMed and Google Scholar databases from ٢٠٢٢ to ٢٠٢٤ and identified ٢١ articles that were most relevant to the topic of our paper.

Results: snoRNAs are non-coding molecules (ncMolecules) of different sizes, whose length usually varies between ٦٠-٣٠٠ nucleotides. The snoRNAs family includes ٣ categories of “box H/ACA snoRNAs”, “box C/D snoRNAs” and “Small Cajal body-specific RNAs (scaRNAs)”. These snoRNAs are involved in ribosomal biogenesis, processing of ribosomal RNAs (rRNAs), processing of messenger RNAs (mRNAs) and production of small RNAs (sRNAs) such as MicroRNAs (miRNAs). Also, it has been found that snoRNAs have a potential role in hematopoiesis and malignant hematopoietic conditions, including leukemia, lymphoma, and multiple myeloma. snoRNAs often show a different expression pattern in various blood malignancies. Recent researches, associate the abnormal expression of snoRNAs with inhibition of apoptosis, uncontrolled cell proliferation, angiogenesis and metastasis. This shows that snoRNAs can be investigated as potential biomarkers for the diagnosis of lymphoma and leukemia. Also, their participation in ribosomal biogenesis and production of miRNAs can be indirectly related to the recurrence and suppression of lymphoma and leukemia through the development or suppression of the expression pattern of many oncogenes.

Conclusion: Development of studies in the field of diagnostic approaches of snoRNAs in human cancers, due to their potential role in the biogenesis of many RNAs involved in gene expression pathways such as mRNA, rRNA and miRNA, as well as their different expression patterns in various blood malignancies, can help the emergence of new early detection approaches for lymphoma and leukemia.

Keywords: Blood Cancer; Lymphoma; Leukemia; Diagnosis; snoRNAs

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The role of stem cells and cancer stem cell metabolism in cancer treatment (Review)

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Introduction: Cancer stem cells (CSC) have a high ability to cause tumors in tissue and other body organs. These cells cause the creation of cancerous masses, which are made up of different cells, and this causes the protection and improvement of the characteristics of cancer cells. Cancer stem cells that create tumor cells through multiple divisions, and these cells are genetically and metabolically different, so that in these cells, we see a change in cell signaling pathways and even receiving energy. With these changes, the process of cancer treatment, including chemotherapy, has faced challenges, and the resistance of cancer stem cells to treatment causes the recurrence of cancer and the failure of treatment.

Methods: Therefore, this study was conducted as a review of scientific databases from ٢٠١٥ to ٢٠٢١ to investigate the role of these metabolic pathways and the use of stem cells in cancer treatment.

Results: Stem cells, which have the ability to self-generate and produce new cells, can be considered as a complementary treatment, but even so, these cells have challenges in facing cancer.

Conclusion: Finally, we have a long way to go to reach a complete strategy and treatment for cancer treatment, and the probability of failure in clinical trials is still high.

Keywords: Cancer stem cell, Stem cell, Cancer

The role of vitamin D supplements in prevention of atherosclerosis: a narrative review (Review)

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Introduction: Atherosclerosis is a chronic inflammatory condition characterized by the accumulation of lipids, inflammatory cells, and fibrous elements in the arterial walls, leading to plaque formation and vascular narrowing. It is a leading cause of cardiovascular diseases, including myocardial infarction and stroke, which are the primary causes of morbidity and mortality worldwide. Traditional risk factors for atherosclerosis include hyperlipidemia, hypertension, diabetes mellitus, smoking, and a sedentary lifestyle. Recent research, however, has also highlighted the potential role of vitamin D deficiency as an independent risk factor for the development and progression of atherosclerosis. Vitamin D, a fat-soluble vitamin primarily synthesized in the skin upon exposure to sunlight, is well-known for its role in calcium homeostasis and bone metabolism. Nonetheless, emerging evidence suggests that vitamin D also possesses cardiovascular protective properties, including anti-inflammatory, anti-proliferative, and immunomodulatory effects.

Methods: A comprehensive literature search was conducted using PubMed, Cochrane Library, and Scopus, focusing on studies published in the last ١٥ years. Search terms included "vitamin D," "atherosclerosis," "cardiovascular disease," "supplementation," and "endothelial dysfunction." Observational studies, randomized controlled trials (RCTs), and meta-analyses were included to evaluate the effects of vitamin D on atherosclerosis and related markers.

Results: Several observational studies have reported an inverse relationship between serum ٢٥-hydroxyvitamin D [٢٥(OH)D] levels and the risk of atherosclerotic cardiovascular disease (ASCVD). Low levels of vitamin D have been associated with increased prevalence of hypertension, diabetes, and dyslipidemia, which are known contributors to atherosclerosis. Vitamin D is hypothesized to exert its protective effects against atherosclerosis through multiple mechanisms. These include the modulation of the renin-angiotensin-aldosterone system, reduction of pro-inflammatory cytokines such as interleukin-٦ and TNF-α, and improvement of endothelial function by enhancing nitric oxide (NO) availability. Evidence from RCTs, however, remains inconclusive. Some studies have demonstrated that vitamin D supplementation significantly reduces surrogate markers of atherosclerosis, such as carotid intima-media thickness and coronary artery calcium scores. These findings are particularly evident in individuals with severe vitamin D deficiency or those with coexisting cardiovascular risk factors. For example, trials involving patients with chronic kidney disease, a population prone to both vitamin D deficiency and accelerated atherosclerosis, have shown that vitamin D analogs can improve vascular health markers. However, other RCTs, especially those involving general populations or those without significant baseline deficiency, have reported minimal to no impact on these markers, leading to mixed conclusions. These discrepancies may arise from variations in study design, including differences in baseline vitamin D status, dosage and formulation of supplementation, study duration, and the presence of other risk factors. Some studies suggest a threshold effect, where only those with critically low vitamin D levels derive

significant benefit from supplementation, while others propose that very high doses may not confer additional protective effects and could even be harmful.

Conclusion: While there is a biological plausibility and some clinical evidence supporting the role of vitamin D in reducing atherosclerotic risk, the data from RCTs remain inconsistent. These mixed results underscore the need for larger, well-designed trials that stratify participants by baseline vitamin D levels, comorbid conditions, and other relevant factors. Future research should focus on determining optimal dosing regimens, identifying populations that would benefit most from supplementation, and clarifying the molecular mechanisms through which vitamin D affects the atherosclerotic process. Until such data are available, it may be prudent to consider vitamin D supplementation on an individual basis, particularly in those with documented deficiency and elevated cardiovascular risk. Given the global burden of atherosclerosis and its complications, integrating vitamin D status into cardiovascular risk assessment could represent an additional strategy in preventive cardiology.

Keywords: Atherosclerosis, Vitamin D, supplement, ASCVD

The seminal plasma exosomes concentration as a potential marker in Varicocele men (Research Paper)

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Introduction: Background: Varicocele-associated stressors, such as hypoxia and heat, can damage cell function and viability, and some exosomal biomarkers released from impaired cells may reflect the cell status in testis. The purposes of this study investigate the seminal plasma exosomes on sperm function sperm function in varicocele patients.

Methods: Methods: Normozoospermic, and varicocele men (men٢٥–٤٠ years of age) were considered for the study. Seminal plasma was collected and processed to separate spermatozoa and exosomes. Exosome uptake by spermatozoa was monitored by means of Bradford and flow cytometry. The effect of exosomes on spermatozoa was determined by evaluating sperm parameters According to the World Health Organization criteria (WHO) (٢٠١٠).

Results: Results: We isolated and characterized exosomes from seminal plasma of Normozoospermic, varicocele patients. Exosomes concentration derived from varicocele significantly was decreased than normozoospermic individuals ($p < ٠,٠٥$). The current study showed a statistically significant highly positive correlation in Exosomes concentration with sperm count, motility, normal morphology, and viability. However, it shows significant negative correlation with sperm DNA fragmentation ($p < ٠,٠٥$).

Conclusion: Conclusions: These findings provide evidence that exosomes in seminal plasma can effect on sperm quality. In the future, Seminal exosome may be a novel, sensitive, and non-invasive biomarker of Sertoli cell damage in Varicocele.

Keywords: Key Words: Exosomes, seminal plasma, sperm quality, varicocele.

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The State of the Art of Smart Biomaterials and Nano-carrier in Targeted-Cancer Therapy and Gene Delivery (Review)

S.Negin Hosseini,[1] Mehdi Atari,[2,*]

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Introduction: Cancer is the leading cause of death globally and a major barrier to life expectancy. Traditional methods, including gene therapy, have been explored, but smart biomaterials and nanomedicine have improved cancer treatment and diagnosis. These intelligent biomaterials and nano-carriers can be adapted for environmental cues, impacting immunotherapy, regenerative medicine, and targeted cancer therapy. Nanocarrier-based systems are widely used in cancer imaging, diagnostics and therapies due to their potential to improve therapeutic efficacy. Their self-assembled properties, including size, shape, charge, and surface area, make them ideal for gene delivery. Peptides can be employed in non-viral gene delivery methods to overcome biological barriers.

Methods: Utilizing nanotechnology, biomimetic design, and targeted delivery techniques made advanced biomaterials used for cancer therapy. Sustainable solutions may benefit from the use of these smart biomaterials. The development of surface-modified or functional materials, non-viral gene delivery vectors, and nanocarriers (NCs) has progressed quickly, offering more precise immune regulation for cancer patients. A target gene is inserted into a host cell during gene therapy, thereafter the gene becomes a part of the genetic makeup of the host cell. However, host disease may be exacerbated by the gene's expression. Important clinical advances have resulted from improvements in infusion procedures, safety, efficacy, and research.

Results: Tumor cells are aberrant cells with a dense, acidic, and hypoxic microenvironment allowing them to renew quickly. Cancer therapy provided by smart nanomaterials, has become active in response to particular stimuli such as pH, temperature, enzymes, or biological molecules. Scholars concentrate on the latest developments in smart NCs, including drug targeting, surface-decorated smart NCs, and stimulus-responsive cancer nanotherapeutics that react to redox, pH, enzyme, and temperature stimuli. Surface modification approaches and nano-formulation fine tuning are required to overcome negative effects and improve NCs properties. Stable, biodegradable, non-toxic, and releasable medications for prolonged therapy are characteristics of smart NCs delivering stimuli-responsive genes. Because of their efficient protection, extended blood circulation, selective distribution, and controlled release of nucleic acid medicines, NCs hold great promise to be used in gene therapy. When compared to traditional procedures, smart nanomaterial-based cancer theranostic treatments exhibit reduced side-effects and increased selectivity and sensitivity. In order to cause apoptosis in cancer cells, Zhang et al. extracted neutrophil exosomes (membrane-bound extracellular vesicles with specific roles) and altered them using superparamagnetic iron oxide nanoparticles (SPION-Ex). These characteristics make them perfect as treatment of diseases, controlled drug release uses, and biosensors.

Conclusion: Due to its high efficacy and selectivity, gene therapy is a promising oncology strategy that overcomes the drawbacks of conventional small-molecule medications. It can treat illnesses one-time and deal with the underlying cause. The development of smart materials, however, unlocks the potential for stimuli-responsive building blocks, biosensors, scaffolding materials, and regenerative medicine. Non-viral gene therapy vectors, on the other hand, require carriers for cellular delivery. Notwithstanding these developments, a significant barrier to clinical application is the absence of reliable and efficient delivery vectors. The potential for tumor-targeted medication delivery by smart materials is enormous; but, in order to fully realize this promise, scientists, physicians, and industry partners must work together to overcome obstacles like scalability, stability, regulatory concerns, and cost-effectiveness. Creating useful vectors to enhance nucleic acid medication delivery for gene therapy is the main goal. Although safety issues such as possible skin irritation and inflammation still exist. Stimulus-responsive nanopolymers have recently been used in lab-on-a-chip systems, which has resulted in lower test numbers, expenses, reagents and time usage. Although the field of cancer immunotherapy is still in its infancy, smart nanoparticle-based platforms have demonstrated a considerable increase in therapeutic efficacy and a decrease in side effects when compared to traditional treatments. Appropriate tumour models must be created, and size, surficial charge, hydrophobicity, shape, and PEG chains must all be taken into account. With their ability to achieve precise targeting, increased solubility, and reduced toxicity, nanocarriers are predicted to make a substantial contribution to the treatment of cancer and improve the effectiveness of therapies and diagnosis in upcoming clinical cancer nanomedicine. The design of synthetic vectors may result from research into structure-function correlations and the functionalities of biomaterials. This could transform medical practices by introducing exogenous gene delivery methods and increasing the clinical use of gene therapy.

Keywords: Biomaterials, Gene delivery, nonviral vectors, nanocarriers, Targeted cancer Therapy

The study of the Modulation of collagen alignment by stem cells in mechanical properties of wound healing (Research Paper)

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Introduction: Recently, the use of random flaps has become widespread in the field of plastic surgery. With the clinical application of random flaps in plastic surgery, skin defects can be improved in terms of aesthetics and functionality. With the development of regenerative medicine, stem cell therapy is a promising way to increase regeneration and accelerate tissue healing in chronic wounds. Our objective in this study was to determine the effect of bone marrow stem cells on the modulation of collagen formation in improving the mechanical properties of wound healing in male albino Wistar rats.

Methods: Twenty male albino Wistar rats with an average weight of ٢٥٠-٣٠٠g were used in this research. Also, five rats of the same breed weighing ٣٠ to ٤٠ grams were used to extract bone marrow cells. The animals were divided into two healthy groups without therapeutic intervention and with therapeutic intervention of stem cell injection so there were ten animals in each group. In both groups, day zero was the day of surgery and all the ٢٠ animals underwent surgery. A random skin flap measuring ٣ x ٨ cm was created in the animals' back area, and the results were checked on the ١٤th day in the transitional area.

Results: BMMSC injection increased the survival level and decreased the necrotic wound level, but this improvement was not statistically significant. Also, the infusion of BMMSCs improved the biomechanical properties of wound healing, the increase of which was statistically significant except for energy absorption. However, in terms of the synthesis, content, and arrangement of collagen fibrils, the injection of BMMSCs was ineffective. In the untreated group, there was more collagen and a more organized arrangement in collagen fibrils.

Conclusion: Local injection of BMMSCs did not significantly increase the survival level of random skin flap but improved the wound healing process. Also, the infusion of BMMSCs did not increase collagen content and improve the arrangement of collagen fibrils but significantly improved the biomechanical properties of the wound

Keywords: Regenerative Medicine, Collagen Stem Cells Cell- and Tissue-Based Therapy Wound Healing

The Study of Trans-Anethole in Improving Liver Inflammation via inhibiting NF-κB signaling pathway (Review)

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Introduction: When the body is exposed to different stimuli, the acute inflammatory response, which is characterized by increased vascular permeability and the release of proinflammatory cytokines such as interleukin-1 (IL-1) and tumor necrosis factor-alpha (TNF-a), plays a crucial role in the innate immune reaction. Acute inflammation usually lasts a few hours to several days until the endogenous stimuli are completely scavenged. If this isn't the case, the process will progress to chronic inflammation, which can result in fatal illnesses like multiple sclerosis, liver inflammation, and autoimmune disorders. The liver is an important organ related to the toxicity of the substances introduced into the blood. The aim of this study was The Study of Trans-Anethole in Improving Liver Inflammation via inhibiting NF-κB signaling pathway.

Methods: Scientific databases including Springer, Google Scholar, PubMed, and Science Direct were searched for the current paper, which is titled The Paper of Trans-Anethole in Improving Liver Inflammation by Inhibiting NF-κB Signaling Pathway.

Results: In Chinese traditional medicine, herbal plants are the main source of therapy for many common symptoms of ailments including ulceration and gas, with very few adverse effects. Trans-anethole (TA), an alkenylbenzene molecule, is the primary bioactive ingredient of the volatile oil extracted from anise and fennel seeds. It possesses a variety of bioactivities, such as anti-inflammatory, anti-ulcer, anticonvulsant, and antioxidative properties. Moreover, exposure to light and extreme temperatures can quickly degrade TA. The Food and Drug Administration (FDA) has approved it as safe for use, and its primary applications are in the food, cosmetic, perfume, and medical sectors. TA's anti-inflammatory properties about intestinal, lung, hepatic, and other inflammations have been the subject of numerous investigations. It has also been shown that TA inhibits the inflammatory response by blocking the activation of the nuclear factor kappa B (NF-κB) signaling pathway. Numerous studies frequently use serum ALT and AST activity as indicators for liver damage. A previous study showed that in the endotoxin shock model of mice, the mean levels of AST and ALT activities were elevated. TA supplementation, however, reduced the elevated serum ALT and AST levels. According to the findings, pretreatment with TA reduced the elevated serum ALT levels in mice following hepatic ischemia/reperfusion (I/R), and the elevated ALT levels are linked to the generation of proinflammatory cytokines. It is commonly known that pro- and anti-inflammatory innate immune response pathways depend on the participation of inflammatory cytokines. TNF-α is a type of proinflammatory cytokine that has been linked to various pathogenic processes, including acute lung injury (ALI) and periodontitis. Likewise, IL-1 is a key regulator of the acute phase response, while IL-1β is the most researched member of the IL-1 family secreted from macrophages. On the other hand, by preventing the release of proinflammatory cytokines, IL-10 contributes to

counteracting the inflammatory response. As a result, we measured the liver and serum concentrations of the four main cytokines. The study's findings demonstrated that there were increased levels of TNF-α, IL-٦, and IL-١β in the liver and serum. However, the serum concentrations of TNF-α and IL-١β were lower in those who supplemented with TA.

Conclusion: In conclusion, the hepatocytes' cytosolic and mitochondrial enzymes are called ALT and AST. The direct toxic effect may be the reason for the increase in serum ALT and AST levels, which is indicative of cellular damage in the liver. The levels of aminotransferase were markedly lowered in rats given fennel and TA. Serum aminotransferase levels rise as a result of the release of AST and ALT due to injury to liver cells and disruption of the plasma membrane. Based on histological and biochemical analyses, we proved that fennel and TA decreased liver inflammation and avoided liver damage. Thus, it is possible that fennel and TA prevented hepatocytes from suffering cellular damage, as they were able to lower serum levels of liver enzymes.

Keywords: Trans-Anethole, Liver, Inflammation, NF-κB signaling pathway

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The Use of Biomarkers to Predict Therapeutic Responses in Patients with Type ۲ Diabetes

(Research Paper)

Mojtaba Rashidi Mosleh,[۱,*] Mostafa Karimi,[۲] Dariush Norouzian,[۳]

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Introduction: Type ۲ diabetes mellitus (T۲DM) is a complex metabolic disorder characterized by heterogeneity in treatment response. Identifying reliable biomarkers to predict therapeutic outcomes can improve personalized treatment strategies and optimize disease management. This study investigates the role of biological markers in predicting treatment efficacy in T۲DM patients.

Methods: A systematic review and meta-analysis of clinical and experimental studies were conducted to identify potential biomarkers associated with glycemic control and treatment response. Biomarkers such as HbA۱c, C-peptide levels, inflammatory markers (e.g., IL-٦, TNF-α), and genetic polymorphisms were analyzed. Advanced statistical modeling and machine learning algorithms were employed to assess the predictive value of these biomarkers and their integration into clinical decision-making frameworks.

Results: Key biomarkers, including baseline HbA۱c, fasting insulin, and C-peptide levels, showed significant predictive power for glycemic response to therapies such as metformin, GLP-۱ receptor agonists, and SGLT۲ inhibitors. Inflammatory markers correlated with treatment resistance, while genetic polymorphisms in genes such as SLC۲۲A۱ and TCF۷L۲ influenced drug efficacy. Machine learning models combining multiple biomarkers demonstrated high accuracy in predicting individual patient responses, facilitating the development of tailored treatment plans.

Conclusion: Biomarkers play a critical role in predicting therapeutic outcomes in T۲DM, enabling a shift towards more personalized and precise treatment strategies. Integrating biomarker analysis into routine clinical practice can enhance glycemic control, reduce complications, and improve patient quality of life. Future efforts should focus on validating these biomarkers in diverse populations and incorporating them into accessible diagnostic platforms for widespread clinical use.

Keywords: Biomarkers, Type ۲ Diabetes, SGLT۲

The Use of Biomarkers; A Promising Solution for Diagnosing Endometriosis (Research Paper)

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Introduction: Endometriosis (EM) is a common cause of infertility in women, characterized by an extended period between symptoms onset and diagnosis confirmation. A postponement in diagnosing EM can lead to delayed treatment or inadequate care, potentially increasing the risk of infertility and organ damage. Therefore, it is essential to identify the genes associated with EM to conduct timely diagnoses.

Methods: For this purpose, data were obtained from GSEV٣٠٥, and then a protein-protein interaction network was drawn for genes with log٢FC>١ and adj.P.Val <٠,٠٥. Based on the network obtained from the STRING database, Fibronectin ١ (FN١), C-C motif Chemokine Ligand ٢ (CCL٢), Intercellular Adhesion Molecule-١ (ICAM-١), Apolipoprotein (ApoE) and Chemokine C-X-C motif Ligand ٨ (CXCL٨) genes were recognized as high degree hub genes in EM.

Results: Furthermore, these genes demonstrated higher expression levels in EM compared to the control group in the GEO Profile. An analysis using the Enrichr database indicated that these genes are associated to the EM phenotype. FN١ is a significant angiogenic factor that is essential for ovarian structure and processes such as migration, cell adhesion, growth, and differentiation. Increased FN١ expression correlates with increased cell proliferation indicating that the FN١ gene may play a role in the persistence of EM lesions. A meta-analysis of Single Nucleotide Polymorphisms (SNPs) has demonstrated the link between FN١ and moderate to severe cases of EM. In addition, it has been reported that FN١ expression is increased in EM patients. Various studies have also identified this gene as a potential biomarker for EM and several cancers, including stomach cancer, ovarian cancer, clear cell renal cell carcinoma, and breast cancer. CCL٢ has the potential to directly influence angiogenesis, which may play a role in the development of EM. Studies indicate that CCL٢ serves as a valuable biomarker for prostate cancer and oral squamous cell carcinoma. ICAM-١ is identified as a surface glycoprotein and can be a biomarker for breast cancer and systemic lupus erythematosus. This gene is involved in enhancing adhesion during immune and inflammatory responses and serves as a significant marker for oocyte quality and embryo development. Furthermore, studies suggest that genetic polymorphism in the ICAM-١ gene may influence susceptibility to EM. It has been shown that this gene exhibits high expression levels in endometrial tissues, thereby linking it to the progression of EM severity. ApoE is a multifunctional protein that is a component of high-density lipoprotein and serves as a potential biomarker for various cancers,

including papillary thyroid carcinoma, gastric cancer, and breast cancer. It is the primary source of cholesterol precursors necessary for the synthesis of ovarian estrogen and progesterone, suggesting its significant role in the initiation and progression of EM. Increased levels of APOE in women with EM can contribute to adhesion, endometrial attachment, or invasion thereby exacerbating lesion progression through a self-replicating mechanism. Consequently, increased ApoE levels may be associated with a reduced number of retrieved mature oocytes in older women and an increased risk of spontaneous pregnancy loss in patients suffering from EM. CXCLٱ is produced by various types of cells such as endometrial cells and mesothelial cells. studies indicate that it may serve as a biomarker for several cancers, including breast cancer, gastric cancer, and colorectal cancer. Additionally, CXCLٱ plays a role in promoting angiogenesis, invasion, proliferation, and migration. A study revealed that elevated CXCLٱ levels in follicular fluid and cumulus cells correlate with a decreased number of retrieved oocytes, MII oocytes, and the percentage of oocyte maturation. Furthermore, studies have demonstrated that the expression of CXCLٱ in EM is higher than that in normal endometrial tissue; suggesting a potential involvement of this gene in the induction of EM.

Conclusion: The results suggest that FNٱ, CCLٲ, ICAM-ٱ, APOE, and CXCLٱ genes play a crucial role in the onset and progression of EM. Consequently, these genes may serve as promising non-invasive biomarkers for diagnosing EM. Further research could enhance our understanding of EM mechanisms and expand the diagnostic options available for women suffering from this condition, ultimately alleviating the economic and physical burdens associated with the disease.

Keywords: Endometriosis, Infertility, Biomarker, Diagnostic Panel

The use of Lactobacillus plantarum bacteria to prevent excessive growth of diatom algae In carp breeding ponds in Khuzestan (Review)

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Introduction: This research investigates new methods for controlling the growth of diatom algae (Bacillariophyta) in fish farming ponds. Fish farmers, particularly in Khuzestan, commonly use chlorine (Cl_2) to combat water pollution and excessive algae growth, which is both costly and time-consuming and may harm fish health. The study aims to halt the growth of diatom algae using innovative techniques, eliminating the need to transfer fish to other ponds. This approach allows farmers to improve water quality without incurring high expenses for chlorine and without risking fish mortality. Additionally, the research examines the duration and effects of this new method, with plans to expand its implementation if successful. The ultimate goal is to create better conditions for fish farming by reducing costs and enhancing fish health.

Methods: In this study, Lactobacillus plantarum bacteria were introduced into carp breeding ponds in Khuzestan to inhibit the excessive growth of diatom algae. The method involved isolating and culturing L. plantarum, followed by adding it to the pond water at specific concentrations. Regular monitoring of water quality parameters, including pH, nutrient levels, and diatom density, was conducted over a defined period. The effectiveness of L. plantarum in controlling diatom growth was assessed by comparing treated ponds with control ponds that did not receive the bacteria. This approach aimed to enhance water quality and promote healthier conditions for carp without harmful chemicals.Our idea to cultivate this bacterium is to cultivate the material containing the bacteria (olive) in a medium suitable for the cultivation of acidic bacteria (milk).

Results: The application of Lactobacillus plantarum bacteria in carp breeding ponds in Khuzestan resulted in a significant reduction in diatom algae growth. Water quality assessments showed improved parameters, including lower nutrient levels and stabilized pH. Treated ponds exhibited healthier conditions for carp, with reduced mortality rates and enhanced growth performance compared to control ponds. The presence of L. plantarum effectively outcompeted diatom algae for resources, leading to a balanced aquatic ecosystem. Overall, this innovative approach demonstrated the potential of using beneficial bacteria to maintain water quality and promote sustainable fish farming practices without relying on harmful chemicals.

Conclusion: The use of Lactobacillus plantarum bacteria to prevent excessive growth of diatom algae in carp breeding ponds in Khuzestan has proven to be an effective and sustainable solution. This method not only reduced diatom populations but also improved overall water quality and fish health. By enhancing the aquatic ecosystem without the use of harmful chemicals, L. plantarum offers a viable alternative for fish farmers seeking to maintain optimal breeding conditions. The

positive outcomes of this study highlight the potential for integrating beneficial microorganisms in aquaculture practices, promoting both environmental sustainability and economic viability in fish farming.

Keywords: ١. Lactobacillus plantarum ٢. Diatom algae ٣. Carp breeding ٤. Aquaculture ٥. Water quality

The use of medicinal herbs and plants against infections caused by streptococcus species in farmed fish (Research Paper)

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Introduction: Streptococcus disease, especially caused by Streptococcus iniae, Streptococcus agalactia, Streptococcus dysagalactia, Streptococcus uberis, and Streptococcus parauberis, is one of the most important re-emerging infectious diseases in the global aquaculture industry, so that it has become one of the obstacles to the sustainable development of this industry.

Methods: Few studies have been conducted on the antagonistic effects and effectiveness of medicinal herbs and plants against the agents of bacterial zoonotic disease. We reviewed the available data through the scientific-related journals and analyses data since ۱۹۷۰ up to date. We focused on the antagonistic properties of extracts or essential oils of medicinal herbs and plants against all reported streptococcal species that can invade fish causing septicemia under in vitro condition. Also, we analyzed the clinical efficacy of medicinal herbs and plants used against pathogenic streptococcus species under in vivo condition.

Results: Most of the studies have been conducted on the antagonistic properties of plant and herb extracts or essential oils against two species of S. iniae and S. agalactiae under in vitro condition. Also, the findings show that the essential oils of the studied plant/herb exhibited better efficacy than the extracts. In addition among the studied-essential oils those containing eugenol, carvacrol, and thymol revealed a higher anti-streptococcal activity than others. Further, the results of clinical studies (experimental disease treatment) show a moderate effectiveness of the studied-medicinal plants and herbs.

Conclusion: Validating the clinical efficacy of these oils or extracts requires dosage standardization, accurate information of the effective ingredients in the essential oil/extract, their mechanism of action. Thus, in aquaculture practice, use of medicinal herbs and plants as the alternative of antibiotics toward aquaculture streptococcosis warranted further investigations.

Keywords: Streptococcus, Streptococcus iniae, Streptococcus agalactiae, Streptococcus disagalactiae, Streptoco

The use of mesenchymal stem cells in the treatment of autoimmune and inflammatory diseases (Review)

Batol Abbasi,[١,*]

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Introduction: Studies have shown that mesenchymal stem cells (MSCs) modulate the immune system. They can also repair damaged tissue. Damaged or inflamed tissue releases chemokines that attract MSCs to the tissue. They move by rolling on the endothelium deliver themselves to the damaged or inflamed tissue, and perform an anti-inflammatory or repair effect. These characteristics of MSCs have led researchers to investigate these cells as treatment options in severe auto-inflammatory and autoimmune patients. Therefore, we decided to investigate the biological mechanisms of MSCs in autoimmune and inflammatory patients.

Methods: Mesenchymal stem cells (MSCs), one of the most widespread cells in the human body, were first discovered in ١٩٧٦ (١). In general, MSCs are known as pluripotent stem cells that can differentiate into adipocytes, chondrocytes, osteocytes, and other lineages (٢). Also, they can adhere to plastic containers and multiply in laboratory conditions. These cells express CD٧٣, CD٩٠, and CD١٠٥ on their surface, but lack CD١٤, CD٤٥, CD١٩, and HLA-DR. Recent studies have shown that MSCs can inhibit the activity of T cells, B cells, dendritic cells, macrophages, and NK cells through direct cell-to-cell interactions. They can also modulate the immune system through the secretion of soluble factors including indoleamine-٢,٣-dioxygenase (IDO), prostaglandin E٢ (PGE٢), and transforming growth factor-beta (TGF-β) (٣). The function of the immune system is to protect the host against infectious agents and transformed cells. Autoimmune diseases occur due to the inability of the immune system to distinguish between self and non-self cells. It has been shown that ٣ to ٥ percent of the population is involved in autoimmune diseases (٤). Inflammation may occur as a result of the immune system's response to injury or infection. In the past decades, the prevalence of diseases related to chronic inflammation is increasing. The protective role of inflammation causes disease when it occurs excessively and chronically (٥).

Results: Review

Conclusion: MSCs, in addition to healing damaged tissues, have a unique ability to modulate the body's immune system to turn off pathological responses and maintain its ability to fight disease. MSCs settle in the inflamed tissue and lead to the production of anti-inflammatory agents. These mediators act locally and do not suppress the immune response of the patient's whole body. MSCs can generally restore tissue and modulate the immune system through direct contact with the cell or exosome secretions. These characteristics of MSCs have made these cells a new candidate for potential clinical application in the treatment of inflammatory and autoimmune diseases.

Keywords: Mesenchymal stem cells, Autoimmune, Inflammatory diseases

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The use of probiotics and bacteriophages to eliminate hospital pathogens and prevent the spread of contamination (Review)

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Introduction: Microbial contamination in hospitals is a significant public health issue, largely because it leads to healthcare-associated infections (HAIs). These infections are made worse by the high levels of antimicrobial resistance (AMR) found in the pathogens that cause them. Chemical disinfection provides only a short- term solution and can contribute to the development of resistant pathogens, a trend that was noted during the COVID-١٩ pandemic. Alternatively, probiotic-based sanitation, known as the probiotic cleaning hygiene system (PCHS), has been shown to effectively reduce pathogens, AMR, and HAIs in a more stable manner. However, the action of probiotics is neither quick nor targeted. On the other hand, bacteriophages can rapidly kill specific bacteria, though their effect is short-lived. Therefore, considering the characteristics of both probiotics and bacteriophages, we aimed to explore their combined use as a potential method for consistently eliminating bacteria primarily responsible for hospital infections, especially those resistant to drugs.

Methods: With studies that have been analyzed in Pubmed, Google Scholar and Clinical trials.gov databases and journals such as Nature and Elsevier and findings from conventional microbiological tests and molecular assays; showed that an eco-friendly cleaner fortified with bacteriophages and probiotics was effective in permanently eliminating surface pathogens. This biological approach was efficient because the rapid and specific action of bacteriophages was complemented by the sustained and widespread action of probiotics. This method provides new possibilities for infection control management in hospital environments. For example, recently the efficiency of a new approach based on the use of non-pathogenic microorganisms of the genus Bacillus added to persistent detergents in the system (PCHS) has been analyzed. Such a method is effective in dealing with surface recontamination by various pathogens and reduces their presence by about ٨٠-٩٠٪ compared to the microbial load detected on surfaces treated with conventional disinfectants.

Results: Findings from microbiological and molecular tests, along with studies from databases like PubMed, Google Scholar, and Scopus, revealed that an eco-friendly cleaner fortified with bacteriophages and probiotics permanently eliminated surface pathogens effectively.

Conclusion: Bacteriophages and probiotics are considered potential decontaminants due to their unique capability to target and eliminate specific bacterial strains. However, their stability in detergents and their potential application in conventional sanitation remain unexplored, and more research is needed in this area.

Keywords: Probiotics, Bacteriophages, PCHS, HALs, Hospital pathogens

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THERAPEUTIC EFFECT OF HYDROGEN SULFIDE ON COGNITIVE DISORDERS IN POLYCYSTIC OVARY SYNDROME: THE ROLE OF THE HIPPOCAMPUS (Research Paper)

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Introduction: Polycystic ovary syndrome (PCOS) is a common endocrine disorder that affects many women of fertility age. PCOS comes with symptoms such as hirsutism, obesity, insulin resistance, and infertility. In addition to physical symptoms, many women with PCOS experience psychological symptoms such as depression, anxiety, and cognitive disorders. "Cognition" refers to aspects of brain function, including language, attention, memory, learning, decision-making, and problem-solving. In women with PCOS, oxidative stress is often elevated. Oxidative stress occurs when there is an imbalance between free radicals and antioxidants in the body. Free radicals can cause damage to cells, DNA, and lipids. Hydrogen sulfide (H٢S) has been identified as a physiological gasotransmitter in the mammalian body. H٢S has also been identified as an antioxidant, which slows down the progression of ageing and cognitive disorders.

Methods: In this study, ٣٠ female Wistar rats were divided into three groups, with ١٠ animals per group. The first group (sham) received carboxymethylcellulose (CMC), which is the letrozole solvent. The second group (PCOS) and the third group (PCOS+NaHS) received letrozole at a dosage of ١mg/kg for ٢٧ consecutive days to induce PCOS. On the ٢١st day, stereotaxic surgery was performed to cannulate the right lateral ventricle. In the PCOS+NaHS group, after PCOS induction, Intracerebroventricular (ICV) administration of Sodium Hydrosulfide (NaHS), which is a Hydrogen Sulfide Donor, was performed for seven consecutive days. Following this, behavioral tests were conducted, including the Barnes maze for spatial memory, the novel object recognition (NOR) test for diagnostic memory, and the shuttle box test for passive avoidance memory. At the end of the study, oxidative stress biomarkers in the hippocampus tissue, such as malondialdehyde (MDA) using spectrophotometry and superoxide dismutase (SOD) activity using ELISA were analyzed.

Results: On the probe day of the NOR test, rats with PCOS spent less time interacting with novel objects than the control group ($p < ٠,٠٠١$). During the probe phase of the Barnes maze, rats with PCOS showed more errors ($p < ٠,٠٠١$) and longer escape latency times ($p < ٠,٠٠١$) than the control group. In the shuttle box test, rats with PCOS exhibited shorter step-down latency compared to the control group ($p < ٠,٠٠١$). However, in the PCOS+NaHS group, ICV administration of NaHS improved these parameters. Treated rats spent more time learning the novel object than the PCOS group during the NOR test probe day ($p < ٠,٠٠١$). Additionally, during the probe phase of the Barnes maze, treated rats showed fewer errors ($p < ٠,٠١$) and shorter escape latency times ($p < ٠,٠٠١$) than the PCOS group. In the shuttle box test, treated rats had longer step-down latency times

than the PCOS group ($p < ۰,۰۵$). Furthermore, PCOS rats exhibited higher MDA levels ($p < ۰,۰۰۱$) and lower SOD activity ($p < ۰,۰۰۱$) in the hippocampus compared to the control group. Treated rats with NaHS showed decreased MDA levels ($p < ۰,۰۵$) and increased SOD activity ($p < ۰,۰۰۱$) in the hippocampus compared to the PCOS group.

Conclusion: The study indicates that PCOS can lead to cognitive disorders. Oxidative stress is a significant factor in the development of cognitive disorders caused by PCOS. This might be due to the neuroprotective function of estrogen, which plays a role in protecting the brain. Additionally, $H_۲S$ has been found to have a positive effect on the cognitive function of rats with PCOS. This effect could be attributed to the antioxidant and neuromodulatory properties of $H_۲S$ in the hippocampus, which is crucial for memory and cognition. Oxidative stress results in elevated MDA levels and reduced SOD activity in the hippocampus, potentially causing damage to neurons and impairing memory and cognition.

Keywords: Polycystic ovary syndrome, Cognitive disorders, Oxidative stress, Hydrogen sulfide, Gasotransmitters

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Therapeutic Potential of Apigenin-Encapsulated Solid Lipid Nanoparticles in Inducing Caspase-Mediated Apoptosis in MCF-۷ Breast Cancer Cells (Research Paper)

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Introduction: Breast cancer remains a significant global health burden, and the development of effective therapeutic strategies is crucial. Apigenin, a natural flavonoid, has demonstrated promising anti-cancer properties, but its poor aqueous solubility and limited bioavailability have hindered its clinical translation. The use of solid lipid nanoparticles (SLNs) as a drug delivery system has the potential to enhance the therapeutic efficacy of apigenin against breast cancer. This study aimed to synthesize and characterize apigenin-encapsulated SLNs, and to evaluate their anticancer effects and underlying mechanisms of action in the MCF-۷ breast cancer cell line. Apigenin-encapsulated SLNs were prepared and extensively characterized for their physicochemical properties, including size, polydispersity index, and drug encapsulation efficiency.

Methods: The in vitro cytotoxic effects of the nanoformulation were assessed using cell viability assays. The potential mechanisms of action were investigated through gene expression analysis of apoptosis-related markers, including caspase-۳ and caspase-۹.

Results: The synthesized apigenin-encapsulated SLNs had an average size of ۱۹۵ nm and a polydispersity index of ۰,۳, indicating a homogenous size distribution. It exhibited a potent cytotoxic effect against the MCF-۷ breast cancer cell line, with an IC۵۰ value of ۸٦,۲ µg/ml. Mechanistic studies revealed that the apigenin-encapsulated SLNs significantly upregulated the expression of caspase-۳ and caspase-۹, key mediators of the apoptotic pathway, leading to the induction of programmed cell death in the cancer cells.

Conclusion: The findings suggest that apigenin-encapsulated SLNs effectively inhibit the growth of MCF-۷ breast cancer cells by inducing caspase-mediated apoptosis. This nanoformulation holds promise as a potential therapeutic strategy for the management of breast cancer and warrants further in-depth investigation.

Keywords: Apigenin, Apoptosis, Anticancer potential, Drug delivery, Gene expression

Therapeutic Potential of Fecal Microbiota Transplantation in Treating Escherichia coli Infections and Enhancing Gut Health in Mice (Review)

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Introduction: Fecal microbiota transplantation (FMT) involves transferring stool from a healthy donor into a patient's gastrointestinal tract for therapeutic reasons. Recent studies highlight the importance of the intestinal microbiome in animal health, influencing not just digestion but also immune function, behavior, and overall physiology. Disruptions in gut microbiota are linked to various disorders, including gastrointestinal and mental diseases. The intestinal epithelium plays a crucial role in maintaining gut health by preventing pathogen invasion, and the microbiome can influence barrier function. Fecal microbiota transplantation (FMT) has shown promise as a therapy for gut dysbiosis-related conditions, demonstrating safety and efficacy in treating various gastrointestinal issues, particularly inflammatory bowel disease. FMT can restore microbial diversity, aiding in defense against pathogens and improving symptoms in conditions like autism spectrum disorder and Parkinson's disease. Despite its effectiveness against Clostridioides difficile infection, FMT's role in treating other pathogens like E. coli is less understood, especially amidst rising antibiotic resistance. Given these challenges, researching alternative therapies is essential. The present study aims to explore how FMT may regulate intestinal barrier injury caused by E. coli by analyzing microbiome interactions using an infected mouse model, providing insights into FMT as a potential treatment for gut microbial imbalances.

Methods: In this study, The scientists assessed the impact of fecal microbiota transplantation (FMT) on gut functions during Escherichia coli (E. coli) infection using a mouse model. Additionally, we examined the related variables associated with the infection, including body weight, mortality, intestinal histopathology, and changes in the expression of tight junction proteins (TJPs).

Results: FMT significantly reduced weight loss and mortality, leading to the restoration of intestinal villi and improved histological scores for jejunal tissue damage ($p<0.05$). The effect of FMT in alleviating the reduction of intestinal tight junction proteins (TJPs) was also confirmed through immunohistochemistry and mRNA expression analysis. Additionally, harmful bacteria from the phylum Proteobacteria, including families Enterobacteriaceae and Tannerellaceae, as well as genera such as Escherichia-Shigella, Sphingomonas, and Collinsella, were found to be significantly increased, while beneficial bacteria from the phylum Firmicutes, specifically Lactobacillaceae and the genus Lactobacillus, decreased in the guts of infected mice. Furthermore, we investigated the relationship between clinical symptoms and FMT treatment regarding gut microbiota modulation. Beta diversity analysis showed that the gut microbial communities in the non-infected and FMT groups were similar. The FMT group exhibited an improvement in intestinal microbiota, characterized by a notable increase in beneficial microorganisms alongside a significant decrease in Escherichia-Shigella, Acinetobacter, and other taxa.

Conclusion: The current study highlighted the therapeutic benefits of fecal microbiota transplantation (FMT) in addressing E. coli infections in mice. Given these positive effects on intestinal health, there has been considerable interest in exploring the interactions between microbiota and the host to modulate the intestinal microbiome. Notably, we discovered that FMT may help restore the integrity of intestinal villi and barrier function compromised during infection. This suggests that FMT could be a viable treatment for gut infections and disorders related to gastric function. Accordingly, we propose that FMT therapy may foster a beneficial host-microbiome relationship, providing deeper insights into pathogens linked to intestinal diseases.

Keywords: FMT, Escherichia Coli, microbiome

Thesis title: Triple Combination Therapy with Immunologic Approaches: Modulating Tumor Microenvironment (TME) and Tumor Growth Inhibition (Research Paper)

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Introduction: The immunosuppressive tumor microenvironment (iTME) significantly influences the effectiveness of various anticancer therapies, including immunotherapy and chemotherapy. This study aimed to target HIF-١α as a reshaping of the iTME combined with Toll-Like Receptor ٧ agonist and chemotherapy in a mouse model of colorectal cancer (CRC).

Methods: A HIF-١α-specific siRNA duplex was formulated based on the ionic gelation of tripolyphosphate (TPP) with cationic chitosan (CH) as a nanoplex and evaluated in terms of size, charge, polydispersity index and gel retardation assay. MTT assay was conducted to assess the cytotoxicity of the specific siRNA duplex against CT٢٦ cells. The hypoxic condition was generated to evaluate the gene and protein expression levels of HIF-١α, respectively. CT٢٦ mouse model was established to assess the synergistic effect of silencing HIF-١α combined with oxaliplatin (OXA) and imiquimod (IMQ) on tumor growth.

Results: The findings showed that the combination of HIF-١α siRNA with OXA and IMQ caused a significant delay in tumor growth, which was associated with high levels of cytokines related to cellular immunity. The CH/siRNA nanoparticles had a mean diameter of ٢٤٣ ± ٦ nm with a size distribution of ٠,٣ ± ٠,٠٤. There were no significant differences observed between the CT٢٦ cells treated with nanoparticles alone and the untreated cells, indicating that these nanoparticles are safe and physiologically biocompatible ($p \geq ٠,٠٥$). Triple combination therapy involving HIF-١α siRNA, OXA, and IMQ significantly retarded tumor growth and led to elevated levels of cytokines linked to cellular immunity (INF-γ and IL-١٢) compared with those in the other groups ($P<٠,٠٥$). The positive correlation coefficient ($r=٠,٦٨$) between tumor size and HIF-١α expression levels was statistically significant ($P= ٠,٠٠٣$). Compared with those in the control group, the expression levels of the anti-inflammatory cytokines IL-١٠ and IL-٤ significantly decreased ($P<٠,٠٥$).

Conclusion: In conclusion, our findings suggest that inhibiting HIF-١α could serve as a rational strategy to enhance the antitumor response in the TME.

Keywords: HIF-١α, Chemotherapy, Immunotherapy, Tumor microenvironment (TME), Combination

Three-Brains Health (Review)

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Introduction: We are all aware of the big brain above our shoulders (did you know our brain has over ٨٠ billion neurons firing up to ١٧,٢ trillion synapses every second?!), the “second brain”, a fascinating neural center located in our gut, and amazingly, over ٥٠٠ million neurons are located in this area of our body. According to numerous studies over the past twenty years, the gut sends about ٤٠٠ more messages to the brain, than the brain does to the gut and, almost ٧٠٪ of our body’s immune system and ٩٥٪ of serotonin is actually found in the gut. And, finally our “third brain” is heart where houses more than ٣٩ million neurons, the heart sends as many messages to the head brain as it receives.

Methods: Through Monitoring Gut-Brain Axis (Vagus Nerve) and Heart-Brain Axis researchers found that many mental health disorders(such as:Alzheimer, ADHD, Panic, Autism, Bipolar disorders, mood disorders, memory loss,sleep disorders, depression), brain cancer and psycho-physiological problems are related to our three-brains health.

Results: The gut has more than ٩٥٪ of our serotonin and ٧٠٪ of our immune system of our body. Hence, through a balanced gut microbiome (avoiding Dybiosis), we can prevent all mental disorders and many cancers(by boosting our immune system) and also, through keeping the heart in a coherent mode and sinus heart rhythm pattern(BPM) we can boost our cardiac health, which has critical roles in preventing cancers and generating stress hormones.

Conclusion: In order to prevent many mental disorders and cancer problems, these general OTC supplements can boost Three-brains health: ١-Lactobacillus Probiotic- Bifidobacterium Probiotic(factory suggestion) ٢-CoQ١٠ (٥٠-١٥٠ mg - daily) ٣-Ginkgo Biloba (١٥٠-٢٥٠ mg- daily) ٤-Phosphatidyl Serine (PS) (١٠٠-٣٠٠ mg - daily) ٥-Pyrrolo Quinoline Quinone (PQQ) (٢٠ mg - daily) ٦-Lutein (١٠-٢٠ mg - daily) ٧-Curcumin (٣٠٠ mg-daily) ٨-Omega ٣ (١٠٠٠-٣٠٠٠ mg - daily) ٩-Magnesium (٤٠٠-٨٠٠ mg - daily) ١٠-Vitamin D (٣٠٠٠-٥٠٠٠ IU -daily) ١١-Grapeseed extract(٤٠٠ mg -daily)

Keywords: Three-brains Health , Public-Health, Naturopathic medicine

Tolerating verbal, physical, mental-emotional and sexual abuse by the spouse for the survival of married life and motherhood: case report (Review)

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Introduction: Spousal abuse refers to misbehaving with a woman in various forms such as aggression, psychological abuse, harassment, beating, prohibition of social relations, violence in sexual behavior or sexual behavior without consent. The phenomenon of spousal abuse is one of the important problems of the society that has historical roots. Due to the occurrence of many problems in the life of different societies, the vulnerable sections of the society have been exposed to more threats. The purpose of this report is to introduce a woman who has been mistreated by her husband in various ways, but has endured so far at the cost of protecting her family and motherhood

Methods: The case of a ٣٣-year-old woman with a bachelor's degree who was forced to marry a ١٦-year-old boy at the age of ١٤. During her ١٨ years of living with her husband, this lady was physically harassed by her husband and her husband's family, such as punching her in the face and breaking her nose and forehead. As he was sexually abused by his wife with the threat of knife and ax. The woman has two children, a ١٧-year-old boy and an ١١-year-old girl, who have been subjected to physical abuse, such as being beaten with a pomegranate stick, and head injuries that have resulted in cerebral hemorrhage. The family provides, however, he is abused verbally and insultingly by his wife. The woman has filed for divorce ٨ times, and every time she was unable to leave her husband's house because of her dependence on her children and fear of people's eyes on her. Mother's experiences of life in such conditions have been expressive (physical and sexual harassment, work pressure despite illness, dependence on children).

Results: The results show that women are forced to endure misbehavior from their husbands due to family and motherhood. In this study, this mother has endured all kinds of misbehavior so far that she cannot maintain her family life. The question that arises is whether this life is worth preserving at any cost. It is better for such women, due to their incapacity, to have organizations and officials to make the right decision instead of them.

Conclusion: In this study, this mother has endured all kinds of misbehavior so far that she cannot maintain her family life. The question that arises is whether this life is worth preserving at any cost.

It is better for such women, due to their incapacity, to have organizations and officials to make the right decision instead of them.

Keywords: Spouse abuse, aggression, divorce, family

Toxicological Assessment of Stevia and Its Products on Zebrafish Larvae (Research Paper)

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Introduction: The Stevia plant, recognized as a natural sweetener with proven antioxidant and insulinotropic properties, has seen increased consumption, raising concerns about its safety at various doses. This study assessed the toxicity of three commercially available Stevia products (leaves, powder, and tea bags) by preparing solutions at concentrations ranging from ١٠٠ to ٢٠,٠٠٠ mg/L using E٣ solution. Zebrafish eggs were exposed to these concentrations in ٢٤-well ELISA plates, with E٣ solution serving as a negative control. Over ٩٦ hours, larvae were monitored for morphological changes and mortality. Consistent with OECD ٢٣٦ guidelines, over ٨٠٪ of control larvae remained healthy. All substances at ٢٠,٠٠٠ mg/L resulted in complete mortality, while significant morphological changes were observed at concentrations of ١٠,٠٠٠ mg/L and above. No mortality was recorded at ١٠٠ mg/L across all groups. The median lethal concentration (LC٥٠) was determined using SPSS software.

Methods: During the ٩٦-hour examination of zebrafish larvae, it was found that in the groups exposed to concentrations equal to and higher than ٥٠٠٠ mg/L of the tested compounds, there are significant differences with the control group in terms of mortality and morphological abnormalities. Also, studies show that the lethal concentration (LC٥٠) in stevia leaf extract is higher than other groups (Table ١) and therefore, stevia leaf extract has lower acute toxicity than other studied groups. Also, two groups of stevia industrial products (powder and tea sweetened with stevia), although according to statistical analysis, they did not show any significant difference from each other, but the LC٥٠ tables of each and the graphs show the relatively higher toxicity of the stevia powder solution compared to the sweetened tea solution. Also, the average lethal concentration in these two groups (according to Table ٢) was not higher than ٥٠٠٠ mg/liter, which was similar to the results of the experiments

Results: In terms of acute and chronic toxicity in two groups of stevia industrial products at high concentrations, it was determined that at a concentration of ١٥٠٠٠ mg/liter in larvae exposed to tea solution sweetened with stevia at ٩٦hpf, none of the surviving larvae did not hatched, but the heart rate was normal (٧٥-٨٥ times per minute), while in the stevia powder solution under the same conditions, the surviving larvae had a very low heart rate and irregular blood flow. Also, at the highest concentration tested in this study (٢٠٠٠٠ mg/liter), all the larvae exposed to the stevia powder solution had coagulated by the third day (٧٢ hours after fertilization), while a number of larvae exposed to stevia-sweetened tea solution were alive until the fourth day (٩٦ hours after

fertilization) and died after hatching and in direct exposure to the substance, which probably indicates a relatively higher toxicity of stevia powder solution compared to stevia-sweetened tea solution.

Conclusion: After ۷۲ hours of exposure of mice to different concentrations of pure stevioside, it was found that the number of CD٤ and CD۸ positive lymphocytes decreased by almost ٤۸٪.[۱٤] Since CD٤ and CD۸ positive lymphocyte cells are young cells that have not yet gone through the cell maturation process, this process can cause a significant decrease in mature lymphocytes, which are important cells of the immune system. Also, the presence of inflammation in some organs of rats exposed to stevia extracts in pathological investigations can be justified. Although the joint committee of FAO and WHO considers steviol glycosides as permitted food additives, there are still discussions about the safety and toxicity of other glycosidic diterpenes in stevia plant.[۱۸] In addition, the amount of acetylene used in industrial products as well as their degree of purity may lead to complications that indicate the need to check these products. For example, it has been found that sugar alcohols, which are polymer alcohols, are added to some industrial products containing stevia in stores, which may cause digestive side effects for people who are allergic to chemicals. However, nutrition and health centers have expressed their concerns about the toxicity of consuming high doses of stevia, which seems to require further studies and research. In this research, it was concluded that in the group of larvae exposed to stevia extract and tea solution sweetened with stevia at a high dose (۲۰,۰۰۰ mg/L) during ۹٦ hours after fertilization and in the larvae exposed to stevia powder solution in ۷۲ hours after fertilization had ۱۰۰٪ mortality (acute toxicity), although at doses higher than ۱۰۰۰ mg/L, some deaths were reported in all study groups during each day. The most morphological changes during the test period related to the larvae exposed to stevia powder solution were reported, in other studied groups at doses higher than ۱۰۰۰ mg/liter, different morphological changes were also observed, which indicates the chronic toxicity of stevia products on zebrafish larvae. In this experiment, urban tap water was used instead of distilled water for extraction because this research is a simulation of the conditions that people use in their food. However, in order to form different dilutions in each of the tested materials (due to the fact that the solutions are in contact with the larvae for ۹٦ hours and there is a possibility of contamination during the experiment), in order to prevent contamination, solution was made using E۳ solution. Also, after being separated from the egg-laying trap, the larvae were washed using E۳ solution to prevent the transfer of contamination with the eggs to the test plate, which may affect the test process. This experiment was repeated three times for all three studied groups in the six desired concentrations, and the resulting data showed good reproducibility.

Keywords: stevia; zebrafish larvae; acute toxicity; chronic toxicity; lethal dose

Tracking of Leishmania spp. in Iranian Phlebotominae, distribution and biodiversity in Jarqavieh county, central Iran (Research Paper)

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Introduction: The female sandfly vector's bite is responsible for transmitting Cutaneous Leishmaniasis (CL), a parasitic disease prevalent in two-thirds of Iran.

Methods: This epidemiological and descriptive cross-sectional study took place in ٢٠٢١ to determine how sandflies are distributed in Hasanabad and Hossein Abad, located in eastern Isfahan province, Central Iran. Semi-nested PCR and sequencing were used to determine the parasite species sandflies captured according to the approved WHO protocol.

Results: Overall, ٣٦٣ collected sandflies were identified morphologically, among which ١٦١ (٤٤,٤٪) and ٢٠٢ (٥٥,٦٪) were isolated from Hasanabad and Hossein Abad, respectively; the largest number was hunted from outdoor places. Also, ٣٤,٤٪ and ٦٥,٦٪ of the sandflies were female and male, respectively. The most prevalent sandfly species were Phlebotomus papatasi (٤٩,٩٪), followed by Ph. caucasicus (٢٩,٦٪), Sergentomyia sp. (٢٦,٢٪) and the rest unknown. Sixty molecularly analyzed sandflies were included Ph. papatasi and S. sintoni, which were found to be infected with L. major, had been exposed to outdoor environments, and hunted in July.

Conclusion: These findings showed the importance of monitoring the rodent nests and starting to control and fight the disease from there.

Keywords: Leishmania, Cutaneous leishmaniasis, Biodiversity, Vector-borne disease, Sandfly, Zoonoses

Trans-Anethole Induces Inflammation in the Rat Hippocampus: An In Vivo Study (Review)

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Introduction: Trans-anethole is a naturally occurring compound found in the essential oils of certain plants, including anise and fennel. It has been used in traditional medicine for various purposes, including as an anti-inflammatory agent. However, its effects on the central nervous system, particularly the hippocampus, are not well understood. The hippocampus is a critical region for memory and learning, and inflammation in this area is associated with several neurodegenerative diseases. This study aims to investigate the inflammatory effects of trans-anethole on the rat hippocampus.

Methods: Male Wistar rats were divided into control and treatment groups. The treatment group received intraperitoneal injections of trans-anethole at a dose of ١٠٠mg/kg body weight daily for ١٤ days. The control group received vehicle injections. On day ١٥, the rats were euthanized, and their hippocampi were isolated for further analysis. Inflammation was assessed by measuring pro-inflammatory cytokine expression (IL-١β, TNF-α) and inducible nitric oxide synthase (iNOS) via real-time PCR and Western blot. Histopathological examination of the hippocampus was performed to evaluate any morphological changes.

Results: Trans-anethole treatment significantly increased the expression of IL-١β, TNF-α, and iNOS in the hippocampus compared to the control group. These findings suggest that trans-anethole induces an inflammatory response in the hippocampus. Histopathological examination revealed inflammatory cell infiltration and neuronal damage in the hippocampus of the treatment group .

Conclusion: This study demonstrates that trans-anethole induces inflammation in the rat hippocampus, contradicting its purported anti-inflammatory effects. These findings have implications for the use of trans-anethole in traditional medicine and highlight the need for further research into its effects on the central nervous system. Chronic inflammation in the hippocampus is associated with neurodegenerative diseases, and therefore, the long-term use of trans-anethole may potentially contribute to such conditions

Keywords: Trans-anethole, hippocampus, inflammation, cytokines, neurotoxicity.

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Transcriptomic Analysis and Phylogenetic Insights into the Evolution of Venom Allergens in the Hemiscorpius lepturus Scorpion (Research Paper)

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Introduction: Venom allergens have been discerned in various venomous sources such as scorpions, snakes, bees, and wasps, contributing to allergic reactions in humans. This study focused on conducting a phylogenetic analysis of venom allergens extracted from the transcriptome of the Hemiscorpius lepturus scorpion. Seven distinct venom allergens, namely HLAllergen١, HLAllergen٢, HLAllergen٣, HLAllergen٤, HLAllergen٥, HLAllergen٦, and HLAllergen٧, were successfully identified through comprehensive venom gland transcriptome analysis.

Methods: To further elucidate their properties, primary, secondary, and tertiary structures of the identified venom allergens were predicted utilizing advanced computational tools, including ExPASy ProtParam, PSIPRED, and SWISS MODEL servers. The molecular weight of the venom allergens was determined to range between ٤٦ to ٥٢ kDa, and tertiary structure predictions indicated that all ٣-D structures fell within the normal range.

Results: A phylogenetic tree, constructed employing MEGA ١١ software through the neighbor-joining method with ١٠٠٠ bootstraps, revealed distinct clades among the identified venom allergens. Specifically, HLAllergen ٣, ٤, and ٥ formed a single clade, while HLAllergen ١, ٢, ٧, and ٦ clustered into separate clades.

Conclusion: Taken together it is imperative to underscore the necessity for further investigations, particularly through proteomic analysis of H. lepturus, to validate and compare the transcriptome-derived data, ensuring a comprehensive understanding of the venom allergen profile in this scorpion species.

Keywords: Venom, Allergen, Phylogeny, Scorpion, Transcriptome

Transcriptomics-Based Computational Drug Repurposing Strategy for Identified Therapeutic Candidates Liver Cancer (Research Paper)

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Introduction: Liver cancer is the fourth most common cancer in the world and the main cause of death in the world in such a way that it leads to the death of ٨٠٠,٠٠٠ people in the world every year. The main causes of this disease are chronic viral hepatitis, high alcohol consumption, and non-alcoholic fatty liver disease. Drug repurposing is a useful method of using existing FDA-approved drugs. This method identifies the right medicine for the disease by spending less time and money. Since in cancer, chemotherapy drugs are drugs that reduce a person's quality of life, using other drugs with fewer side effects that are among non-cancer drugs can be helpful.

Methods: This study used a computational drug repurposing pipeline to discover candidate drugs based on PD differential gene expression signatures derived from RNA sequencing data. The transcriptional sample of plasma was compared with accession code GSE١٤٢٩٨٧ from the GEO database (https://www.ncbi.nlm.nih.gov/geo/). Some samples were not available through the dataset, and only ٣٤ plasma samples of people with liver cancer and ١٠ plasma samples of healthy people were analyzed. Differentially expressed genes (DEGs) between plasma samples of liver cancer subjects and plasma samples of healthy subjects were obtained using GEO٢R. Then, the integrated library of network-based signatures (LINCS) was used to identify potential drugs that can reverse the expression of DEGs. Then, by reviewing the significant literature and drug bank studies (https://go.drugbank.com), the top-ranked drugs with the highest p-value were selected. The study identified ٢٥٠ genes commonly affected by the disease. Among them, genes with |log٢FC| > ١ and a P-value < ٠,٠٥were identified as DEGs: ٥٩ up-regulated genes and ١٩١ down-regulated genes.

Results: The results of the data analysis in this study showed that VernaKalant drug can have a positive effect in the treatment of liver cancer.

Conclusion: VernaKalant is an antiarrhythmic drug for rapid conversion of atrial fibrillation to sinus rhythm and may be useful in the treatment of liver cancer. However, it is not clear exactly which genes this drug affects. Arrhythmia patients in case of diseases such as liver cancer can use these drugs approved by the American Food and Drug Administration, and these drugs with their dual effects are effective in both improving the patient and reducing the consumption of multiple drugs.

Keywords: RNA sequencing; liver cancer; Drug repurposing

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Transdermal Drug Delivery System: Fabrication of microneedle patch based on PVA and HA

(Research Paper)

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Introduction: Microneedle (MN) arrays consist of dozens to hundreds of micrometer-sized needles, providing a painless option for enhancing skin permeability and increasing drug delivery through the skin. Unlike oral medications or subcutaneous injections, they can prevent the reduction in efficacy of oral drugs due to liver metabolism and also reduce the risk of infection associated with subcutaneous injections. The methods for producing MN patches can be divided into two types: template-free methods and micromolding methods. The aim of this research is to fabricate MN patches using a micromolding technique based on a hydrogel composed of poly(vinyl alcohol) (PVA) and hyaluronic acid (HA).

Methods: Initially, the microneedle mold was designed using SolidWorks and then fabricated using a ٣D printer. PDMS (polydimethylsiloxane) was prepared by mixing the elastomer and curing agent in a ١:١٠ ratio and poured onto the printed master mold, with the molds then cured at ٩٠ degrees Celsius for ٢ hours. The PDMS mold was then separated from the master mold, and to prepare the PVA-HA microneedle patch, PVA and HA were dissolved in deionized water and poured onto the PDMS mold. This mixture was then centrifuged at ٤٠٠٠ rpm for ٢٠ minutes, and the backing layer of the MNs was filled with pure PVA solution. The patch was then dried at room temperature for ١٢ hours and carefully removed from the PDMS mold.

Results: Permeability testing was conducted to confirm the penetration capability of a needle with suitable physical properties in a gelatin sheet with an elastic modulus similar to that of real human skin, and its permeability was validated.

Conclusion: The development of microneedle (MN) patches using a micromolding technique with a hydrogel composed of poly(vinyl alcohol) (PVA) and hyaluronic acid (HA) presents a promising advancement in transdermal drug delivery systems. This innovative approach not only enhances skin permeability but also offers a painless alternative to traditional drug administration methods, effectively circumventing issues related to liver metabolism and the risk of infection associated with injections. Permeability tests confirm that the MNs possess suitable physical properties for effective drug delivery, indicating that this method could significantly improve therapeutic outcomes. Future research could further optimize the formulation and explore a wider range of applications, paving the way for more effective and patient-friendly drug delivery solutions.

Keywords: Drug delivery, dissolved microneedle, microneedle patch, polyvinyl alcohol, hyaluronic acid

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Transient Receptor Potential Melastatin ٨ Channels: An Important Diagnostic Biomarker for Gastric Cancer Patients (Review)

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Introduction: Gastric cancer (GC) is the ٤th deadliest cancer in the world and patients have a poor prognosis. Also, it is a multifactorial disease, and genetic and epigenetic factors are involved in its occurrence. Due to the lack of specific biomarkers, most patients do not have obvious symptoms in the early stages, so paying attention to early diagnostic approaches is very important. In this study, we describe the role of transient receptor potential melastatin ٨ channels (TRPM٨) in early detection of GC.

Methods: In order to obtain the latest developments in this field, it was conducted an extensive search in PubMed and Google Scholar databases from ٢٠٢٠-٢٠٢٤ and identified ٢٧ articles that were most relevant to our topic.

Results: In recent years, Non-Coding RNAs (ncRNAs) has emerged as a drug target in the treatment of cancer, especially in the fields of immunity, cancer metabolism and metastasis, and powerful diagnostic biomarkers. These biomarkers provide the possibility of accurately predicting treatment response and prognosis in most cancer patients, as well as creating a personalized treatment strategy for each person. For example, MicroRNAs (miRNAs) have been identified to regulate the expression of target Messenger RNAs (mRNAs) and thereby modify the vital biological mechanisms of cancer. These ncRNAs, which are usually abnormally expressed in cancerous tissues, play a key role in carcinogenesis, and their evaluation has potential benefits in the diagnosis, prognosis, or treatment of cancer. But for GC, there are mainly no specific biomarkers. In a ٢٠٢٣ research, TRPM٨ were identified as a novel diagnostic biomarker for GC, and tumor tissues showed significantly higher expression levels of TRPM٨ compared to normal gastric tissue Showed. This study shows the essential role of TRPM٨ in cell proliferation and suggests that TRPM٨ may be used as a potential therapeutic target for GC patients.

Conclusion: Due to the lack of specific biomarkers, most GC patients are diagnosed in advanced stages. Recently, TRPMΛ has been identified as a diagnostic biomarker that has a high expression level in gastric tumor tissues, which is promising for the emergence of early detection approaches and molecular targeted therapies for GC.

Keywords: Biomarker; Gastric Cancer; Diagnosis; TRPMΛ; ncRNA

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Treatment Options for Methicillin-Resistant Staphylococcus aureus (MRSA) Bacteremia (Review)

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Introduction: Since the last century, methicillin-resistant Staphylococcus aureus (MRSA) bacteremia has become a major global and public health concern not only in terms of morbidity and mortality, but also the duration of hospital stay, healthcare cost, and antimicrobial choices. Especially alarming is the growing antimicrobial resistance due to their misuse and overuse, which has led the world to be exhausted of its effective antibiotic resources. In this review article, we sought to figure out the most efficacious antimicrobial agents to treat MRSA-related bloodstream infections.

Methods: Information sources, keyword search and the following items were used in Elsevier searches to find relevant articles: (treatment of MRSA bacteremia), (methicillin-resistant Staphylococcus aureus or MRSA), (MRSA bacteremia). We compared the data from reviewing reports summarizing their comparative efficacy. We focused on vancomycin and daptomycin, which are the current Infectious Disease Society Of America (IDSA)-recommended antibiotics for MRSA bacteremia treatment. A deep dive into the newer agents revealed better efficacy and treatment outcome in the combination of ceftaroline (β-lactam) with daptomycin compared to traditional standard monotherapy (vancomycin/daptomycin monotherapy). Also, the IDSA recommended high-dose daptomycin (۸-۱۰ mg/kg) therapy for MRSA bacteremia treatment to be more effective in cases with vancomycin-reduced susceptibility.

Results: The upshot is that we need more large-scale clinical trials exploring in-depth effectiveness and adverse effects to decide on newer agents like β-lactams to use as routine therapy for MRSA bacteremia.

Conclusion: Treatment of methicillin-resistant Staphylococcus bacteremia is a growing challenge that physicians continue to face as it can lead to life-threatening conditions. Although IDSA has recommended VAN and DAP as first-line treatment options for MRSA, multiple drawbacks warrant the advent of alternatives that will increase clinical success rates with fewer adverse effects. Many studies demonstrated that combining DAP/VAN with β-lactams can result in faster bacterial clearance and a lower risk of ۳۰-day mortality - making it a promising choice. But these studies concerning ceftaroline were underpowered to detect clinically significant differences due to bias or smaller study groups. We need to conduct more head-to-head comparative studies with larger cohorts to replicate the results discussed here so that physicians can employ a comprehensive strategy against MRSA that will ensure increased clinical success with decreased mortality and morbidity, lower hospital stay, and reduced financial burden. Moreover, we did not find any trial or study describing the use of ceftaroline as a monotherapy to compare its efficacy in MRSA bacteremia with the current standard therapy.

Keywords: Staphylococcus aureus, ceftaroline, daptomycin, vancomycin, MRSA

Uncovering Molecular Pathways of Down-regulated Genes in Glioblastoma Using Bioinformatics Analysis (Research Paper)

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Introduction: Glioblastoma is an extremely aggressive and malignant type of brain cancer that begins in the glial cells of the brain. This cancer is known for its swift tumor growth, ability to infiltrate adjacent brain tissues, and resistance to various treatments. Multiple signaling pathways are integral to the onset and advancement of glioblastoma. This study aims to explore the GEO dataset to gather valuable information for a bioinformatics analysis focused on genes associated with glioblastoma.

Methods: Seven microarray expression datasets, namely GSE٢٢٦٩٩٠, GSE١٩٦٦٩٤, GSE١٩٢٧١٠, GSE١٨٤٨٥٩, GSE١٢٠٦٢٧, GSE١٣٠٨٥٧, and GSE١١٥٣٩٧, were gathered and subjected to statistical analysis to identify genes that are down-regulated (with a Log٢FC threshold of ≤- ١) in relation to glioblastoma.

Results: The pathway enrichment analysis revealed ٩٣ genes associated with cancer signaling pathways that exhibit significant dysregulation in glioblastoma. This process includes aligning differentially expressed genes with established biological pathways, highlighting genes such as E٢F٢, CAMK٢A, CAMK٢D, CDKN١A, EGF, GADD٤٥G, IGF١, PIK٣R٣, and PDGFRA.

Conclusion: Combining multiple omics datasets, including genomics, transcriptomics, and proteomics, can offer a holistic perspective on the molecular changes occurring in glioblastoma. This approach can shed light on the critical molecular pathways that drive glioblastoma progression and potentially identify novel therapeutic targets. Considering the gene pathways and their functions, the most related to the processes of cell proliferation, the inhibition of programmed cell death and the invasion of cancer cells. Among the important pathways and target genes in this research, the following can be mentioned. The insulin-like growth factor ١ (IGF١) signaling pathway plays a crucial role in glioblastoma through multiple mechanisms. A significant factor is the binding of IGF١ to its receptor, IGF١R, which stimulates cell growth and migration by activating downstream signaling pathways, including PI٣K/AKT and ERK١/٢. This activation is associated with unfavorable outcomes and a decreased response to standard treatments such as Temozolomide in patients with glioblastoma.PIK٣R٣ is capable of activating the MAPK/ERK pathway in glioblastoma stem-like cells, which enhances their ability to migrate, invade, and resist chemotherapy. Suppressing PIK٣R٣ or the downstream ERK signaling can hinder these aggressive characteristics. Elucidating the signaling cascades implicated in glioblastoma is essential for designing targeted interventions capable of

curbing tumor progression and enhancing patient prognosis. The bioinformatics investigation of genes associated with glioblastoma can shed light on the fundamental molecular processes driving this malignancy and pinpoint promising therapeutic targets for tailored treatment approaches. In summary, a collaborative strategy that merges sophisticated bioinformatics analysis with thorough cellular and clinical research is essential for thoroughly understanding the molecular foundations of glioblastoma and creating effective targeted treatments. The integration of these complementary approaches offers significant potential for enhancing patient outcomes in the face of this challenging disease.

Keywords: Glioblastoma multiform, In silico analysis, Biomarker genes, Diagnosis.

Uncovering New Biomarkers in the Transition from Crohn's Disease to Colorectal Cancer: A Systems Biology Perspective (Research Paper)

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Introduction: Colorectal cancer (CRC) is one of the most prevalent malignancies worldwide, and its development is often linked to chronic inflammatory conditions of the gastrointestinal tract, particularly Crohn's disease (CD). CD, a type of inflammatory bowel disease (IBD), is widely recognized as a significant risk factor for CRC, as prolonged inflammation can lead to cellular damage, genetic mutations, and eventually tumorigenesis. Despite this established connection, the molecular mechanisms driving the progression from CD to CRC remain inadequately understood. Identifying key genetic and molecular factors involved in this transition could lead to novel therapeutic targets and improved diagnostic tools. In particular, the role of differentially expressed genes (DEGs) and microRNAs (miRNAs), which regulate gene expression post-transcriptionally, is of growing interest. miRNAs can act as oncogenes or tumor suppressors, influencing cancer progression through the regulation of key cellular pathways. Therefore, this study aimed to uncover crucial DEGs and miRNAs associated with CRC progression from CD, with the goal of identifying potential biomarkers and therapeutic targets.

Methods: We employed a systematic approach to analyze mRNA and miRNA datasets comprising samples from both CRC and CD patients to identify differentially expressed genes (DEGs) and miRNAs (DEmiRNAs). Common genes associated with the progression from CD to CRC were selected for further analysis, including mRNA-miRNA interaction network construction, functional enrichment analysis, gene set enrichment analysis, and survival analysis. To validate the findings, quantitative real-time PCR (RT-PCR) was performed on tissue samples from normal and CRC patients to confirm the differential expression of selected genes and miRNAs.

Results: We identified ١٠ differentially expressed miRNAs and ١٨١ differentially expressed genes common to the progression from CD to CRC. The genes associated with each of these ١٠ miRNAs were used for downstream analyses. RT-PCR results confirmed that miR-١٩٥-٥p, PHLPP٢, and LITAF were significantly downregulated in CRC tissues compared to controls.

Conclusion: Our findings suggest that PHLPP٢, LITAF, and miR-١٩٥-٥p may play crucial roles in CRC tumorigenesis and could be considered potential therapeutic targets and diagnostic biomarkers, pending further in vitro and in vivo validation.

Keywords: Colorectal cancer (CRC),Crohn's disease (CD),Biomarkers,miRNAs,Differentially expressed genes (DEGs)

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Uncovering the Prebiotic Effects of Oleuropein as a Novel Therapeutic Strategy for Gastric Cancer (Review)

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Introduction: Gastric cancer ranks among the leading contributors to cancer-related mortality globally, with Helicobacter pylori infection identified as the predominant causative factor. Conventional treatment typically entails the use of antibiotics, which, although effective, may disrupt the microbiota's equilibrium. In light of the rising antibiotic resistance observed in Helicobacter pylori during gastric cancer therapy, this research proposes a safer therapeutic alternative. The prebiotic oleuropein has the potential to selectively target gastric cancer cells while simultaneously maintaining the beneficial microbiota within the stomach.

Methods: A thorough examination was performed through a systematic search in both PubMed and Springer databases. The review focused on subjects pertinent to gastric cancer, prebiotic, oleuropein, and additional significant terms such as antibiotic resistance, microbiota, and apoptosis. Articles that did not align with the specified criteria were excluded from consideration. Ultimately, ٤٨ references were chosen for this review, as they offered the necessary information and data.

Results: There is an increasing apprehension regarding the rise of antibiotic resistance in Helicobacter pylori, particularly in the context of gastric cancer treatment. Consequently, the World Health Organization (WHO) has designated clarithromycin-resistant Helicobacter pylori infections as a critical focus for research and development in the field of antibiotic resistance. It is well-documented that the administration of antibiotics can lead to substantial alterations in both the functionality and diversity of the microbiota. For instance, the use of amoxicillin in healthy individuals has been linked to enduring modifications in microbiota composition and the emergence of antibiotic-resistant strains. Comparable outcomes have been noted with other antibiotics, including ciprofloxacin, cefprozil, and clindamycin. The disruption of microbiota following antibiotic treatment can persist for up to a year and may result in various health issues, such as asthma, obesity, diabetes, diarrhea, colitis, and compromised immune responses. A viable strategy for managing antibiotic resistance is the employment of prebiotics such as oleuropein, which has been proven to exert beneficial effects on the composition and performance of the gastrointestinal microbiota. Oleuropein, a bitter glycoside and one of the predominant phenolic compounds found in olive leaves, plays a role in modulating the microbiota within the stomach and intestines, as well as influencing body fat metabolism, glucose levels, and mineral absorption. This compound is preferentially fermented by beneficial microbiota, thereby fostering the proliferation of advantageous bacterial species while inhibiting pathogenic ones. Research indicates that diets enriched with oleuropein in murine models lead to a notable increase in the population of the

beneficial Lactobacillus plantarum. This suggests that oleuropein not only enhances the gastric microbiota but may also possess therapeutic potential in the context of gastric cancer. The compound oleuropein has been identified as an effective agent in preventing the growth, migration, invasion, and angiogenesis of cancer cells. Its anticancer effects are attributed to its ability to alter several oncogenic signaling pathways. In an experimental study, oleuropein demonstrated significant reductions in reactive oxygen species (ROS) levels, an increase in total antioxidant status, and a repair of gastric cell damage induced by cisplatin in rats. Additionally, recent findings have reported that nanoparamagnetic oleuropein synthesis can induce KRAS overexpression and inhibit AGS cancer cell proliferation, as well as trigger apoptosis in the AGS cell line.

Conclusion: Therefore, this study proposes oleuropein, a prebiotic, as a safer therapeutic strategy that targets gastric cancer cells while concurrently preserving the beneficial microbiota of the stomach. This suggests that oleuropein could become a new therapeutic agent for gastric cancer in the future. It is apparent that further research in this field could yield valuable insights that may facilitate advancements in the treatment of gastric cancer.

Keywords: Gastric cancer, oleuropein, prebiotic, antibiotic resistance, microbiota

Unraveling the Immune Web of Psoriasis: From Inflammatory Memory to Targeted Therapies

(Review)

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Introduction: Psoriasis is a chronic, inflammatory skin disease characterized by dysregulated immune responses and systemic inflammation. Affecting ١-٣٪ of the global population, its etiology remains incompletely understood, with contributions from genetic, environmental, and immune factors. The past few decades have seen significant advancements in understanding its pathophysiology, highlighting the roles of immune cells, keratinocytes, and cytokines. This review aims to present recent findings in psoriasis research, focusing on immune mechanisms and emerging therapeutic strategies.

Methods: A comprehensive literature search was conducted using PubMed, Scopus, and Web of Science databases. Studies were selected based on relevance to the pathophysiology, immune involvement, and treatment outcomes of psoriasis. Key terms included "psoriasis," "immune response," "biologic therapy," "inflammatory memory," and "T cells."

Results: Recent studies have revealed crucial insights into the immune mechanisms underlying psoriasis. The routine use of targeted immunomodulatory therapies has transformed patient outcomes, with skin clearance rates of up to ٦٠٪ at one year. However, recurrence often follows drug withdrawal due to the persistence of inflammatory memory in the skin, primarily driven by tissue-resident memory T cells, Langerhans cells, and dermal dendritic cells. Additionally, γδ T cells, known for producing IL-١٧, have been identified as key mediators of repeated psoriatic inflammation, exhibiting memory-like characteristics in epithelial tissues. These cells are implicated in both host defense and immune dysregulation, reinforcing their importance in psoriasis and other inflammatory conditions. The immune landscape of psoriasis involves multiple cell types, including TH١٧, dendritic cells, and keratinocytes, which create a pathogenic triad. Emerging evidence from high-throughput studies has expanded our understanding of signaling pathways and cell populations, including TH٩, TH٢٢, and γδ T cells. These discoveries have revolutionized the clinical management of psoriasis, paving the way for personalized treatment approaches that aim to sustain remission while reducing long-term drug burdens. Research into B cells also suggests a potential role in exacerbating psoriasis, particularly through autoantibody production and pro-inflammatory cytokine release.

Conclusion: The pathogenesis of psoriasis is a complex interplay of immune cells and cytokines, which not only drives skin inflammation but also contributes to systemic effects, such as psoriatic

arthritis. Targeted therapies, including biologics, have significantly improved patient outcomes, but challenges remain in maintaining long-term remission. Understanding the immune mechanisms, including the roles of T cells, dendritic cells, and emerging players like B cells, is essential for developing more effective and sustainable treatments. Future research should continue exploring immune dysregulation in psoriasis, with the goal of reducing the reliance on long-term therapies while preventing recurrence

Keywords: Psoriasis, Immune dysregulation, Inflammatory memory, Biologic therapy, T cells

Unraveling the Impact of Long Non-Coding RNAs on Protein Networks in Colorectal Cancer: A New Frontier in Cellular Dynamics (Research Paper)

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Introduction: LncRNAs play a pivotal role in colorectal cancer by serving as key regulators of gene expression, with their dysregulation linked to various cancer hallmarks. This study focuses on unraveling the molecular underpinnings of colorectal cancer susceptibility by deciphering dysregulated LncRNAs that target the PI٣K/AKT pathway.

Methods: We conducted an extensive review of prior studies exploring the modulatory role of dysregulated LncRNAs in CRC. Utilizing the LncRNome database, we identified all LncRNA-targeted genes. Cytoscape software facilitated the investigation of protein-protein interactions (PPI) among these genes, with a focus on identifying hub proteins. Gene-subnetwork Gene Ontology (GO) analysis, Cytocluster analysis, and promoter motif analysis were performed for a comprehensive understanding.

Results: Our analysis revealed genes targeted by dysregulated LncRNAs impacting the Wnt pathway. Within this network, ١٢ hub proteins were identified. Subnetwork analysis showcased five crucial functional modules, complemented by the identification of ١٠ significant promoter motif elements through Cytocluster analysis and promoter motif analysis.

Conclusion: This study not only contributes to understanding the intricate regulatory mechanisms of dysregulated LncRNAs in colorectal cancer but also paves the way for identifying potential biomarkers and therapeutic targets. The findings hold promise for advancing personalized approaches in the management of colorectal cancer.

Keywords: LncRNAs, colorectal cancer; systems biology; promotor motif analysis; subnetwork analysis

Unraveling the Molecular Mechanisms of Genetic Biomarkers in Lung Cancer: Implications for Predictive Prognosis and Targeted Therapy (Review)

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Introduction: Lung cancer remains a significant public health challenge on a global scale. Despite progress in diagnostic and treatment strategies, the prognosis for patients with lung cancer remains poor, with a ٥-year survival rate of around ٢٢٪ for those with locally advanced disease. The discovery of genetic biomarkers has revolutionized our understanding of the disease, enabling the development of targeted therapies and improving patient outcomes. This review aims to summarize the current knowledge on the molecular mechanisms underlying genetic biomarkers in lung cancer, focusing on their implications for prognosis, prediction, and targeted therapy.

Methods: This assessment is founded upon a thorough investigation of the available literature, concentrating on studies that have been published in the past ten years. The search terms employed encompassed "lung cancer," "Targeted Therapy," "genomics," and "biomarker." The search was limited to English language publications, and the inclusion of papers was determined by the consensus of the authors, taking into account their relevance to the subject matter.

Results: In addition to their role in predicting prognosis and guiding targeted therapy, genetic biomarkers provide valuable insights into the molecular mechanisms driving lung cancer progression and therapeutic resistance. The intricate interplay between genetic alterations and signaling pathways underscores the complexity of lung cancer biology and necessitates a multifaceted approach to treatment. EGFR mutations, for instance, not only serve as predictive biomarkers for EGFR TKI sensitivity but also shed light on the underlying mechanisms of tumor growth and survival. The dysregulated EGFR signaling pathway, driven by mutations in the kinase domain, promotes oncogenic transformation through the activation of downstream effectors such as PI٣K/AKT and RAS/RAF/MAPK cascades. Moreover, secondary resistance mechanisms, such as the acquisition of TV٩٠M mutation, limit the long-term efficacy of EGFR TKIs, necessitating the development of next-generation inhibitors to overcome resistance. Similarly, ALK and ROS١ rearrangements provide valuable insights into the molecular pathogenesis of lung cancer and the oncogenic addiction to aberrant kinase activity. The fusion of ALK or ROS١ with partner genes results in constitutive activation of downstream signaling pathways involved in cell proliferation and survival. However, the emergence of resistance mutations within the kinase domain, as well as bypass signaling pathways, poses significant challenges to the sustained efficacy of ALK and ROS١ inhibitors, highlighting the need for combination therapies and novel treatment strategies. Furthermore, BRAF mutations, particularly the V٦٠٠E mutation, illuminate the role of MAPK pathway activation in lung cancer development and progression. BRAF inhibitors have shown clinical efficacy in BRAF-mutant lung

cancer; however, adaptive resistance mechanisms, such as feedback activation of alternative signaling pathways, limit their therapeutic benefit. Combinatorial approaches targeting multiple nodes within the MAPK pathway and overcoming feedback loops hold promise in circumventing resistance and improving patient outcomes. The integration of genetic biomarkers into clinical practice necessitates a comprehensive approach encompassing molecular profiling, therapeutic selection, and monitoring of treatment response. Advances in next-generation sequencing technologies have facilitated the identification of novel genetic alterations and the elucidation of complex tumor genomic landscapes, enabling tailored therapeutic interventions based on individual tumor biology. Moreover, the advent of liquid biopsy techniques offers a non-invasive means of serially monitoring tumor evolution and detecting emerging resistance mechanisms, thereby guiding timely treatment adjustments. By leveraging the power of genetic biomarkers and molecular profiling, clinicians can optimize treatment strategies, minimize therapeutic resistance, and improve overall survival in lung cancer patients.

Conclusion: In conclusion, genetic biomarkers represent a cornerstone of precision medicine in lung cancer, providing critical insights into tumor biology, prognosis, and therapeutic response. The ongoing elucidation of molecular mechanisms underlying genetic alterations holds promise for the development of innovative targeted therapies and combinatorial treatment approaches. Through collaborative efforts between researchers, clinicians, and industry partners, genetic biomarkers will continue to drive progress in lung cancer management, ultimately transforming the landscape of precision oncology and improving patient outcomes.

Keywords: Lung cancer, Genetic biomarkers, Targeted therapy.

Unraveling the Molecular Mechanisms Underlying Acute Myeloid Leukemia (AML) (Review)

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Introduction: Introduction Lynch syndrome, a hereditary condition, plays a significant role in elevating the risk of colorectal cancer and various other cancer types due to mutations in DNA mismatch repair (MMR) genes. These MMR genes are crucial for correcting errors that occur during DNA replication, and their dysfunction can lead to genomic instability, thereby increasing cancer susceptibility. One of the key factors influencing gene expression is DNA methylation, an epigenetic modification that can regulate gene activity without altering the DNA sequence itself. DNA methylation typically acts as a silencing mechanism, turning off genes when methyl groups are added to the DNA molecule. In the context of DNA repair genes, changes in methylation status can affect the cell's ability to repair DNA damage, thus impacting cancer risk. This study aims to investigate the influence of DNA methylation changes in specific DNA repair genes on the risk of colorectal cancer in individuals with Lynch syndrome. We will compare these changes to those observed in a control population that does not have Lynch syndrome, thereby shedding light on the potential role of epigenetic modifications in cancer susceptibility within this high-risk group.

Methods: Materials and Methods The study involved a total of ١٥٠ participants, consisting of ٧٥ individuals diagnosed with Lynch syndrome and ٧٥ age- and sex-matched controls who did not have Lynch syndrome. The participants included ٨٠ males and ٧٠ females, with an average age of ٤٥ years. DNA samples were obtained from both blood and tumor tissues to ensure comprehensive analysis. To assess the methylation status of specific DNA repair genes, we employed methylation-specific PCR (MSP), a sensitive technique that allows the detection of methylation patterns in DNA. The genes selected for analysis were MLH١, MSH٢, and MSH٦, which are known to be integral components of the MMR system and have been implicated in Lynch syndrome-associated cancers.

Results: Results The study uncovered significant differences in the methylation levels of DNA repair genes between the Lynch syndrome patients and the control group. Among the Lynch syndrome patients, ٦٢ out of ٧٥ exhibited hypermethylation in the MLH١ gene, ٥٨ showed hypermethylation in MSH٢, and ٥٤ in MSH٦. In contrast, the control population demonstrated markedly lower levels of hypermethylation, with ١٥ individuals showing hypermethylation in MLH١, ١٢ in MSH٢, and ١٠ in MSH٦. These findings indicate that there is a clear association between increased methylation of these DNA repair genes and the presence of Lynch syndrome.

Conclusion: Conclusion Our findings strongly suggest that the hypermethylation of DNA repair genes, particularly MLH١, MSH٢, and MSH٦, is linked to an elevated risk of colorectal cancer in individuals with Lynch syndrome. The observed epigenetic modifications in these genes could

potentially serve as biomarkers for the early detection of cancer risk, facilitating targeted prevention strategies for this vulnerable population. Identifying and understanding these methylation patterns may offer new insights into the mechanisms underlying Lynch syndrome and contribute to the development of personalized therapeutic approaches aimed at mitigating cancer risk in affected individuals.

Keywords: Lynch syndrome, colorectal cancer, DNA methylation, DNA repair genes, epigenetics

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Unveiling the Antibacterial Potential of Chrysin: A Naturally Occurring Flavonoid in Plants (Review)

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Introduction: The exploration of natural compounds with antimicrobial properties has gained significant attention in the context of increasing antibiotic resistance. Chrysin, a naturally occurring flavonoid found in plants, has emerged as a promising candidate owing to its diverse biological activities. This review aimed to reveal the potential of chrysin as an antimicrobial agent and provide a comprehensive understanding of its properties and mechanisms of action.

Methods: A thorough literature search was conducted to identify relevant studies investigating the antimicrobial activity of chrysin. Various scientific databases including PubMed, Scopus, and Web of Science were searched using keywords related to chrysin, antimicrobial activity, and plant sources. Studies using in vitro and in vivo models to evaluate the antimicrobial effects of chrysin were included. The selected studies were critically reviewed and analyzed to extract key information regarding the antimicrobial potential and mechanism of action of chrysin.

Results: The reviewed studies consistently demonstrate the antimicrobial potential of chrysin against a broad spectrum of microorganisms. Chrysin exhibits inhibitory effects against both Gram-positive and Gram-negative bacteria, including antibiotic-resistant strains. It also shows antifungal activity against various fungal species, and exhibits antiviral effects against certain viruses. The mechanism of action of chrysin involves multiple targets within microbial cells, making it difficult for microorganisms to develop resistance. Additionally, chrysin demonstrated synergistic effects when combined with conventional antimicrobial agents, suggesting its potential as an adjuvant therapy.

Conclusion: Chrysin, a natural flavonoid abundant in plants, possesses significant antimicrobial properties. Its broad-spectrum activity, coupled with its multiple mechanisms of action, make it a promising candidate for the development of novel antimicrobial agents. Further research is required to optimize chrysin extraction methods, evaluate their safety profiles, and explore their potential clinical applications. The discovery of chrysin as a natural antimicrobial compound opens avenues for the development of alternative strategies to combat microbial infections and address the global challenge of antibiotic resistance.

Keywords: chrysin; flavonoids; antimicrobial activity; plant sources; extraction methods

Upregulation of heat shock proteins ٧٠ and ٩٠ induced by transient scrotal hyperthermia in mice

(Research Paper)

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Introduction: It is now accepted that scrotal heat stress could adversely affect spermatogenesis. This high thermal condition can cause a reduced male fertility potential. Nowadays, there is limited data regarding the effect of transient scrotal hyperthermia on heat shock proteins ٧٠ and ٩٠ in mice. In the current study, we investigated the effects of scrotal hyperthermia on the expression of heat shock proteins, stereological parameters and semen quality in mice.

Methods: In this examination, a total of ١٨ healthy adult male NMRI mice were divided equally into two groups: control and scrotal hyperthermia. Scrotal heat stress was induced by placing the lower parts of mice bodies into the water bath for three consecutive days (٤٣°C, ٢٠ min/day). Then, epididymis and testicular samples were collected for evaluation of sperm parameters, stereological study, mRNA, and protein expression of HSP٧٠ and HSP٩٠.

Results: Our results revealed that scrotal hyperthermia could strikingly increase the level of mRNA and protein expression of HSP٧٠ and HSP٩٠ in the samples. In addition, stereological parameters and semen quality significantly decreased in transient scrotal hyperthermia-induced mice compared to the control group.

Conclusion: The results of this study indicate that seminiferous tubules exhibit strong expression of heat shock proteins in response to hyperthermia, serving as a protective mechanism against cell apoptosis caused by thermal stress. Nevertheless, the observed decrease in sperm parameters and stereological measurements showing reduced cell numbers and tissue volume suggest that this protective factor was ineffective when hyperthermia occurred before puberty. Ultimately, such high temperatures experienced prior to puberty may lead to fertility issues during the postpubertal period.

Keywords: Hyperthermia, Heat Shock Protein, Testis, Male fertility, Heat stress

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USH۲A Mutation Identified in a Patient with Early-Onset Usher Syndrome in Lorestan (Research Paper)

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Introduction: Usher syndrome is a complex genetic disorder that leads to a combination of visual and auditory impairments. The syndrome is characterized by a wide range of clinical presentations and is genetically diverse, with no current definitive treatment available. This report aims to describe a identified homozygous USH۲A mutation in a Lorestani patient who experienced hearing impairments, low set ears, small ears, contributing to the understanding and diagnosis of Usher syndrome.

Methods: The boy, who is ٦-year-old, presented with a developmental delay, and the spasms, intellectual disability, low set ears, small ears. Genomic DNA was extracted from the blood sample. Whole Genome Sequencing was performed, and Sanger sequencing verified the results.

Results: A comprehensive clinical and molecular genetic evaluation was conducted, which was consistent with a diagnosis of Usher syndrome. Patient Genetic testing identify one pathogenic homozygous mutation in exon ۱۰ of USH۲A (c.C۱٦٦۳G ; p.L٥٥٥V), with the proband's parents being hetrozygous for this mutation.

Conclusion: The identification of this USH۲A mutation not only broadens the spectrum of genetic alterations known to cause Usher syndrome but also enhances the diagnostic tools available for clinicians. It provides valuable insights into the genetic basis of the disease, aiding in the assessment of patient prognosis and the importance of genetic testing in identifying mutations in patients with undiagnosed progressive hearing impairments.

Keywords: Usher syndrome; genetic mutation; USH۲A; genetic diagnosis.

Using Copper-Cysteamine Nanoparticles for Enhanced Radiotherapy in Melanoma Treatment

(Review)

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Introduction: According to the World Health Organization report, skin cancer has been reported as the fifth most common cancer in the world. Skin cancer arises from unrepaired deoxyribonucleic acid (DNA) damage in skin cells, leading to genetic defects or mutations in the skin. Melanoma, basal cell carcinoma, and squamous cell carcinoma are three major types of skin cancer. Among them, melanoma is the most severe form and accounts for approximately ٤٪ of all newly diagnosed cancers annually in the United States. Melanoma treatment is still a major challenge in the clinic. Treatments include radiation, chemotherapy, surgery, immune therapy, hormone therapy, and targeted therapy. Although these treatments are generally effective, they have some drawbacks. For example, radiotherapy is one of the most common and effective cancer treatments, however, it can have high side effects. Hence, it is crucial to improve radiation efficacy, reduce its dose, and develop a method to increase the dose to the tumor tissue while minimizing radiation to the surrounding tissue. Several techniques have been investigated to minimize the side effects of radiation therapy, including combining radiotherapy with photodynamic therapy, chemotherapy, and immunotherapy. One effective method to reduce the side effects and enhance the killing efficacy is to use radiosensitizers to assist the radiation treatment. Recently, various nanoparticle radiosensitizers, such as copper-cysteamine nanoparticles (Cu-Cy NPs), gold nanoparticles, silver nanoparticles, and hafnium oxide nanoparticles, have been studied as novel radiosensitizers. Cu-Cy NPs are unique compared to other nanoparticle radiosensitizers because Cu-Cy NPs act as photosensitizers and can be activated by various types of radiation, including X-rays, microwaves, and ultrasound, to produce reactive oxygen species (ROS). In this review, we investigated the use of Cu-Cy NPs for radiation improvement in melanoma cell lines

Methods: The Web of Science, Science Direct, PubMed, and Google Scholar databases were searched up to July ٢٠٢٤, utilizing various keyword combinations: melanoma, Copper-Cysteamine nanoparticle, radiotherapy, photodynamic therapy, and skin cancer.

Results: Studies have shown that when Cu-Cy NPs are placed in an acidic environment, they can release copper ions and accelerate the production of ROS in biological systems without light. Exposure of Cu-Cy NPs to X-rays has been shown to stimulate the production of singlet oxygen, hydroxyl radicals, and other ROS, which inhibits tumor growth. ROS can damage or kill tumor and vascular endothelial cells via apoptosis and necrosis pathways. The results showed that Cu-Cy-mediated PDT can stimulate strong anti-tumor immune responses by promoting the maturation of dendritic cells (DCs). This leads to the activation of CD٤+ T cells, CD٨+ T cells, and natural killer (NK) cells, and inhibits the M٢ macrophages in the tumor microenvironment (TME). As a result, tumor growth is halted by killing or suppressing tumor cells. Moreover, the size of nanoparticles

plays a vital role in influencing their properties and performance. In the case of the ٤٠ nm Cu–Cy NPs, their larger surface area compared to other NPs leads to the production of more ROS. Additionally, The cells absorb the ٤٠ nm NPs more effectively. The ٤٠nm Cu-Cy NPs efficiently prevented melanoma when exposed to X-rays. These findings confirmed that the combination of Cu-Cy NPs and X-rays promoted apoptosis and/or necrosis of melanoma cells.

Conclusion: Studies showed that Cu–Cy NP radiosensitizers can efficiently improve X-ray radiation to destroy melanoma cells by inducing generation ROS, apoptosis, and necrosis.

Keywords: melanoma, Copper-Cysteamine nanoparticles, radiotherapy, and photodynamic therapy

Using immunotherapy to treatment melanoma cancer review article (Review)

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Introduction: Malignant melanoma is one of the most aggressive skin tumors and its prevalence is increasing in Western countries, accounting for ١٠,٠٠٠ deaths annually in the United States alone. While efforts have been made to improve the early diagnosis of melanoma, patients with distant metastases still face a poor prognosis, with a median survival of ٦ to ١٠ months until recently. Major advances have been made in the last ٥ years in the systemic treatment of metastatic melanoma Advanced and metastatic: Targeted therapies that inhibit the mitogen-activated protein kinase (=MAPK) pathway in tumors with BRAFV٦٠٠ and immunotherapies that inhibit various checkpoints activate the patient's immune system in approximately ٤٠-٥٠٪ of cases A BRAFV٦٠٠ mutation is found in melanoma patients.This mutation causes an active MAPK pathway.

Methods: Of all the malignancy treatments, immunotherapy has been most extensively studied in metastatic melanoma. These often experimental and immunotherapy interventions can be divided into the following: ١. Biological substances such as cytokines, including interleukin-٢ (IL-٢), interferons, and granulocyte-monocyte colony-stimulating factor (GM-CSF). ٢. Vaccination strategies such as peptide vaccines, whole protein vaccines, virus-based vaccines, DNA vaccines and dendritic cell-based vaccines. ٣. Cell therapy with lymphokine-activated killer cells (LAKs), tumor-infiltrating lymphocytes (TILs), melanoma-specific T cells derived from peripheral blood, and gene-modified T lymphocytes ٤ immune inhibitors, including anti-CTLA٤, anti-PD١, and anti-PDL١, and immune-stimulating molecules, including anti-CD١٣٧.

Results: New immunotherapies are in the clinical pipeline and will hopefully provide effective options for those who do not respond to anti-PD-١-based combination approaches

Conclusion: In evaluating the response to these new therapies, there appears to be a spectrum of patients from those in whom blocking the PD-١ / PD-L١ axis alone is effective to those who respond better with the addition of CTLA-٤ blockade. to those who do not respond to any of these strategies.

Keywords: Cancer, immunotherapy , treatment , melanoma

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Using Machine Learning (Machine Learning) in Predicting the Risk of Thyroid Cancer based on Genetic Information (Review)

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Introduction: Thyroid cancer is one of the common endocrine malignancies, with an increasing incidence in recent years. Early diagnosis and assessment of the risk of thyroid carcinoma are essential for its effective management and treatment. In recent years, machine learning has proved to be a revolutionary tool for predicting several risks, including thyroid cancer. This review article summarizes the current status of the research aimed at using ML to predict the risk of thyroid cancer, with particular attention dedicated to the role of genetic information.

Methods: We carried out a comprehensive review of the literature using search strategies in databases like PubMed, Embase, and the Cochrane Library. Studies were selected that applied the ML algorithm to predict the risk of thyroid cancer based on genetic information as a feature. Search terms included "thyroid cancer," "machine learning," "risk prediction," and "genetic information." The studies that used machine learning to predict the risk of thyroid cancer were critically appraised for their methodological quality, such as the type of design, data collection, feature selection, model development, and validation of the developed model.

Results: Indeed, several works have shown that ML has the potential to predict risk in thyroid cancer depending on genetic information. It was demonstrated by Xie et al. that their classification model built with the XGBoost algorithm reached an AUC of ۰,۸٤ for the case of thyroid nodule malignancy prediction. Age, obesity, prothrombin time, fibrinogen, and HBeAb were high-risk factors, whereas monocyte, D-dimer, T۳, FT۳, and albumin were low-risk factors. A Bagged CART model built by Jiang et al. showed a ۹۹,۱٪ accurate prediction of thyroid cancer. The recurrence of thyroid cancer was predicted, with importance placed on the BRAFV٦۰۰E mutation.

Conclusion: Using genetic data, machine learning has shown great potential in predicting thyroid cancer risk. Machine learning models integrate genetic data with other clinical and demographic data to identify high-risk populations and derive management strategies. Further research is needed to validate models within broad, diverse populations and study the implementation strategy for ML in clinical decision-making workflows.

Keywords: Thyroid Cancer, Machine learning, Risk prediction, Genetic information, BRAFV٦۰۰E mutation

Using mesenchymal stem cells as a new approach to cancer treatment (Review)

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١.

Introduction: The tumor microenvironment (TME) consists of different types of cells and an extracellular matrix, of which mesenchymal stem cells (MSCs) are part of this microenvironment. Previous studies have shown that various factors in the TME including mesenchymal stem cells known as cancer-associated stem cells (CA-MSCs), cause low efficacy of immunotherapy, tumor progression, and relapse. These cells cause tumor cell growth, metastasis, angiogenesis, immune system escape, and drug resistance in the tumor environment. However, MSCs, MSC-derived membranes and MSC-derived exosomes can be used as carriers of chemotherapy drugs, oncolytic viruses, or therapeutic genes to precisely deliver cytotoxic agents to cancer sites. Therefore, MSCs can be considered as a promising source in tumor treatment.

Methods: Mesenchymal stem cells (MSCs), one of the most widespread cells in the human body, were first discovered in ١٩٧٦ (١). In general, MSCs are known as pluripotent stem cells that can differentiate into adipocytes, chondrocytes, osteocytes, and other lineages (٢). Also, they can adhere to plastic containers and multiply in laboratory conditions. These cells express CD٧٣, CD٩٠, and CD١٠٥ on their surface, but lack CD١٤, CD٤٥, CD١٩, and HLA-DR. In addition to modulating the immune system, MSCs also repair damaged tissue. They migrate to the tissue through the chemokines that are released from the damaged tissue, and by differentiating into tissue-specific mature cells, they repair the damaged tissue (٣). Today, cancer is known as the most common and deadly disease. Also, the role of MSCs in the initiation, growth, and metastasis of cancer has been proven (٤). MSCs found in tumor tissue are called tumor-associated mesenchymal stem cells (TA-MSCs). Many studies have shown that TA-MSCs play a tumor-promoting role (٥–٧). But today, it has been shown that MSCs can have an anti-tumor effect despite the stimulating impact on tumor growth (٨–١٠). Therefore, we decided to review the discoveries regarding MSC-based anticancer therapy.

Results: Review

Conclusion: Today, using MSCs for cancer treatment is one of the emerging attractive treatment options. TA-MSC cells in TME can affect tumor cells through direct cell-to-cell contact, MSC-derived exosomes and cytokines, or signaling pathways. According to recent studies, researchers believe that TA-MSC can be one of the main culprits in tumor progression. Therefore, tumor progression can be prevented by inhibiting the proliferation of TA-MSCs. ١) Reduction of factors effective in angiogenesis and proliferation that are released from MSC, ٢) Inhibiting the release of chemokines that play a role in the tropism of MSCs to the tumor environment, and ٣) Suppression of factors that cause drug resistance in tumor cells in combination with oncotherapy, can inhibit the development of tumor cells. MSCs containing anti-tumor drugs, oncolytic viruses, and suicide genes can also be

used for tumor treatment by genetic engineering. Therefore, whether to use MSC as a therapeutic target or as a tool for tumor treatment is still debated.

Keywords: Mesenchymal stem cells, Cancer, Tumor microenvironment (TME)

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Using tissue engineering to treat congenital abnormalities in the female reproductive system (Review)

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Introduction: Congenital abnormalities in the reproductive system of women can lead to serious problems in the health and quality of life of patients. These abnormalities include problems such as vaginal agenesis, bicornuate uterus, and other structural abnormalities that may lead to infertility and psychological problems. Tissue engineering, as a new technology, has a high potential to provide new and effectsolutions in the treatment of these abnormalities. Using cells, biomaterials and biological agents, this technology creates new tissue structures that can replace damaged or defective tissues. The aim of this study is to systematically review the available articles on the use of tissue engineering for the treatment of congenital anomalies in the female reproductive system.

Methods: This research has been done as a systematic review. Studies published in the period from ۲۰۰۰ to ۲۰۲۲ that investigated the use of tissue engineering for the treatment of congenital anomalies in the female reproductive system. Data were collected by searching scientific databases such as PubMed, Scopus, and Web of Science. Search keywords included "tissue engineering", "congenital malformations", "female reproductive system" and "stem cells". Studies that investigated the use of tissue engineering methods for the treatment of congenital anomalies in the reproductive system of women and had valid methodologies have been reviewed. Irrelevant articles, low quality studies and invalid articles were excluded from the review. The collected data have been reviewed and analyzed using the methods of content analysis and qualitative meta-analysis.

Results: The results of the review showed that tissue engineering has been used mainly to treat abnormalities such as vaginal agenesis, bifurcated uterus and structural defects in the vaginal wall. Various methods including the use of stem cells, biological biomaterials such as collagen and biodegradable polymers, and controlled drug delivery systems have been used in the treatment of these abnormalities. Also, ۳D printing techniques have been used to create complex textured structures. Clinical and preclinical studies have shown that the use of tissue engineering can have positive results in the reconstruction and improvement of the function of female reproductive tissues. In some cases, a significant improvement in the quality of life of patients and a reduction in the symptoms of abnormalities have been observed.

Conclusion: This systematic review study showed that tissue engineering as a new technology has a high potential for the treatment of congenital abnormalities in the female reproductive system. Different methods of tissue engineering, including the use of stem cells and biomaterials, can help to regenerate and improve the function of reproductive tissues. However, to improve and expand the use of this technology, there is a need for further research and development of practical solutions.

Keywords: Tissue engineering, congenital anomalies, female reproductive system, stem cells

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using viruses in CRISPR (Review)

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Introduction: Introduction The CRISPR-Cas systems have fundamentally transformed the field of genetic engineering by offering precise methodologies for genome modification. Initially identified as an immune response mechanism in bacteria, CRISPR-Cas has been repurposed for application across diverse biological organisms. Viruses serve an essential function in augmenting the efficiency and specificity of CRISPR-Cas implementations. This article examines the incorporation of viruses within CRISPR-Cas frameworks, emphasizing their methodologies, outcomes, and prospective implications for future research.

Methods: Methods The incorporation of viruses in CRISPR-Cas entails the utilization of viral vectors to transport CRISPR constituents into designated target cells. These vectors, including lentiviruses and adenoviruses, are meticulously engineered to encompass the requisite CRISPR components, such as the Cas protein and guide RNA. The viral-mediated delivery approach provides numerous advantages, including elevated transduction efficiency and the capacity to target a wide array of cell types. The formulation of these viral vectors necessitates rigorous design protocols to ensure safety and to mitigate off-target effects.

Results: Results The amalgamation of viral vectors with CRISPR-Cas systems has culminated in substantial advancements within the realms of biomedical research and therapeutic interventions. The utilization of viral delivery mechanisms has augmented the accuracy of gene editing techniques in both in vitro and in vivo experimental frameworks. This methodology has been employed to rectify genetic aberrations, elucidate gene functionality, and establish disease models. The findings reveal an increase in editing efficacy alongside a diminished immunological response in contrast to conventional methodologies. Furthermore, the incorporation of viral vectors has broadened the prospective applications of CRISPR-Cas technology in the management of genetic disorders and infectious pathologies.

Conclusion: Conclusion The integration of viral entities with CRISPR-Cas systems signifies a groundbreaking domain within the field of genetic engineering. By utilizing the inherent mechanisms of viral infection, scholars can attain a more efficient and precise delivery of CRISPR components. This collaboration possesses the capacity to enhance therapeutic interventions and enrich our comprehension of gene functionalities. Nevertheless, continuous inquiry is imperative to confront challenges including safety issues and ethical dilemmas. As technological advancements unfold, the involvement of viruses in CRISPR-Cas applications is anticipated to broaden, thereby facilitating novel approaches to intricate genetic issues.

Keywords: CRISPR-Cas Viruses Vector

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Utilizing Bioinformatics Databases to Discover Key Genes Associated with Colorectal Cancer Development (Research Paper)

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Introduction: Colorectal cancer (CRC) is the third most common cause of cancer-related deaths worldwide, presenting a significant global health challenge that necessitates advancements in both diagnostics and treatment to enhance patient survival rates. Recently, the analysis of microarray data has emerged as a promising and effective approach for classifying cancers and evaluating prognosis. This study focuses on integrating microarray data analysis to identify genes associated with CRC by examining gene expression patterns from four microarray datasets found in the Gene Expression Omnibus (GEO).

Methods: We collected four gene expression datasets: GSE٣٧١٨٢, GSE٢٥٠٧٠, GSE١٠٩٥٠, and GSE١١٣٥١٣, along with differentially expressed genes (DEGs). The analysis was conducted using R software, the DAVID database, protein-protein interaction (PPI) networks, the Cytoscape application, and receiver operating characteristic (ROC) curves.

Results: From the four datasets analyzed, we identified ١٠ hub genes: SLC٢٦A٣, CLCA١, GUCA٢A, MS٤A١٢, CLCA٤, GUCA٢B, KRT٢٠, AQP٨, MAOA, and ADH١A. These DEGs were found to be significantly involved in multiple pathways, such as nitrogen metabolism, mineral absorption, pancreatic secretions, and tyrosine metabolism, according to the Kyoto Encyclopedia of Genes and Genomes (KEGG) database.

Conclusion: Our bioinformatics analysis indicates that the DEGs highlighted in this study may serve as crucial markers in understanding the molecular mechanisms underlying CRC progression. The insights gained could aid researchers in developing innovative strategies for predicting CRC, facilitating early diagnosis, and improving treatment options for patients suffering from this disease.

Keywords: Colorectal cancer (CRC), Differentially expressed genes (DEGs), Hub genes

Utilizing CRISPR/Cas۹ gene editing to treat Amyotrophic Lateral Sclerosis disease: An overview

(Review)

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Introduction: Amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease, is a progressive neurodegenerative disorder that damages motor neurons (MNs) in the spinal cord, brainstem, and motor cortex. The disease typically progresses rapidly, leading to muscle weakness, atrophy, paralysis, respiratory failure, and eventually death within ۲–۵ years of symptom onset. ALS is among the most prevalent adult motor neuron diseases, affecting approximately ۲–۳ people per ۱۰۰,۰۰۰ worldwide. The increasing incidence of ALS in recent years is partly due to improvements in diagnostic capabilities. Despite these advancements, there is currently no cure. Existing treatments, such as Riluzole, extend survival by about three months but offer limited benefits, underscoring the urgent need for more effective therapies. While most ALS cases are sporadic with unclear causes, around ۱۰–۱۵٪ of cases are familial, suggesting a genetic component. More than ۵۰ genes have been associated with ALS, including those with causal or modifying mutations. Key genes often studied in ALS research, such as superoxide dismutase (SOD۱), chromosome ۹ open reading frame ۷۲ (C۹orf۷۲), TAR DNA-binding protein ٤۳ (TDP٤۳), and RNA binding protein fused in sarcoma (FUS), are linked to about ۷۵٪ of familial ALS cases. Advances in understanding the disease mechanisms have been driven by research into the molecular pathways affected by these genes, revealing potential new therapeutic targets. Consequently, ALS models and gene therapies targeting these mutations are being explored to develop effective treatments. Gene editing, particularly using CRISPR/Cas۹, presents a promising approach for treating ALS by correcting pathogenic mutations. This technology is increasingly being adopted in clinical research. CRISPR/Cas۹ is favored for its simplicity and cost-effectiveness compared to other genome-editing methods such as transcription activator-like effector nucleases (TALENs) and zinc finger nucleases (ZFNs). This review focuses on the evolution of gene editing tools, emphasizing CRISPR/Cas۹ for gene correction and the development of disease models and gene therapies for ALS.

Methods: Searched in ۳ databases; PubMed, Scopus and Web of Science with the related terminol¬ogy of ALS, CRISPR and Lou Gehrig's disease. Also, relevant articles from ۲۰۲۰ until now are reviewed to mention gene therapy for ALS

Results: Recent research has explored the use of cellular models to correct genetic defects associated with ALS using CRISPR-Cas۹ technology. This study reports the results are highly accurate, with corrections being approximately ۹۹٪ precise. The analysis of on-target and off-target effects shows GC content ranging from ٤۰-٦۰٪, as measured by the RNA/DNA GC Content Calculator. This finding is significant for the effectiveness of single-guide RNAs (sgRNAs) used in CRISPR-Cas۹ treatments. The targeted region in the mutant SOD۱ gene is located near the start codon, with the CRISPR-Cas۹ system inducing double-strand breaks, indicated by black highlights on the CAG repeats

and orange or yellow highlights on the sgRNA cassettes. Additional validation includes the measurement of minimum free energy (MFE), which assesses the structural stability of sgRNAs using the Mfold web server and RNA structure webserver. These tools predict the most stable structures of oligonucleotides at ٣٩°C, providing graphical representations of MFE structure, the thermodynamic ensemble of RNA structures, and centroid structures. These results suggest that CRISPR-Cas٩ offers a promising therapeutic approach for ALS. Encouraged by the success of CRISPR technology and its suitable sgRNAs, researchers and pharmaceutical companies are exploring this strategy for future treatments. CRISPR's ability to modify gene function and alter DNA sequences opens new possibilities for correcting genetic disorders. This technology has already proven efficient for site-specific genome editing in single cells and whole organisms. The study highlights CRISPR as a potential future treatment for genetic disorders like SBMA. Despite these promising developments, these methods cannot fully capture the complexity of biological systems in living organisms. Further research involving animal models and human clinical trials is essential to validate the safety and efficacy of CRISPR-Cas٩ as a treatment for ALS.

Conclusion: This review examines recent research utilizing CRISPR/Cas٩-mediated gene correction to explore the pathophysiology of ALS through patient-derived iPSCs. Despite its simplicity and broad applicability, CRISPR/Cas٩ technology has certain limitations. A significant concern is the risk of off-target effects, which occur when Cas٩ and sgRNA inadvertently target non-specific DNA sites due to reduced specificity. Additionally, the efficiency of gene correction via the HDR mechanism is low (<١٪). To improve HDR rates, strategies such as timed delivery with cell cycle synchronization and inhibition of key NHEJ molecules are necessary. Since the identification of mutant SOD١ as a genetic cause of ALS in ١٩٩٣, over ٢٠ genes associated with ALS have been discovered. However, more than ٨٠٪ of ALS patients lack identifiable genetic variants. This suggests that ALS may involve various mechanisms and genetic causes. The integration of genetic information, advanced CRISPR/Cas٩ genome engineering techniques, and in vitro disease modeling with iPSCs is expected to advance the identification of disease-causing mutations and deepen our understanding of ALS pathology. This approach holds the potential to thoroughly investigate ALS mechanisms, paving the way for the development of effective treatments and ultimately a cure for the disease.

Keywords: CRISPR/cas٩, ALS, Lou Gehrig's disease, gene therapy

Utilizing machine learning algorithms for the diagnosis of skin diseases (Review)

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Introduction: The increasing global prevalence of skin diseases, ranging from benign conditions to life-threatening malignancies, highlights the need for rapid, accurate, and accessible diagnostic methods. Traditional diagnostic approaches, including clinical observation and histopathology, are time-consuming, subject to human error, and dependent on specialist availability. The integration of machine learning (ML) algorithms into dermatology offers a transformative solution, utilizing computational power to enhance diagnostic accuracy, improve patient outcomes, and simplify clinical workflows. This abstract explores the latest advancements in machine learning applications for diagnosing skin diseases and addresses the challenges of their integration into clinical practice.

Methods: Machine learning, specifically deep learning algorithms like convolutional neural networks (CNNs), has emerged as a powerful tool in image recognition, with significant success in medical image analysis. In dermatology, CNNs have been employed to classify a wide array of skin diseases, analyzing visual data from clinical and dermoscopic images. CNNs, designed to mimic the human brain's neural networks, can autonomously learn features such as color, texture, and shape, enabling the detection of subtle variations in skin lesions that are often imperceptible to the naked eye. These models have shown diagnostic accuracy comparable to or exceeding that of experienced dermatologists in identifying conditions such as melanoma, basal cell carcinoma, and other skin cancers. One of the most promising applications of ML in dermatology is in the detection of malignant melanoma. Early diagnosis is critical for melanoma, as it significantly improves survival rates. Machine learning models, trained on large datasets such as the International Skin Imaging Collaboration (ISIC) dataset, have demonstrated the ability to accurately distinguish between malignant melanoma and benign lesions, such as nevi. These algorithms can analyze high-resolution dermoscopic images and identify patterns in pigmentation, border irregularity, and asymmetry that are indicative of malignancy. Beyond cancer diagnosis, ML algorithms have been utilized to identify and classify a broad spectrum of dermatological conditions. For instance, ML models have been used to assess inflammatory skin diseases such as psoriasis, atopic dermatitis, and rosacea. These algorithms, trained on both clinical images and patient data, can accurately differentiate between these conditions, even when they present with overlapping symptoms. Additionally, ML-based tools have been developed for the automated assessment of acne severity, providing dermatologists and patients with real-time, objective evaluations that can guide treatment decisions.

Results: One key advantage of machine learning is its ability to learn and improve over time. By continuously feeding ML models with new data, their diagnostic performance can evolve, offering more accurate and reliable results. This capacity for continual learning allows ML tools to adapt to

the changing landscape of dermatological diseases, such as the emergence of new disease patterns, drug-resistant strains, or shifting epidemiological trends. Moreover, ML algorithms can facilitate personalized treatment strategies by analyzing patient-specific data, such as genetic information, medical history, and treatment response, to predict the most effective therapies for individual patients. Despite these advancements, several challenges remain in the widespread implementation of ML algorithms for diagnosing skin diseases. One major limitation is the lack of large, diverse datasets representative of different skin tones, age groups, and geographic regions. Many current ML models have been trained on datasets that predominantly feature lighter skin tones, which may result in reduced diagnostic accuracy for patients with darker skin. Another challenge is the interpretability of machine learning models. Deep learning algorithms, particularly CNNs, function as "black boxes," meaning their decision-making processes are not always transparent. Clinicians may be hesitant to adopt these tools without a clear understanding of how diagnoses are made. To overcome this barrier, there is growing interest in developing explainable AI (XAI) systems that offer insights into the reasoning behind ML-generated diagnoses. This transparency can increase trust in AI-assisted diagnostics and facilitate their integration into routine clinical workflows. Ethical considerations and regulatory approval are also important factors in the deployment of ML in dermatology. The collection and use of patient data for training ML models raise concerns about privacy, consent, and data security.

Conclusion: In conclusion, machine learning algorithms hold immense promise for revolutionizing the diagnosis of skin diseases. Their ability to analyze vast amounts of visual data, recognize patterns, and continuously improve diagnostic performance can enhance the accuracy and efficiency of dermatological diagnoses.

Keywords: Machine Learning (ML) Dermatology Convolutional Neural Networks (CNNs) Skin Disease Diagnosis

Validity and reliability of the Persian version of the questionnaire to assess the ergonomic knowledge of computer professionals (Research Paper)

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Introduction: The prevalence of musculoskeletal disorders among people with frequent use of computers varies from ٤٠٪ among students to more than ٧٠٪ among university employees. In order to plan education with the aim of filling the knowledge gaps regarding the principles of ergonomics, it is necessary to know the level of knowledge of people in this field. In the conducted search, only one questionnaire was found that evaluates people's knowledge and not its external appearance. Considering the importance of the mentioned components and the strengths of this tool, including a special design for evaluating ergonomic knowledge of working with computers and the use of perceived indicators, we decided to translate and psychometrically evaluate the questionnaire of ergonomic knowledge of working with computers in Iranian society during this research.

Methods: The current research was a translation and psychometric study of tools, and its purpose was the validity and reliability of the questionnaire for evaluating ergonomic knowledge of working with computers. The questionnaire for evaluating knowledge of computer ergonomics was translated into Farsi. Then the translated questionnaire was re-translated into the original language by a third person. Then the translation and re-translation were reviewed by the research team and sent to the designer of the questionnaire for approval. Then the translated questionnaire was completed by the computer user and a question was asked whether the person understood the items or not. In order to check the formal and qualitative validity of the translation of the questionnaire, ١٠ computer users were given their opinion about the difficulty in understanding the concepts, ambiguity and inappropriate perceptions, and the appropriateness and relevance of the items. In order to check the quantitative face validity, the computer user was asked to record his opinion about the importance of each item. To check the content validity of the tool using a qualitative method, ٥ experts were provided and their opinions were presented in a specialized group (plan implementers) and applied to the options. Also, CVR and CVI were evaluated for content validity. Finally, ICC was calculated with ٢٠ computer users. In the stage of construct validity assessment, among the computer users who met the criteria for entering the study, they were selected by the available method and after obtaining informed consent, they were invited to participate in the research.

Results: After the Persian translation of the questionnaire, the CVI and CVR of the questions were evaluated, and ۱۲ questions were removed based on the content validity ratio of less than ۰,۷۵, and the CVI of the remaining ۲۳ questions was equal to ۰,۹۹. Also, in the quantitative face validity part, all questions (۲۳ questions) had an acceptable impact factor (more than ۱,۵). The ICC coefficient was equal to ۰,۸۱۳ (confidence interval ۰,۵۱۵, ۰,۹۲۸ and p<۰,۰۰۱). In order to check the validity of the construct, ۳۲۸ people were evaluated. The ratio of male and female students was approximately equal. The average age of the participating students was ۲۵,۵±۲۵,٦۵ years. Also, the majority of studied students were studying in fields related to medical sciences. In the factor analysis of ۲۳ questions, ٤ questions were removed from the questionnaire due to the factor loading of less than ۰,۳ and the single-factor structure was able to explain about ۳۰٪ of the total variance of the instrument score.

Conclusion: Translation and publication of a practical tool for evaluating ergonomics knowledge prevents the emergence of various versions. In this study, our results showed that the ۱۹-question version of the computer ergonomic knowledge evaluation questionnaire has good validity and reliability and can be used to evaluate ergonomic knowledge. However, in order to improve the factor variance, it is recommended to add knowledge questions and changes in the questionnaire options, as well as increase the study population.

Keywords: Validity; reliability; Ergonomic; Questionnaire

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Viral Metagenomics in Stray and Domestic Dogs; A Systematic Review (Review)

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Introduction: Many human viral infections have a common origin between humans and animals, and if a virus can adapt and replicate in its new human host, human-to-human transmission may occur, leading to an epidemic such as the ۲۰۰۹ H۱N۱ influenza pandemic. to be Therefore, the prediction of emerging zoonotic infections will be an important challenge for public health officials in the coming decades. Viral metagenomics is a powerful tool for exploring new viruses in different human and animal tissue and feces samples and responding to this challenge.

Methods: We systematically reviewed studies that used this tool to examine the feces of stray and domestic dogs. By searching PubMed, Google Scholar, and Web of Science databases using the keywords “viral metagenomics,” “dog,” “stray dog,” “domestic dog,” “intestinal virome,” and “faecal virome,” ۵۱۷ We identified the study and finally after screening, ۳۳ articles were analyzed.

Results: Studies have shown a high diversity of viruses of Astroviridae, Coronaviridae, Circoviridae, Picornaviridae, Caliciviridae, Herpesviridae, Parvoviridae, Microviridae, Siphoviridae, Ackermannviridae families in the fecal virome of healthy dogs. Also, the results showed that stray dogs may have new viral species of Astroviridae, strains of Coronaviridae that have a common potential between humans and animals, and the virus that causes hepatitis E. Due to the lack of vaccination and contact with infected animals, stray dogs are mostly infected with enteric viruses such as parvovirus and canine adenovirus. and due to the interaction with different ecosystems, the diversity of environmental phages and viruses of the Microviridae and Siphoviridae families was also higher in stray dogs. The results also showed the different virome composition of dogs with diarrhea compared to healthy dogs, and known intestinal pathogens such as parvovirus and coronavirus were present in both healthy dogs and dogs with diarrhea, and astrovirus in dogs with Acute diarrhea was significantly higher.

Conclusion: This systematic review provides an overview of the current state of knowledge on viral metagenomics in domestic and stray dogs and highlights the importance of ongoing research and surveillance to prevent viral disease transmission.

Keywords: Viral Metagenomics, Dog, Faecal Virome

Water Purification by Bacteria (Review)

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1. -
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Introduction: Water purification is a critical process in ensuring access to clean drinking water, especially in areas where conventional treatment methods may be impractical. One innovative approach that has gained attention in recent years is the use of bacteria for water purification. This method leverages the natural abilities of certain bacteria to break down pollutants and contaminants, offering a sustainable and effective solution to water quality issues.

Methods: The Role of Bacteria in Water Purification Bacteria play a vital role in the natural ecosystem, particularly in the biogeochemical cycles that help maintain environmental balance. In the context of water purification, specific strains of bacteria can metabolize organic matter, degrade harmful substances, and even remove heavy metals from contaminated water. This process is often referred to as bioremediation, where microorganisms are used to clean up polluted environments. One of the most significant advantages of using bacteria for water purification is their ability to thrive in diverse environments, including those with high levels of pollutants. For instance, certain bacteria can survive in extreme conditions, such as high salinity or low oxygen levels, making them suitable for treating wastewater from various sources, including industrial effluents and agricultural runoff. Mechanisms Bacterial water purification can occur through several mechanisms: Biodegradation: Many bacteria can break down organic pollutants into less harmful substances. For example, bacteria such as Pseudomonas and Bacillus species are known for their ability to degrade hydrocarbons, which are common in oil spills.١ Bioaccumulation: Some bacteria can absorb heavy metals and other toxic substances from water, effectively removing them from the aquatic environment.٢ Nitrification and Denitrification: These are essential processes in the nitrogen cycle facilitated by specific bacteria. Nitrifying bacteria convert ammonia into nitrites and then nitrates, while denitrifying bacteria convert nitrates back into nitrogen gas, thus reducing nitrogen pollution in water bodies.٣ Phosphate Removal: Certain bacteria can also help in the removal of phosphates from water, which is crucial in preventing eutrophication—a process that leads to excessive growth of algae and depletion of oxygen in water bodies.٤ Pathogen Reduction: Some bacteria can outcompete or inhibit the growth of pathogenic microorganisms, thereby improving the safety of water supplies.٥ Biofilm Formation: Bacteria often form biofilms on surfaces in water treatment systems. These biofilms can trap and degrade contaminants, providing a habitat for a diverse community of microorganisms that work together to purify water.٦ Coagulation and Flocculation: Some bacteria can produce extracellular polymeric substances that help in coagulating suspended particles in water. This process aids in the removal of solids and improves the clarity of water.٧ Reduction of Heavy Metals: Certain bacteria can reduce heavy metals, such as chromium and lead, to less toxic forms. This is particularly useful in treating industrial wastewater.٨ Anaerobic Digestion: In low-Oxygen environments, specific bacteria can break down organic matter, producing biogas and

reducing the volume of waste. This process is often used in sewage treatment.[٩] Phytoremediation Support: Bacteria can enhance the effectiveness of plants in removing contaminants from water through a process called rhizoremediation, where bacteria associated with plant roots help degrade pollutants.[١٠]

Results: Advantages Bacteria are strong candidates as water purifiers because they enhance the water quality beside other features such as Cost-Effectiveness, Sustainability, Biodegradability, Adaptability and Minimal Energy Requirements. Challenges There are challenges associated with using bacteria for water purification. One significant concern is the potential for pathogenic bacteria to contaminate the water supply. Therefore, it is crucial to select non-pathogenic strains for purification processes and to monitor their effectiveness regularly. Additionally, the efficiency of bacterial purification can be influenced by various factors, including temperature, pH, and the presence of competing microorganisms. Optimizing these conditions is essential for maximizing the effectiveness of bacterial treatment systems.[١١]

Conclusion: Water purification by bacteria represents an innovative approach to addressing global water quality challenges. By harnessing the natural capabilities of microorganisms, we can develop sustainable and cost-effective solutions for providing clean drinking water. As research continues to advance in this field, it is likely that bacterial purification methods will become increasingly integrated into water treatment practices worldwide, contributing to healthier ecosystems and communities. While there are challenges to overcome, the potential benefits of using bacteria for water purification make it a compelling area for further exploration and implementation.

Keywords: Water purification-Bacteria

Whey protein beverage, homeostatic balancer of energy production and obesity reduction by regulating UCP١ gene expression (Research Paper)

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Introduction: Introduction and Aim: The effect of high protein diets on weight management has always been controversial. The nutrients in whey protein have introduced this combination as the king of proteins which has potential benefits in weight management, obesity prevention and improvement of metabolic parameters. In this study, whey protein used to formulate a protein beverage and the effect of this nutrient composition on UCP١ gene expression was evaluated.

Methods: Materials and Methods: In this study, ٢٠ male mice divided into four groups: placebo, treatment with whey protein supplement, exercise, and simultaneous treatment with supplement and exercise. Then the liver tissue sample was take and the expression of UCP١ gene in the liver under the influence of the supplement evaluated.

Results: Results: The studies showed that mice supplemented with whey protein beverage gained less weight than other groups. They also showed an increase in UCP١ expression and energy consumption as a result of whey protein supplementation.

Conclusion: Conclusion: This supplement increases the expression of the UCP١ gene as the protein responsible for cellular respiration in the liver and heat production in brown fat tissue, by inhibiting the proton gradient across the mitochondrial inner membrane during the process of oxidative phosphorylation, it can create homeostatic balance in the body. Therefore, with the results of this research, this beverage can be considered as an important protein in reducing the development of obesity.

Keywords: Keywords: UCP١, Whey Protein, Obesity, Energy Metabolism, Supplement.

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Whole Cell-Based Drug Delivery: Emerging Frontiers (Review)

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Introduction: Recently, whole cell-based drug delivery systems (WC-DDS) have emerged as a prominent area of research. The selection of specific cell types for drug delivery, while preserving their structure and function, is of significant value.

Methods: All articles containing the terms "drug delivery" and "Whole Cell" were reviewed without any historical limitations.

Results: Whole Cell delivery systems (WCDS) can be classified into three categories: 1. Whole Cell-Cell Delivery Systems (WC-CDS): These systems aim to achieve cell-based therapies, such as the injection of stem cells into joints, the heart, etc. 2. Whole Cell-Gene Delivery Systems (WC-GDS): These systems are designed to address genetic deficiencies, for instance gene therapy for inherited disorders like cystic fibrosis or hemophilia. 3.Whole Cell-Drug Delivery Systems (WC-DDS): That is the focus of this article, these systems aim to protect, deliver, and release drugs at the target tissue. This category encompasses both therapeutic and diagnostic agents. Within the WC-DDS category, various cell types have been utilized for targeted drug delivery: a. Blood cells, such as RBC, have a history of carrying drugs like antibiotics and enzymes to diverse target tissues, including the spleen, liver, and lungs. b. Stem Cell, (NSCs and MSCs), have been used in both natural and synthetic forms to deliver drugs to target tissues. c. Cancer cells use of cancer cell membrane-coated nanoparticles (NPs) for cancer therapy. d. Bacteria (like OMVs) for targeted cancer drug delivery. e. Immune cells, such as macrophages, dendritic cells, and T cells, possess inherent capabilities to migrate towards sites of inflammation or tumors

Conclusion: The introduction of new cell types and innovative applications within this domain will undoubtedly open new horizons for this technology.

Keywords: Whole Cell-Based Drug Delivery Cell-Based Therapies Gene Therapy Targeted Drug Delivery Cancer Thera

Zika virus (Review)

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Introduction: Zika virus is a flavivirus transmitted through mosquitoes and therefore it is classified in the group of arboviruses. Most arboviruses cause zoonoses that are usually dependent on non-human animal species for maintenance in the wild. These viruses are transmitted to humans through non-human animals and can be dangerous for humans. This transmission usually takes place through mosquitoes or ticks, which act as vectors for these viruses. Although most Zika virus infections are characterized by subclinical or mild influenza-like illness, severe manifestations including Guillain-Barré syndrome in adults and microcephaly in infants born to infected mothers have been described. The World Health Organization has announced that Zika was first identified in Uganda in ۱۹٤۷ in a species of monkeys called rhesus through a yellow fever surveillance network, and for the first time in humans in ۱۹۵۲ The country of Tanzania was seen. Then it was reported in Southeast Asia and then in Brazil. This virus does not have a specific drug treatment or vaccine. Since Zika virus infection is a self-limiting disease, the treatment approach is more supportive and based on limiting the symptoms of this disease, and it is recommended to rest the patient. The most important difference between Zika virus infection and other infections transmitted through arthropods is the ability of this virus to affect the fetus through the placenta in pregnant mothers.

Methods: In this review study, a systematic search was conducted across reputable scientific databases to examine articles and resources related to the Zika virus. To ensure comprehensive coverage, the following strategies were employed for search methods, inclusion and exclusion criteria for articles, and quality assessment of the selected studies: ۱. Databases and Scientific Resources To gather scientific articles, searches were conducted in databases such as PubMed, Scopus, Web of Science, and Google Scholar. These databases were chosen for their broad collections of articles in the fields of medical sciences, virology, and epidemiology. Additionally, data from organizations such as the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) were used to access epidemiological data. ۲. Keywords and Search Strategy To ensure complete coverage of the topic, the following keywords were used: *Zika Virus*, *Zika Transmission*, *Zika Outbreak*, *Zika Prevention*, *Zika Vaccine*, and *Zika Epidemiology*. These keywords were searched in the titles and abstracts of the articles, and Boolean operators such as "AND" and "OR" were used to combine the keywords. ۳. Inclusion and Exclusion Criteria - Inclusion Criteria: Articles published between ۲۰۱۵ and ۲۰۲٤ that directly addressed the Zika virus and related topics (such as outbreaks, transmission, clinical symptoms, prevention, and treatment) were included. Only articles written in English and published in peer-reviewed, reputable scientific journals were considered. - Exclusion Criteria: Articles that addressed unrelated topics, were of low quality, or lacked reliable data were excluded from the review. Additionally, duplicate review articles or brief conference reports were also omitted. ٤. Article Selection Process Initially, the search results

from the databases were reviewed, and articles were filtered based on their titles and abstracts. Articles that appeared relevant to the topic were selected for further detailed review. After this phase, the full texts of the selected articles were downloaded and thoroughly reviewed to confirm their relevance to the research objectives. In total, [number of articles] articles were chosen for final analysis. ٥. Data Analysis and Synthesis Once the final selection of articles was made, the available data were extracted and categorized. The information collected included routes of Zika virus transmission, clinical effects and disease complications, control and prevention methods, and advancements in vaccines. This information was qualitatively analyzed, and the results of various studies were compared to identify similarities and differences. ٦. Quality Assessment of Articles To ensure the scientific quality of the reviewed articles, the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) tool was used. Articles were evaluated based on various parameters, including research methodology, data quality, and statistical methods used. Only high-quality articles with proper study designs were included in this review. ٧. Study Limitations One limitation of this study was the lack of access to certain articles due to access fees. Additionally, articles published in languages other than English that might contain important information were not included in this review. Another limitation was that some studies might not have been updated and may not reflect the most recent data.

Results: Zika virus is a virus of the Flaviviridae family and the Flavivirus genus, which is mainly transmitted to humans through the bites of infected Aedes mosquitoes (especially Aedes aegypti and Aedes albopictus). The virus was first identified in Zika forests in Uganda in ١٩٤٧, but in recent decades it has spread more widely in different parts of the world, becoming a public health crisis. Symptoms of this virus include mild fever, skin rashes, joint pain, red eyes, headache and muscle pain. And these symptoms usually appear ٢ to ٧ days after the mosquito bite. The ways of transmission of this virus can be mentioned through the bite of infected mosquitoes, transmission from mother to fetus, sexual transmission and transmission through blood. So far, no effective vaccine has been found for this virus and the only way is to prevent it.

Conclusion: Despite significant advances in the understanding of this virus, significant challenges remain in the field of effective prevention and treatment. Although efforts to develop a vaccine continue and progress has been made in controlling mosquito populations, insufficient access to global health resources continues to hamper the ability to contain the spread of the virus. Additionally, the long-term effects of the Zika virus, especially on infants and people with weakened immune systems, require more research.

Keywords: Arbovirus , Glynn Barr , Microcephaly , Mosquito