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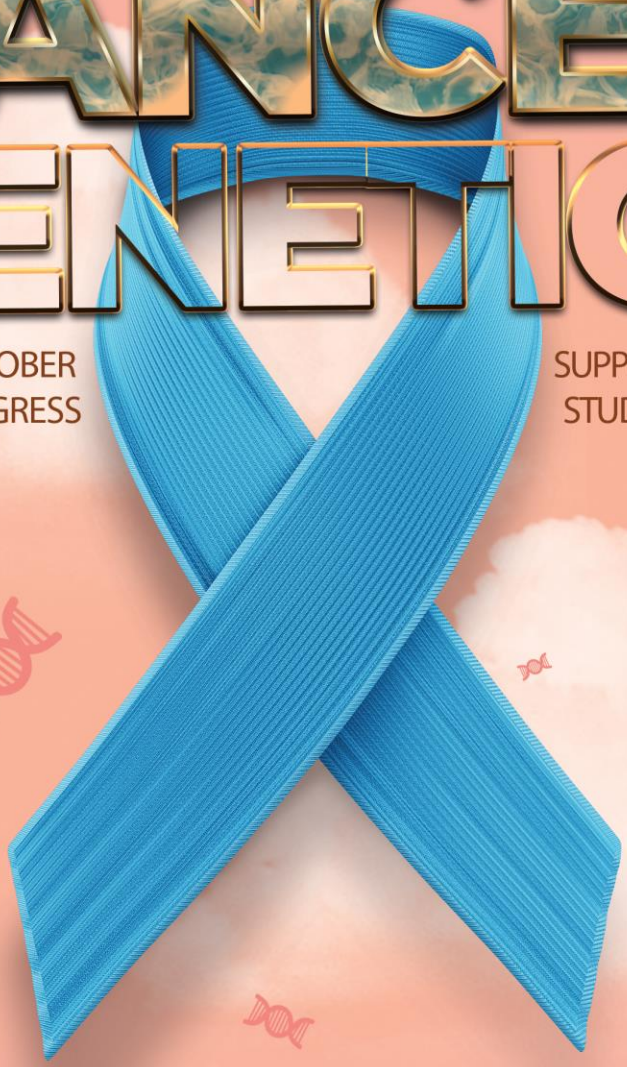

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1. **A computational approach to identify the biomarker based on the RNA sequencing data analysis for colorectal cancer (Research Paper)**

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Introduction: Colorectal cancer (CRC) remains one of the most common cancers in the world. Previous studies have shown that some genetic changes are closely associated with the occurrence of CRC. RNA sequencing (RNA-seq) is one effective approach to finding the heterogeneous gene expressions of diseases that helps discover new functional genes as prognostic biomarkers. Besides, It is well-known that microRNA (miRNAs) biomarkers have emerged as a powerful screening tool, as they are highly expressed in CRC patients and easily detectable in several biological samples. The bioinformatics method is cost-effective and time-saving when studying the role of miRNAs-mRNA. Therefore, in this study computational models were used to identify colon cancer-related biomarker by RNA-seq analysis.

Methods: The RNA sequencing of 20 colorectal tumor samples with 20 matched adjacent normal colorectal tissue under the accession code GSE142279 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 GEO2R. The 1000 top up regulated genes were imported into the STRING (version 12.0, http://string-db.org) database to identify the interactive association between the proteins. Then, the all interactions with a significant combined score >0.9 were selected for further analysis. The appropriate gene with the highest degrees of connectivity were selected as hub genes. The targetSacn database is a specialized collection of microRNA-mRNA targeting relationships. These databases were used to obtain hub gene-associated miRNA.

Results: This study identified 4250 genes with |log2FC|>1 and P-value <0.01 as DEGs: 2009 upregulated and 2241 downregulated genes. BYSL, Bystin like, was identified as one of the best hub gene in STRING which hsa-miR-138-5p can suppressed the BYSL expression in

CRC. BYSL plays a role in a variety of cancers, and mutations in the BYSL gene will significantly increase tumourigenesis and progression. BYSL was characterized as an important gene for cell proliferation, migration and invasion in human carcinoma. Down-regulation of miR-138-5p has also been reported in various cancers. This miRNA have been categorized as a tumor suppressor. Of note, this bioinformatic results confirmed that targeting BYSL is an important mechanism of the tumor-suppressive function of miR-138-5p in CRC. Moreover, TargetScan indicating that the seed region of miR-138-5p contains 1 complementary sites within position 2293-2299 of BYSL 3' UTR.

Conclusion: Taken together, our findings from RNA sequencing analysis provide the first clues regarding the role of miR-138-5p as a tumor suppressor in CRC by inhibiting BYSL translation. The results also provide valuable insights into the regulation of miR-138-5p and BYSL for future research and therapeutic development.

Keywords: Colorectal cancer; RNA sequencing; miRNA; miR-138-5p; BYSL

2.

A review of evaluation and management of lung cancer in patients with interstitial lung disease (Review)

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Introduction: Patients with interstitial lung disease increase the risk of developing lung cancer, the consequences and possible pulmonary complications due to invasive methods and toxicity caused by lung cancer treatment, which should be done with careful and potential management decisions.

Methods: In order to identify studies aimed at evaluating and managing lung cancer in patients with interstitial lung disease, this systematic review was conducted by searching Google Scholar, Science Direct, PubMed databases based on the keywords Lung cancer, Interstitial lung disease, Treatment. After reviewing the summary of the articles and checking the title, irrelevant articles were removed and the full text of the articles was searched and the articles related to the topic were included in the study.

Results: According to studies, symptom-based assessment for lung cancer in patients with interstitial disease overlaps with lung cancer symptoms and often includes shortness of breath, cough, and functional limitations. Physical examination findings and other symptoms can rarely occur as a direct consequence of interstitial lung disease; Among them, hemoptysis, weight loss, chest pain, obesity, pleural effusion and lymphadenopathy are significant. Therefore, these features should prompt investigation of lung cancer and further possible tests to evaluate possible causes.

Conclusion: The risk of complications and mortality in patients with interstitial lung disease will be higher compared to patients with lung cancer who do not suffer from this disease, and the treatment should be proportional to the individual risks associated with the diagnosis and severity of the patient's interstitial lung disease.

Keywords: Lung cancer, Interstitial lung disease, Treatment

3.

A Review of investigating the potential of vaccines in the prevention and treatment of prostate cancer (Review)

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Introduction: Prostate cancer (PCa) is a common malignancy in men worldwide. This disease occurs mostly in countries with high Human Development Index (HDI). Among the factors affecting the development of this cancer are genetics, race and ethnicity, family history and unhealthy diet. People with PCa are diagnosed through prostate biopsy, digital rectal examination, and prostate-specific antigen analysis Prostate-Specific Antigen (PSA) testing. In cases of progression and metastasis of this cancer, treatment is done through radiotherapy or radical prostatectomy. Over the past few decades, the focus on the development of vaccines has been introduced as a way to treat cancers, particularly PCa. Currently, the Sipuleucel-T (Provenge) vaccine is the only vaccine approved by Food and Drug Administration (FDA) for PCa treatment. Studies show that in the future, PCa vaccines can be used to activate and increase T cells in tumors, be used as part of a hybrid approach with factors that enhance tumor-resistant immune mechanisms. There has also been a lot of research done to find new therapeutic approaches such as traditional medicine, immunotherapy, gene therapy and nanotechnology. The aim of this study is to review prostate cancer, factors affecting the development of disease, prevention, diagnosis and treatment of it, including vaccines and a review of diverse therapeutic approaches in the future.

Methods: The research method used in this review included an extensive study. Search and analysis of scientific literature, including peer-reviewed papers, research papers, and clinical studies of databases such as PubMed, Scopus, and Google Scholar were used to collect related publications. Search terms include « prostate cancer», «vaccine therapy for cancer» and « prostate cancer treatment».

Results: PCa After lung cancer Lung Lung, is the second leading cause of death worldwide. Current treatments for this cancer are only useful for a small number of patients and have many side effects. In this study, the potential of vaccines in the prevention and treatment of PCa was examined ،Vaccines have been shown to play an effective role in the management and treatment of PCa. Due to the increasing prevalence of PCa and the risk factors associated with the disease ،The use of proprietary vaccines and non-specific vaccines specifically designed to stimulate immune responses can be used to control cancer ،important strategies and strategies are promising and effective. In addition, there are a variety of treatment options available for PCa, including hormonal treatments, chemotherapy, radiotherapy, and radical prostatectomy ،New hormonal treatments such as abyrotron, apalotamide, and ejaculationotamide are considered effective methods. Due to recent advances in precision medicine and the use of new technologies such as mRNA vaccines, emerging perspectives on PCa treatment have been provided . Vaccinations for PCa not only have the ability to help boost the immune system, but also allow for personalization of treatments based on genetic characteristics. Finally, more research is needed in this area to improve and optimize current treatments and introduce new techniques . This holistic approach has the potential to improve treatment outcomes as well as improve the quality of life of patients with PCa.

Conclusion: cancer vaccines, especially anti-PCa vaccines, are expected to benefit from improvements in the speed, cost and efficiency of molecular sequencing, artificial intelligence, and cell engineering.

Keywords: Prostate cancer, Prostate-specific antigen, Vaccine, Gene therapy

4.

A review of osteoclast inhibitors in primary breast cancer (Review)

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Introduction: Breast cancer is the most common cancer in women worldwide. The prognosis for completely cured early breast cancer is usually very good, in part because of systemic therapies that reduce the risk of recurrence.

Methods: To identify studies aimed at the role of osteoclast inhibitors in primary breast cancer, this systematic review was conducted in Google Scholar, Science Direct, and PubMed databases based on keywords Breast cancer, Osteoclast inhibitors, and Osteoporosis. 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 shown, osteoclast inhibitorshave been evaluated as anticancer treatments in an adjunctive setting to improve breast cancer outcomes, treatment with the help of these inhibitors, either for the management of osteoporosis or as an adjuvant treatment, is generally They are well tolerated and reduce the risk of osteoporosis and fractures. Therefore, the prevention of bone loss related to breast caccer, avd the treatment of osteoporosis and osteopenia should be considered first with adequate nutrition (calcium and vitamin D), regular exercise with weight bearing and healthy lifestyle behaviors.

Conclusion: Osteoporosis is associated with an increased risk of fracture and can be associated with significant morbidity, mortality, disfigurement, loss of self-esteem, as well as health care costs. Thus, systemic therapies used to treat primary breast cancer may be associated with loss of bone mineral density and increased risk of osteoporotic fractures.

Keywords: breast cancer, osteoclast inhibitors, osteoporosis

5.

A review of the epidemiology and risk factors of skin cancer in solid organ transplant recipients (Review)

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Introduction: The skin is the most common site for malignancy, with organ transplant recipients requiring chronic immunosuppression and contributing to an increased risk of skin cancer. In particular, squamous cell carcinoma of the skin and basal cell carcinoma are often identified.

Methods: In order to identify studies aimed at epidemiology and risk factors of skin cancer in solid organ transplant recipients, this systematic review was conducted in Google Scholar, Science Direct, PubMed databases based on the keywords Skin cancer, Organ transplant, Safety system. After reviewing the summary of the articles and checking the title, irrelevant articles were removed and 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, several factors such as patient characteristics, transplant type, severity, type and duration of immunosuppression, geographical location and exposure to sunlight can affect the probability of skin cancer in these patients. The incidence of skin cancer in organ transplant recipients varies by geographic location, with squamous cell carcinoma of the skin and basal cell carcinoma accounting for more than 90% of skin malignancies in organ transplant recipients.

Conclusion: The role of immunosuppression as a precipitating factor for the development of skin cancer in organ transplant recipients is generally accepted, and the effect of these specific factors is also unclear; Although the overall level of immunosuppression appears to be an important factor in the development of skin cancers.

Keywords: Skin cancer, Organ transplant, Immune system

6.

A review of the pathology and prognostic factors of colorectal cancer (Review)

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Introduction: Colorectal cancer is a common and deadly cancer worldwide, and the risk of developing this cancer is influenced by environmental and genetic factors. This cancer can be diagnosed after the onset of symptoms or through screening of asymptomatic people.

Methods: This systematic review was conducted to identify studies aimed at the pathology and prognostic factors of colorectal cancer, searching Google Scholar, Science Direct, PubMed databases based on the keywords Colorectal cancer, Pathology, Prognostic. After reviewing the summary of the articles and checking the title, the irrelevant articles were removed and 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, the most powerful tool to evaluate the prognosis after potentially curative surgery for colorectal cancer is the pathological analysis of the resected specimen. Right and left colon cancers are microscopically similar and appear to have a similar prognosis when presenting with regional disease. However, in the setting of metastatic disease, at least some data suggest a worse prognosis for those with a right-sided primary tumor.

Conclusion: Prognostic determinants are the most important outcome indicators after resection of colorectal cancer in the pathological stage at presentation. However, more recent data suggest that tumor size may be an adverse prognostic factor for colorectal cancer.

Keywords: Colorectal cancer, Pathology, Prognosis

7.

A review of the role of microbial products in the development of colorectal cancer (Review)

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Introduction: Colorectal cancer (CRC) is the third most common malignant cancer and the second leading cause of cancer-related death in the world. There are many microbes in the intestine that have the ability to process and use ingested food, and their products play a significant role in causing this cancer.

Methods: In this systematic review, to identify studies aimed at the effect of the role of microbial products in the development of colorectal cancer, a search was conducted in Science Direct, Google Scholar, PubMed databases based on the keywords Colorectal cancer, Microbial products, Prevention. After reviewing the summary of the articles and checking the title, the irrelevant articles were removed and the full text of the articles was searched and the articles related to the topic were included in the study.

Results: Human gut microbiome is a complex community consisting of bacteria, archaea, viruses and eukaryotes. Also, the intestinal microbiome can affect the chemotherapy of colorectal cancer, and the simultaneous use of Bifidobacterium long and Bifidobacterium short can improve cancer control and significantly reduce tumor progression.

Conclusion: Colorectal cancer is a multifactorial disease and microbial dysbiosis in the human intestine has been identified as a risk factor. However, the molecular mechanisms that underlie the effects of intestinal microbial products have not yet been fully elucidated, and the effect of some products on this cancer is still controversial, but in short, intestinal microbial products play an important role in prevention. They have cancer from this.

Keywords: Colorectal cancer, Microbial products, Prevention

8.

A review of the role of telomerase in the response of breast cancer to treatment

(Review)

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Introduction: Breast cancer is the most common cancer in the world, which is the cause of death caused by this particular type of cancer, affects women in developed and developing countries. Prevention and early detection are very important factors for prognosis that should be considered.

Methods: To identify studies aimed at the role of telomerase in the response of breast cancer to treatment, this systematic review was searched in PubMed, Science Direct, and Google Scholar databases based on the keywords Telomerase, Breast cancer, 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 topic were included in the study.

Results: According to the studies, one of the prominent characteristics of cancer cell is the ability to divide indefinitely, which makes them immortal, and the telomeres that shorten with each cell division in normal cells are shortened by the telomerase enzyme in cancer cells. are regenerated, which is expressed in more than 85% of cancers. In this way, the low effectiveness of treatments has led to the search for new combined and more effective treatment methods, including the involvement of telomerase inhibitors and telomerase-tergeted immunotherapy.

Conclusion: Telomerase may have different functions and high enzyme activity in cancer cells is related to poor cell sensitivity to treatments; Therefore, telomerase has become a potential target for cancer therapy.

Keywords: telomerase, breast cancer, treatment

9.

A Thorough Review of Current and Emerging Techniques for Screening and Diagnosing Ovarian Cancer. (Review)

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Introduction: Ovarian high-grade serous carcinoma (HGSC) is a highly aggressive form of gynecological cancer, with a 5-year survival rate of under 50%. The high mortality associated with HGSC is primarily due to late diagnoses, as many patients are not identified until the disease has progressed significantly. Currently, there are no standardized screening tests for ovarian cancer, highlighting the urgent need for new diagnostic methods that can identify the disease at earlier stages when treatment is more effective. The development of effective screening strategies has been particularly difficult due to the low incidence of ovarian cancer in the general population and a significant lack of sensitive and specific biomarkers. This review provides a comprehensive overview of ovarian cancer diagnostics, focusing on innovative techniques that utilize novel protein, genetic, epigenetic, and imaging biomarkers, along with advanced diagnostic technologies for the noninvasive detection of HGSC, especially in women at higher risk due to germline mutations like BRCA1/2. Finally, we explore the potential for these approaches to be translated into clinically applicable solutions for the early screening and diagnosis of ovarian cancer, aiming to enhance patient outcomes in both the general population and those at high risk.

Methods: Current Screening Techniques Transvaginal Ultrasound (TVU) :-1 TVU is a primary imaging modality used to visualize the ovaries and detect abnormalities. 2- CA125 Serum Biomarker: CA125 is a protein that is often elevated in women with ovarian cancer. :3- Pelvic Examination A physical examination by a healthcare provider to check for abnormalities. Emerging Techniques Multi-Modal Biomarker Panels -1 Combining multiple biomarkers (e.g., HE4, ROMA index) with CA125 to improve diagnostic accuracy. Liquid Biopsy -2 A minimally invasive test analyzing circulating tumor DNA (ctDNA) or exosomes in blood samples. MRI and CT -3 Advanced imaging techniques that provide detailed views of the pelvic region. Genetic Testing Testing for genetic mutations (e.g., BRCA1/2) associated with increased ovarian cancer risk.

Results: Treating recurrent ovarian cancer presents significant challenges, and despite advancements in therapeutic options, several controversies persist. Ongoing research is addressing these issues, including studies on secondary cytoreduction, maintenance therapy, and the prognostic value of CA 125 levels. The primary objective remains to establish optimal treatment strategies that enhance outcomes for ovarian cancer patients.

Conclusion: there is considerable optimism due to a deeper understanding of the various causes of this diverse group of diseases, which is leading to the identification of new biomarkers. Innovations in non-invasive diagnostic methods, such as liquid biopsies, Pap smear analysis, and pan-cancer approaches, are being propelled by advanced machine learning algorithms. Additionally, emerging technologies like microchip and nano-based platforms are just beginning to be explored. A range of new cancer biomarker types—including microRNAs (miRNAs), extracellular vesicles (EVs), autoantibodies, the cancer microbiome, and metabolomics—are rapidly being developed, paving the way for novel diagnostic strategies. Furthermore, advancements in imaging technologies show promise for enhancing sensitivity and accuracy in detecting low-volume disease

Keywords: ovarian cancer,diagnostic,emerging,screening,HGSC

10.

Advancing Cancer Diagnosis: The Role of Biopsy Techniques (Research Paper)

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Introduction: Biopsy is one of the cornerstone techniques in cancer diagnosis, providing critical information about the nature of tumors. Through the extraction and analysis of tissue samples, biopsy methods enable the detection of malignancies, assessment of tumor type, and understanding of cancer progression. Traditional biopsy techniques, such as surgical and needle biopsies, have long been used to obtain tissue samples for histopathological examination. However, advancements in biopsy methods, including liquid biopsy, are revolutionizing the way cancer is detected and monitored. Liquid biopsy, in particular, offers a non-invasive approach, allowing for the analysis of circulating tumor cells (CTCs), cell-free DNA (cfDNA), and other biomarkers in the blood. This review explores the various biopsy techniques, their applications in cancer diagnosis, and their potential to improve patient outcomes through early detection and personalized treatment strategies.

Methods: This review is based on an extensive analysis of recent studies and clinical trials that have utilized different biopsy techniques for cancer diagnosis. The focus is on comparing traditional tissue biopsies with emerging methods like liquid biopsy. We examined the technical aspects of each method, including sample collection, processing, and analysis. Special attention was given to liquid biopsy due to its non-invasive nature and its ability to provide real-time insights into tumor dynamics. The review also addresses the challenges associated with biopsy techniques, such as the accuracy of detection, the potential for false negatives, and the integration of biopsy data with other diagnostic tools.

Results: Biopsy techniques have been instrumental in the accurate diagnosis of various cancers. Traditional tissue biopsies remain the gold standard for histopathological analysis, providing definitive diagnoses and guiding treatment decisions. However, liquid biopsy has emerged as a promising alternative, particularly for its ability to detect cancer at earlier stages, monitor treatment response, and identify genetic mutations without the need for invasive procedures. Studies have shown that liquid biopsy can detect minimal residual disease (MRD) and predict recurrence in certain cancers, making it a valuable tool

for ongoing patient management. Additionally, liquid biopsy allows for the detection of tumor heterogeneity, which is crucial for the development of personalized treatment plans.

Conclusion: Biopsy techniques continue to play a vital role in cancer diagnosis, with significant advancements enhancing their effectiveness and application. While traditional tissue biopsies provide essential histopathological information, liquid biopsy represents a new frontier in non-invasive cancer detection and monitoring. As these technologies evolve, they hold the potential to transform cancer diagnosis, enabling earlier detection, more precise treatment, and better patient outcomes. Future research should focus on optimizing biopsy methods, improving the sensitivity and specificity of liquid biopsy, and integrating these techniques into standard clinical practice to fully leverage their benefits in cancer care.

Keywords: Biopsy, cancer diagnosis, liquid biopsy, tissue biopsy, personalized medicine

11.

AI-Enhanced Liquid Biopsy: Revolutionizing Early Cancer Detection and Personalized Treatment (Review)

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2.

Introduction: Early detection and personalized treatment are critical for improving cancer survival rates, yet traditional diagnostic methods, such as tissue biopsies, are invasive and often fail to capture tumor heterogeneity or early-stage cancer mutations. Liquid biopsy, a minimally invasive method that analyzes circulating tumor DNA (ctDNA), circulating tumor cells (CTCs), and other biomarkers from body fluids, has emerged as a promising tool in oncology. However, the vast amount of genetic and molecular data generated from these biopsies requires advanced analytic tools for accurate interpretation and clinical application.

Methods: Artificial intelligence (AI) offers a powerful solution to the limitations of traditional liquid biopsy analysis. By integrating machine learning and deep learning algorithms, AI enhances the detection and interpretation of subtle genetic variations and tumor-related biomarkers that might otherwise go unnoticed. AI-driven models can detect cancerous mutations at very low frequencies, enabling earlier diagnosis than standard techniques. These models are particularly effective in detecting ctDNA signals in patients with early-stage cancers or in those with minimal residual disease (MRD), allowing for earlier intervention and monitoring of recurrence. AI-enhanced liquid biopsy also plays a vital role in personalizing cancer treatment. Machine learning algorithms can process large datasets to identify specific genetic and molecular signatures associated with different tumor types, subtypes, and stages. This information can guide oncologists in selecting the most effective treatment regimens, reducing the risk of trial-and-error approaches and improving patient outcomes. For instance, by identifying actionable mutations in genes such as EGFR, KRAS, and BRAF, AI-enhanced liquid biopsies help tailor targeted therapies to individual patients, offering a precision medicine approach that optimizes therapeutic efficacy while minimizing side effects. Furthermore, AI improves the efficiency and accuracy of longitudinal monitoring. By continuously analyzing liquid biopsy samples over

time, AI algorithms can track the evolution of the tumor, detect emerging resistance mutations, and assess the patient's response to treatment. This dynamic monitoring enables timely adjustments in treatment plans, potentially preventing relapse or progression. In this way, AI-enhanced liquid biopsy offers a real-time, non-invasive alternative to traditional biopsy methods, which are often unable to capture the full complexity of tumor evolution and resistance mechanisms.

Results: One of the most exciting applications of AI-enhanced liquid biopsy lies in cancer screening programs. AI's ability to detect minute genetic alterations makes it particularly useful for identifying cancers that are typically challenging to diagnose early, such as pancreatic, ovarian, and colorectal cancers. By analyzing cfDNA and other biomarkers in asymptomatic individuals or those at high risk, AI-enhanced liquid biopsy offers the potential to detect cancers at an early, more treatable stage, significantly improving survival rates. This advancement could revolutionize cancer screening and prevention strategies, moving towards earlier and more accurate detection. However, despite these advantages, challenges remain. Integrating AI into clinical workflows requires overcoming technical, ethical, and regulatory hurdles. The development of robust, generalizable AI models depends on access to large, diverse datasets, raising concerns around data privacy and equity in healthcare. Additionally, clinical validation and regulatory approval are essential to ensure the reliability and safety of AI-enhanced liquid biopsy before it can be widely implemented.

Conclusion: In conclusion, AI-enhanced liquid biopsy represents a transformative shift in the landscape of cancer detection and treatment. By applying AI to the vast and complex datasets generated by liquid biopsy, clinicians can achieve earlier detection, more personalized treatment strategies, and improved monitoring of cancer progression and treatment response. As ongoing research and clinical trials continue to refine AI algorithms and validate their clinical utility, AI-enhanced liquid biopsy is poised to become an integral tool in the future of precision oncology. With the potential to improve patient outcomes, reduce the burden of invasive procedures, and enable earlier intervention, this technology holds promise for revolutionizing cancer care.

Keywords: Circulating tumor DNA, Artificial Intelligence, Early Cancer Detection, Personalized cancer treatmen

12.

AI-Powered Healthcare: Transforming Cancer Treatment Through Advanced Technologies **(Review)**

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Introduction: Artificial Intelligence (AI) is changing the healthcare services by making early detection better, diagnostic processes more efficient, medicines more personalized, and treatment plans more streamlined. Some examples of AI in healthcare are Machine Learning (ML), Convolutional Neural Networks (CNNs), Artificial Neural Networks (ANNs), Natural Language Processing (NLP), and Predictive Analytics (PA). This article reviews how AI is being used to treat cancer. More specifically, it looks at how robots, ML algorithms, and NLP are changing the way cancer is treated. It's being used to change how cancer is found, how treatments are planned, how new drugs are discovered, and how patients are watched. It's also used to deal with the issues and problems that come up with these tools. It is very important to find cancer early and correctly so that patients can get the right medicine at the right time and have better outcomes. This big change in healthcare shows how AI can make things better and how important it is for oncology to use these new tools to help cancer patients get better care.

Methods: We used the most recent articles from Google Scholar, Pubmed and SID in this review article. The main part of our work was a detailed discussion of the best ways to look over and correctly evaluate old studies. We looked at how specific terms like "Artificial Intelligence," "Transforming Cancer Treatment," and "Advanced Technologies" were used to make sure the topic was covered in depth.

Results: The way cancer is treated is changing because of ML and AI. These technologies are helping to diagnose, predict, and plan the treatment. AI's good ability to look at medical data has helped find cancer earlier, make more accurate guesses about how it will grow, and make more personalized treatment plans. They canalso figure out how the immune system will respond, find proteins in cancer, and improve the effectiveness of immunotherapy. Models built on AI have been made to guess how long people with different kinds of cancer will live. AI has issues, like the need for good data and stress over privacy. It can only be used in medical picture systems, so it can't be used in ML. That being said, AI is still getting better at making predictions and is being used in healthcare systems as more research is done. Some of the most important ways that AI is helping to improve and speed up testing methods are in finding cancer earlier. CNNs are very good at finding tumors and other strange growths, especially when they look at medical pictures and find trends. AI also makes it easier to automatically group tumors, which is useful for planning surgeries and radiation therapy. Genomic data can be looked at by AI programs, especially those that use ANNs and ML models to find mutations and signals that are linked to cancer. This helps doctors figure out how to treat people. It is also being added AI to systems that watch over patients. This will help cancer patients be better cared for. AI has a lot of potential, but it also has some problems and ethical issues that need to be fixed. Some of these are the quality and availability of the data needed to teach AI models, worries about privacy and security, and the need to be clear about how AI makes decisions.

Conclusion: AI has the ability to make clinical trials, drug research, and the process of developing new treatments much better. This game-changing technology also suggests ways to make pathology and histopathology tests better so that cancer can be diagnosed more accurately and reliably. AI-powered technologies are changing the way cancer is treated by making it easier to find the disease earlier, making treatment more personalized, and eventually improving patient outcomes. It is important to note, though, that putting AI to good use in cancer care will depend on solving important problems like getting data, protecting privacy, and thinking about what is right and wrong. Accepting that AI can provide personalized care is a key step toward the future of cancer treatment, as it holds the promise of better, more patient-centered healthcare solutions.

Keywords: Artificial Intelligence, Transforming Cancer Treatment, and Advanced Technologies

13.

Alteration of Lung Microbiota in Smokers and its Association with Lung Cancer Development (Review)

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Introduction: The human lung, once thought to be a sterile environment, is now recognized as a complex ecosystem hosting diverse microbial communities. This lung microbiota plays an essential role in maintaining pulmonary health and immune homeostasis. However, alterations in the lung microbiome have been associated with various respiratory diseases, including chronic obstructive pulmonary disease (COPD), asthma, and lung cancer. Smoking is one of the leading causes of lung microbiota dysbiosis, which may contribute to cancer development. Cigarette smoke contains over 7,000 chemicals, many of which are toxic or carcinogenic. These substances can disturb the natural lung microbiota, leading to bacterial imbalances, immune dysregulation, chronic inflammation, and an environment conducive to tumorigenesis. This review focuses on how smoking alters the lung microbiota and how these alterations contribute to the transition from a healthy state to cancerous conditions.

Methods: For this review, a systematic search of existing literature was conducted using databases such as PubMed, Scopus, and Google Scholar. Studies from the last 5 years were considered to evaluate how smoking-induced changes in the lung microbiome correlate with lung cancer development. Search terms included "lung microbiota," "lung microbiome dysbiosis," "smoking," "cigarette smoke and microbiome," and "lung cancer." Articles were screened for relevance, and only those that explicitly examined lung microbiota changes in smokers, ex-smokers, or lung cancer patients were included. A total of 20 studies were reviewed, focusing on the characterization of lung microbiota in smokers and their potential association with oncogenesis.

Results: Several studies have documented significant shifts in the composition of the lung microbiota in smokers compared to non-smokers. In healthy individuals, the lung microbiome is dominated by phyla such as Bacteroidetes, Firmicutes, and Proteobacteria. However, in smokers, there is a noticeable increase in the abundance of pathogenic

bacteria such as Streptococcus, Neisseria, and Haemophilus, which are associated with inflammation and infection. Simultaneously, beneficial bacteria, including those from the genera Prevotella and Veillonella, are significantly reduced in smokers. These shifts lead to a pro-inflammatory environment, promoting tissue damage, immune suppression, and abnormal cell growth. Chronic exposure to cigarette smoke promotes a state of continuous inflammation and oxidative stress, which facilitates lung tissue damage. Smoking also alters the mucosal immune system by impairing normal clearance mechanisms, such as the mucociliary escalator, which allows pathogens to persist in the lung environment. Alterations in microbial diversity and function were found to enhance the activity of pro-carcinogenic pathways, including those involving NF-kB and STAT3, leading to uncontrolled cell proliferation and impaired immune surveillance. One key mechanism linking smoking-induced microbiota changes to cancer is the overrepresentation of Proteobacteria in the lungs of smokers. Proteobacteria, including Haemophilus and Pseudomonas, produce various virulence factors, including lipopolysaccharides (LPS), which contribute to chronic inflammation and create a microenvironment conducive to cancer development. Studies also found that Neisseria, another bacterial genus elevated in smokers, is associated with increased lung cancer risk through its ability to promote inflammatory signaling. Another important finding from these studies is that microbial dysbiosis persists even after smoking cessation. While quitting smoking does reduce inflammation and improve lung function over time, ex-smokers still harbor a microbiota profile that differs significantly from that of non-smokers. This residual dysbiosis may explain why former smokers remain at higher risk for lung cancer, even decades after quitting. Notably, long-term changes in bacterial diversity and composition may contribute to carcinogenesis through persistent inflammation and immune dysregulation. Additionally, several studies report a significant correlation between specific microbial species and the presence of lung cancer. For example, an increase in Acinetobacter, Rothia, and Streptococcus species was observed in lung cancer patients compared to healthy controls, suggesting these bacteria may play a role in tumor development or progression. Furthermore, the presence of certain bacterial metabolites and by-products in the lung microenvironment can promote DNA damage and inhibit apoptosis, further accelerating the cancerous transformation of lung epithelial cells.

Conclusion: This review highlights the critical link between smoking-induced alterations in lung microbiota and the development of lung cancer. By disrupting the natural balance of lung microbial communities, smoking creates a pro-inflammatory environment conducive to cancer initiation and progression. Understanding the microbial dynamics in the lungs of

smokers and their potential as biomarkers or therapeutic targets may pave the way for novel preventive and treatment strategies in lung cancer management. References Yu, H., et al. (2023). The composition of lung microbiome in lung cancer: a systematic review and meta-analysis. BMC Microbiology, 21(1), 1-10. Zhao, H., et al. (2021). The lung microbiome in COPD and lung cancer: Exploring the potential of metal-based drugs. International Journal of Molecular Sciences, 22(15), 8044. Wang, Y., et al. (2023). The human microbiome: A promising target for lung cancer treatment. Frontiers in Immunology, 14, 1325. Wu, J., et al. (2022). The lung microbiota in cancer: A review. Cancer Letters, 550, 138126. Huang, Y., et al. (2021). The role of the lung microbiome in lung cancer: A systematic review. Journal of Thoracic Oncology, 16(10), 1549-1558. Chen, Y., et al. (2022). The lung microbiome and its association with lung cancer: A review. Clinical and Experimental Pharmacology and Physiology, 49(12), 1135-1144. Li, X., et al. (2023). The lung microbiome and its role in lung cancer: A review. Cancer Management Research, 15, 61-72.

Keywords: Lung Cancer; Lung Microbiota; Cigarette

14.

An Effective Therapeutic Strategy in Non-Small Cell Lung Cancer: Targeting Glutaminolysis to Disrupt the Balance of Oxidative Phosphorylation and Tricarboxylic Acid Cycle (Review)

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Introduction: According to the statistics of the World Health Organization (WHO), lung cancer is the main cause of cancer deaths in the world, of which more than 80% is non-small cell lung cancer (NSCLC). Most NSCLC patients have a 5-year survival rate of less than 15-20% and are diagnosed in advanced stages. Metabolism is the main factor in the development of tumor cells, and according to recent researches, cancer cells rely on two main energies: Oxidative Phosphorylation (OXPHOS) and aerobic glycolysis (a phenomenon known as the Warburg effect). Targeting the Tricarboxylic acid cycle (TCA) can prevent the development of OXPHOS, and with the addition the positive regulation of OXPHOS, a constant feedback between OXPHOS and the TCA cycle is necessary, and the TCA cycle constitutes the main center of cellular metabolism, this can be an effective therapeutic strategy. Therefore, paying attention to effective diagnostic and treatment approaches is of great importance. In this study, we demonstrate some of the effective therapeutic strategies in NSCLC that focus on cellular metabolism including OXPHOS and the TCA cycle.

Methods: It was conducted an extensive search in PubMed and Google Scholar databases with the keywords “lung cancer”, “NSCLC”, “Glutaminolysis”, “TCA” and “Clinical” in the last 5 years and Identifying 45 articles relevant to the main topic of this paper.

Results: Recent advances have identified glutamine as an essential nutrient for cancer cells that provides significant capacity to fuel diverse metabolic pathways in cancer cells. These pathways include the TCA cycle, maintenance of redox homeostasis and synthesis of cellular structures such as nucleic acids, fatty acids, glutathione and other amino acids. A great number of researches are currently focused on glutaminase (GLS) inhibition, some of which are in clinical trial stages and have resulted in potent antitumor effects. Glutaminolysis is a metabolic pathway that converts glutamine into various metabolites related to the TCA cycle and produces antioxidants that are necessary for the survival of tumor cells. Glutaminase catalyzes the initial step of this metabolic pathway, therefore, is very important in cancer metabolism and tumor development. Cancer cells exhibit altered metabolism that provides many potential targets for cancer therapy, including elevated glycolysis, OXPHOS, glutaminolysis, and elevated heme levels. TCA cycle intermediates are largely obtained through increased glutaminolysis. Mitochondrial glutamate is converted to α-ketoglutarate catalyzed by glutamate dehydrogenase 2 (GLUD2) or glutamic oxaloacetic transaminase 2 (GOT2). This α-ketoglutarate undergoes reductive carboxylation in the TCA cycle to produce citrate, then citrate is exported to the cytosol via SLC25A1 and converted to oxaloacetate and acetyl-CoA by ATP citrate lyase (ACLY), and finally, it is used in the synthesis of fatty acids and steroids. Therefore, developing tumors show the ability to oxidatively process glutamine to generate energy through the TCA cycle. Increasing glutamine transport and glutaminolysis, enables many types of cancer to extract a large part of their energy and macromolecules. It has also been mentioned in recent research that the inhibition of increased glutamine transport and glutaminolysis (the conversion of glutamine to glutamate by glutaminase or GLS) is to support the excessive conversion of glucose to lactate and the export of citrate from mitochondria to the cytosol. It may be an effective therapeutic strategy for cancer treatment. However, cancer cells show altered metabolism and are capable of metabolic reprogramming, escaping from apoptosis, tending to adapt and creating resistance through compensatory pathways. Therefore, a complete understanding of the changes in the TCA cycle in NSCLC will be useful for developing new and effective therapeutic approaches

Conclusion: Despite the dysregulated and altered metabolism of cancer cells, the TCA cycle is a central core in the metabolism of normal and cancer cells, and its targeting is an effective therapeutic strategy. Glutaminolysis is one of the selective pathways of cancer cells for the synthesis of TCA cycle precursors, metabolic reprogramming and escaping

from apoptosis. Its inhibition can prevent the synthesis of TCA cycle precursors and disrupt OXPHOS in NSCLC.

Keywords: Lung cancer; NSCLC; Glutaminolysis; TCA; Clinical

15.

An Examination of the Potential Cancer Risks Associated with Intracytoplasmic Sperm Injection (ICSI) (Review)

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Introduction: Intracytoplasmic sperm injection (ICSI) has emerged as a prevalent form of assisted reproductive technology aimed at facilitating conception for individuals facing fertility challenges. Although ICSI has enabled numerous individuals to achieve parenthood, there exists a persistent discourse regarding its possible long-term health ramifications, particularly concerning the cancer risk in progeny. Numerous investigations have scrutinized the correlation between fertility treatments, including ICSI, and the incidence of cancer development in children. Comprehending the potential risks is essential for couples contemplating ICSI, as well as for healthcare professionals tasked with providing informed counsel.

Methods: This review article amalgamates the findings from the extant literature regarding the potential nexus between ICSI and cancer risk in children. The analysis is predicated upon the data elucidated in the selected documents, which encompass studies that explore the following dimensions: 1. Correlation between fertility treatment and cancer risk in children 2. Risks of congenital anomalies and pediatric cancer associated with conception via assisted reproductive technology 3. Likelihood of live birth following IVF/ICSI interventions in female early-onset cancer survivors 4. Correlation between prolonged in vitro culture to the blastocyst stage and the risk of pre-malignant gestational trophoblastic disease (GTD) subsequent to IVF/ICSI.

Results: The extant literature concerning the potential association between ICSI and cancer risk in children reveals a heterogeneous landscape. Some research has suggested a slightly higher chance of certain cancers, like retinoblastoma and hepatoblastoma, in kids born via assisted reproductive methods, particularly ICSI. Conversely, other investigations, including one evaluating a substantial UK national database, reported no significant correlation between extended embryo culture to the blastocyst stage (a prevalent practice in ICSI) and the risk of pre-malignant GTD, such as molar pregnancy. It is imperative to acknowledge that the underlying fertility complications, parental age, and various lifestyle

factors may also influence the identified associations, necessitating further research to elucidate these intricate relationships.

Conclusion: The prevailing evidence concerning the potential association between ICSI and cancer risk in children remains inconclusive. While certain studies have proposed a plausible augmented risk, the overall findings are characterized by variability. Continuous research and longitudinal monitoring of health outcomes are crucial for yielding more definitive insights. Couples contemplating ICSI are advised to engage in discussions regarding the potential risks and benefits with their healthcare practitioners to arrive at an informed decision. Also, larger and prolonged studies are required to advance our comprehension of the detailed interactions between assisted reproductive technologies, including ICSI, and the incidence of cancer in children

Keywords: Icsi, cancer, risk,

16.

An overview Comparative Effectiveness of Phage Therapy and Conventional Antibiotics in Treating Antibiotic-Resistant Infections: A Molecular Perspective **(Review)**

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Introduction: The rise of antibiotic-resistant infections poses a critical challenge to modern medicine. As traditional antibiotics lose their effectiveness, alternative therapies such as phage therapy are garnering attention. This article delves into the molecular mechanisms underpinning the efficacy of phage therapy compared to conventional antibiotics in combating antibiotic-resistant infections. Antibiotic resistance typically arises through several molecular mechanisms. These include the production of enzymes like beta-lactamases that degrade antibiotics, modifications of target sites that reduce drug binding, increased efflux of antibiotics from bacterial cells, and alterations in metabolic pathways to bypass the effects of antibiotics.

Methods: Bacteria can acquire resistance genes via horizontal gene transfer, further exacerbating the problem. Conventional antibiotics combat bacterial infections through various mechanisms. Beta-lactams, such as penicillin, inhibit cell wall synthesis by targeting penicillin-binding proteins. Aminoglycosides, like gentamicin, disrupt protein synthesis by binding to the bacterial ribosome. Fluoroquinolones, such as ciprofloxacin, interfere with DNA replication by inhibiting DNA gyrase and topoisomerase IV. While these mechanisms are effective against susceptible bacteria, they become ineffective when resistance mechanisms are present. Phage therapy employs bacteriophages, viruses that specifically infect and lyse bacteria. Bacteriophages recognize and attach to specific receptors on the bacterial surface, inject their genetic material, and hijack the bacterial machinery to produce progeny phages. The bacterial cell eventually lyses, releasing new phages to infect other bacterial cells. This process, known as the lytic cycle, is highly specific to the target bacteria and does not affect human cells or beneficial microbiota.

Results: Comparative studies have shown that phage therapy can be as effective, if not more so, than conventional antibiotics in treating antibiotic-resistant infections. For instance, phage therapy has demonstrated success in treating chronic infections such as

those caused by Pseudomonas aeruginosa, a pathogen known for its resistance to multiple antibiotics.

Conclusion: Clinical trials and compassionate use cases have reported promising outcomes, including the resolution of infections unresponsive to antibiotics. However, challenges remain, such as the need for personalized phage preparations, regulatory hurdles, and the potential for phage resistance.

Keywords: Clinical trials Antibiotics Phage therapy

17.

An overview of Cancer stem cells: from origin to therapeutic implications (Review)

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Introduction: The link between cancer and stemness has a deep-rooted history, which is summarized here. It started in the mid-19th century with the first theory about the embryonic origins of cancer and progressed through studies on embryonal carcinoma cells in the mid-20th century. This journey has culminated in the modern cancer stem cell theory, which proposes that a small group of tumor cells with stem-like traits drives tumor growth. However, over the last fifteen years, various studies have consistently urged a reassessment of the cancer stem cell paradigm. Cancer stem cells (CSCs), also known as tumor-initiating cells (TICs), are characterized as cells that can sustain themselves through self-renewal. They demonstrate a high level of resistance to current treatment strategies and are a key cause of cancer relapse.

Methods: Cancer stem cells (CSCs) are self-renewing cell types found in various liquid and solid tumors, playing a role in tumor initiation, growth, resistance, recurrence, and metastasis following treatment. The identification of CSCs relies on the expression of specific cell surface markers, which vary by tumor type. There is a dynamic interaction between CSCs, cancer cells, and non-CSCs, influenced by signals from both CSCs and the tumor microenvironment (TME), including the CSC niche. Among the most significant cells in this process are cancer-associated fibroblasts, which facilitate both the differentiation of CSCs and the dedifferentiation of non-CSCs, leading to a CSC-like phenotype. It is widely accepted that cancer stem cells (CSCs) serve as the primary "seeds" for tumor initiation, development, metastasis, and recurrence. CSCs have evolved and exhibit significant heterogeneity. For instance, breast CSCs display varying patterns of surface biomarkers, such as CD44+, CD24−, SP, and ALDH+. Additionally, melanoma stem cells, whether CD271− or CD271+, are capable of forming tumors in SCID mice. This heterogeneity has also been observed in other cancers, including glioblastoma, prostate cancer, and lung cancer. The complexity of CSC heterogeneity highlights the need for more effective biomarkers to accurately identify CSCs and differentiate between their various subtypes. Stem cell niches are specialized regions within tissues that create specific

microenvironments to support and enhance the self-renewal capacity of cancer stem cells (CSCs) and their ability to produce differentiated progeny. The concept of the stem cell niche was initially introduced by Schofield, who showed that successful transplants could only occur when stem cells were sourced from the bone marrow. He also suggested that the stem cell niche plays a crucial role in determining stem cell fate, as the behavior of stem cells is shaped by their interactions with other cells in the niche. Cancer stem cells (CSCs) are known to contribute to prolonged tumor growth, the spread of cancer to distant organs, and the eventual recurrence of the disease following chemotherapy and/or radiotherapy. These cells exhibit a gene signature associated with epithelial-mesenchymal transition (EMT), which is linked to their ability to proliferate and migrate to remote locations. Furthermore, DNA mutations and factors within the tumor microenvironment (TME) may influence CSCs, pushing them toward a metastatic phenotype.

Results: Given their resistance to traditional cancer treatments, cancer stem cells (CSCs) have led to the exploration of various alternative strategies, such as immunotherapy, gene therapy, molecular inhibition, and combination therapies. Immunotherapy, in particular, holds significant potential for targeting CSCs. For example, vaccines that incorporate antigens from CD133+ hepatocellular carcinoma cells can stimulate specific cytotoxic lymphocytes, thereby effectively eliminating CSCs associated with hepatocellular carcinoma. Radiotherapy (RT) continues to be a viable treatment option for various cancers. Advances in medical imaging and dose delivery technology have paved the way for three-dimensional conformal treatment. Standard RT is based on five radiobiological principles: DNA damage repair, cell redistribution during the cell cycle, repopulation, reoxygenation of hypoxic tumor regions, and radiosensitivity—collectively referred to as the "5 Rs" of radiobiology. The goal of this fractionated regimen is to eliminate tumor cells while minimizing harm to the surrounding healthy tissues.

Conclusion: Eliminating cancer stem cells (CSCs) poses significant challenges, as current treatments often fail to target them effectively. Systematic research has yet to provide a reliable method to overcome chemotherapy resistance, limiting our understanding of CSCs' role in tumor heterogeneity. Despite these obstacles, there is optimism that ongoing investigations will eventually lead to effective cancer prevention and treatment strategies.

Keywords: Cancer stem cells cancer therapy tumor microenvironment (TME)

18.

Antiproliferative activity of sesquiterpene lactone britannin on ovarian cancer cell line SKOV3 (Review)

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Introduction: Ovarian cancer is the eighth most frequent cancer and fifth most common cause of death in women in the world. Britannin is a sesquiterpene lactone with anticancer effects on different cancers. We aimed to evaluate the antiproliferative effect of britannin on ovarian cancer cell line SKOV3.

Methods: The antiproliferative effect of britannin on SKOV3 cells was assayed using the MTT method. Briefly, SKOV3 cells were seeded into 96-well microplates and left for 24 hours to adhere to the wells. Afterward, the cells were treated with different doses of britannin (0-100 µM) for 24, 48, and 72 h. The medium was discarded and the cells were treated with MTT solution for 4 h. Subsequently, the MTT solution was replaced with DMSO 1% solution. Finally, the absorbance of formazan crystal was read at 570 and 630 nm and the proliferation rate of SKOV3 cells was calculated.

Results: Treatment of SKOV3 cells with various concentrations of britannin for 24 h had no remarkable effect on the proliferation rate of this cancer cell line. However, britannin treatment for 48 significantly inhibited the proliferation of these cells with an IC50 value of 7.8 µM compared to the controls. This sesquiterpene lactone also significantly decreased the proliferation of SKOV3 cells 72 h after treatment (IC50 = 7.5 µM).

Conclusion: According to the results of the MTT assay in the present investigation, britannin prevented the proliferation of human SKOV3 cells by exerting cytotoxic effects on these cancer cells. This may suggest britannin as a natural compound for the suppression of ovarian cancer growth.

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

19.

Artificial Intelligence for breast cancer detection (Review)

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Introduction: AI technology is increasingly vital for breast cancer diagnosis due to rising patient numbers and limited pathologist resources. Computer-aided diagnosis (CAD) tools and deep learning (DL) methods have shown promise in enhancing accuracy and early detection. Studies like HASHI have demonstrated AI's effectiveness in handling large histopathology images and classifying malignancy levels. AI systems also assist in identifying metastasis locations and improving diagnostic efficiency. Despite challenges, integrating AI into clinical workflows shows potential for enhancing diagnostic accuracy and efficiency, ultimately aiding in early breast cancer detection and reducing avoidable deaths. For decades, research has focused on automated breast cancer detection in mammography to support radiologists. Despite advancements like digital mammography (DM) and digital breast tomosynthesis (DBT), radiologists' evaluations remain crucial. Even experienced radiologists can miss cancerous lesions or recall healthy women, adding to their workload. Since the 1990s, CAD systems using machine learning (ML) have helped radiologists by highlighting suspicious areas, but high false positive rates limited their acceptance. Recently, DL AI systems have shown significant improvements in detection accuracy, potentially enhancing or partially replacing radiologists' roles. This review highlights AI's development, benefits, and ongoing challenges in breast cancer detection.

Methods: The evaluation of breast AI technology focuses on comparing AI techniques with traditional methods. Advances in computational power and digital data have significantly improved AI in medical imaging. AI includes machine learning (ML) and deep learning (DL), each with unique methods. Traditional computer-aided detection (CADe) and diagnosis (CADx) tools from the 1990s used ML to process image features, requiring extensive manual input. In contrast, DL techniques like deep neural networks (DNN) and convolutional neural networks (CNN) autonomously learn from data, improving tasks like image segmentation and classification with minimal human intervention. Training AI systems relies on high-quality data, involving thorough pre-processing and maintaining patient privacy. AI models use various learning paradigms, including supervised,

unsupervised, and reinforcement learning. Effective training also involves data augmentation and transfer learning to overcome dataset limitations. Validating AI systems requires independent, generalizable models using diverse datasets to ensure fairness and robustness. Explainable AI (XAI) techniques, such as attribution maps, enhance transparency in AI decision-making, building trust and facilitating clinical integration by providing clear insights.

Results: Deep learning (DL)-based AI systems have significantly improved breast cancer detection by increasing screening accuracy and reducing false positives and negatives. These systems can identify subtle abnormalities that human observers might miss. However, challenges like inconsistent datasets, biases, and regulatory issues hinder widespread adoption. Choosing the right AI system for clinical use requires evaluating factors such as accuracy, application, and compatibility with local populations and equipment. Regular audits are recommended to ensure safety and effectiveness, and access to performance metrics and training data is essential for informed decisions. Future AI advancements should incorporate diverse data sources, including historical and contralateral images, to enhance predictive accuracy. Techniques like federated learning and increased clinical data availability will support these improvements. Recent trials, such as MASAI and ScreenTrustCAD, have shown that AI can improve cancer detection rates and reduce recall rates. The ongoing AITIC trial suggests AI could automate the review of low-risk exams. The main challenge is deciding whether to use these results or conduct local trials to adapt AI for specific screening needs.

Conclusion: AI technology shows great potential for improving breast cancer screening by enhancing accuracy and reducing radiologists' workload. Deep learning (DL)-based AI systems have outperformed traditional methods, sometimes even surpassing human radiologists. These systems help reduce observer variability and minimize false positives and negatives. To integrate AI effectively into clinical practice, standardized guidelines and reliable practices are necessary to ensure fairness and robustness. Ongoing research and validation are crucial to build clinical trust and confirm AI's efficacy. Collaboration among researchers, clinicians, and regulatory bodies is essential to address challenges and implement AI in screening programs. While traditional computer-aided detection (CAD) systems had high false positive rates, recent DL advancements have improved performance. High-quality data and effective preprocessing are vital for AI training, using various learning paradigms and data augmentation techniques. International initiatives are

working on guidelines to enhance AI transparency and reliability. Continued research and validation are key for successfully integrating AI into routine breast cancer screening.

Keywords: Artificial intelligence, Breast imaging, Breast cancer, Mammography, Screening

20.

Artificial Intelligence in oncology: Enhancing diagnosis and treatment (Review)

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Introduction: The world of cancer treatment is being transformed by artificial intelligence, which is improving the accuracy of cancer diagnosis and prognosis. AI algorithms, like convolutional neural networks (CNN) and support vector machines (SVM) are now being utilized in the diagnostic process. For example, Google's LYNA (LYmph Node Assistant) and SMILY (Similar Medical Images Like Yours) are making strides in breast cancer detection. LYNA achieved a 99% success rate in identifying breast cancer on slides. Additionally, AI is playing a role in precision oncology by aiding in predicting outcomes and determining optimal treatment plans by assessing responses to treatment strategies.

Methods: A thorough review of 10 journal articles from databases such as PubMed, Google Scholar, and Scopus was conducted to gather data on advancements in AI applications within the field of oncology focusing specifically on diagnostic methods and treatment approaches. This review of sources including primary research studies and systematic reviews offers a comprehensive analysis of how AI shapes the oncology landscape.

Results: AI models have achieved an accuracy rate exceeding 90% in detecting glioma, breast, and prostate cancers, marking an advancement from a decade ago. Other AI applications such as BANDIT (Bayesian ANalysis to determine Drug Interaction Targets) are being used for the prediction of the target of existing molecules and drugs. Moreover, AI-enhanced imaging tools have increased detection rates in lung and prostate cancers while algorithms analyzing data are uncovering new drug targets and cancer subtypes, thus expanding the horizons of personalized medicine. Yet, there are several challenges including overfitting, black box problem, and discrepancies among facilities, especially in medical imaging.

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Keywords: Artificial Intelligence, Cancer Diagnosis, Precision Oncology, Deep Learning, Cancer Treatment

21.

Assessing the Potential of CERS6-AS1 Long Non-Coding RNA as a Biomarker for Distinguishing Normal Tissue from Tumor Tissue in Transitional Cell Carcinoma Patients: An Exploratory Study (Research Paper)

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Introduction: Objective: In the present study, we aimed to elucidate the role of lncRNA CERS6-AS1 in BC patients to discriminate between tumor tissue and healthy counterparts. Method: This study was conducted on 40 bladder tumor tissues and normal tissue adjacent as a control sample. Initially, we extracted RNA from all samples and used them for cDNA synthesis. Employing the real-time PCR technique, we assessed expression levels of lncRNA CERS6-AS1 in both sample groups. Statistical studies were performed by graphpad prism. The relationship between lncRNA CERS6-AS1 expression levels was examined in relation to variables such as age, gender, smoking history, tumor stage, and tumor grade. Results: We discerned that expression of lncRNA CERS6-AS1 was notably elevated in tumorous tissue compared to healthy counterparts (P-value< 0.001). There was no statistically significant difference between tumor and control samples in terms of gender and age. Moreover, the expression of lncRNA CERS6-AS1 was not correlated with smoking rate, tumor grade, stage, and tumor size. Conclusion: The findings suggest that lncRNA CERS6-AS1 levels may potentially serve as a risk factor for bladder cancer susceptibility. To substantiate our findings, it is necessary to conduct further investigations with expanded sample cohorts and diverse ethnic backgrounds.

Methods: In our study, in the first step, we analyzed the expression pattern of our interest lncRNA, CERS6-AS1, in The Cancer Genome Atlas (TCGA)-Bladder Urothelial Carcinoma (BLCA). To show consistency in the CERS6-AS1 expression in TCGA-BLCA, we investigated its expression in this database using different web tools GEPIA2 (http://gepia2.cancer-pku.cn/) (2), and TNMPLOT (https://tnmplot.com/analysis/) (3) To proceed with molecular analysis, all tissue samples were securely stored in cryovial containers at a low temperature of -80°C. This preservation method helps preserve the samples' integrity and quality for further examination. The QIAGEN real-time PCR device and Rotor-Gene Q were utilized to evaluate the CERS6-AS1 lncRNA expression levels

Results: We discerned that expression of lncRNA CERS6-AS1 was notably elevated in tumorous tissue compared to healthy counterparts (P-value< 0.001). There was no statistically significant difference between tumor and control samples in terms of gender and age. Moreover, the expression of lncRNA CERS6-AS1 was not correlated with smoking rate, tumor grade, stage, and tumor size.

Conclusion: In summary, the findings of the study propose that CERS6-AS1 is overexpressed in bladder cancer (BC) tissues. However, it was observed that the expression levels of CERS6-AS1 were not significantly associated with tumor grade and stage, pathological tumor size, age, gender, or smoking status. These results indicate that CERS6-AS1 may play a role in bladder cancer progression, but its relationship with other clinical factors remains inconclusive. More research is required to explore the exact mechanisms underlying the function of CERS6-AS1 in BC and to determine its potential as a prognostic or therapeutic target.

Keywords: Bladder cancer; Long non-coding RNAs, CERS6-AS1

22.

Association between dietary folate intake and genetic mutations that cause breast cancer (Review)

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Introduction: Breast cancer (BC) is the most diagnosed malignancy worldwide and is a leading cause of half million women deaths annually. Some of the related risk factors that we can name for this disease are menarche, age of first birth or menopause, breastfeeding, excess weight, low physical activity, alcohol consumption, viral infectious agent, and gene mutations. Women who inherit a deleterious BRCA1-2 or MTHFR gene mutations are at risk of developing BC. Evidence shows that there is U-shaped relationship between levels of folate in diet and serum with breast cancer risk. So that both low and high levels of folate in plasma may increase risk of breast cancer, whereas midrange intakes are protective. the issues that are important regarding the intake of folate supplements are the dose and stage of cell transformation at the time of intervention.

Methods: Studies published updated to July 2024 analyzing "the effect of folate on breast cancer related genes" were searched by searching Google Scholar, Pubmed, and Web of Science. Among the screened articles, related articles were reviewed.

Results: The proteins encoded by BRCA1 and BRCA2 are critical checkpoints in cell cycle for repair of single- and double-stranded DNA breaks with homologous recombination, and repairing of stalled or collapsed replication forks. If these genes are mutated, they may disrupt normal cell cycle and lead to carcinoma. Germline genetic mutations in BRCA1 are one hallmark of hereditary BC. Folate is a key factor in one-carbon metabolism, the universal source of methyl donors for DNA methylation that plays important roles in nucleotide biosynthesis and biological methylation reactions. BRCA1 and BRCA2 mutation carriers are more sensitive to folate deficiency-induced genome damage, especially those who develop breast cancer. So adequate folate status may be necessary for the protection of genomic stability and the prevention of BC. Evidence supports that the risk of BC in women who only had mutations in their BRCA1 gene and used folic acid-containing supplements was significantly decreased, compared to women who never used a folic

acid-containing supplement. In the other hand Folate status affects DNA methylation by interacting with the MTHFR C677T polymorphism. MTHFR is a crucial enzyme in folate metabolism, facilitating the conversion of 5,10-methylenetetrahydrofolate to 5-methylenetetrahydrofolate, a methyl donor that is essential for DNA functions. Also Folate may increase breast cancer risk by promoting the silencing of tumor-suppressor genes APC, PTEN, and RARb2 through DNA methylation. Excessive folate intake can disrupt one-carbon metabolism, potentially contributing to breast cancer development.

Conclusion: Since excessive and deficient folate levels are both carcinogens, dietary folate intake should be arranged in normal range by considering suitable dietary patterns (that have enough folate resources) and cooking methods. More researches and studies with large sample size and long follow-up periods are needed to provide more knowledge about relation between folate status and breast cancer risk in high-risk women and suggest ways to control it.

Keywords: Breast cancer, BRCA1/2, MTHFR, "folate"

23.

Blocking microplastic-induced carcinogenesis: Emerging approaches in cancer prevention and environmental safety (Review)

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Introduction: Microplastic pollution is becoming a burgeoning global threat to human health due to the recent discovery of microplastics (MPs) in most ecosystems. MPs are plastic particles, typically less than 5 mm in size, which result from the degradation of larger plastic materials or are intentionally produced for use in packaging materials, personal care products, synthetic textiles, industrial applications, etc. MPs can enter the human body through inhalation, the digestive tract, and skin.

Methods: For 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; microplastic, plastic plastic, cancer, tumor, carcinogenesis, environment, prevention

Results: The accumulation of MPs in the body tissues can potentially result in a range of health issues, including asthma, hypersensitivity pneumonitis, neurological disorders, cardiovascular diseases, diabetes, and obesity. Epidemiological studies have shown that long-term exposure to MPs is highly related to cancer development in humans. These particles can potentially induce carcinogenesis through several mechanisms. Evidence has revealed that prolonged exposure leads to the activation of inflammatory pathways, triggering the release of cytokines and growth factors to promote cell proliferation and survival. Numerous MPs contain endocrine-disrupting chemicals (EDCs), such as bisphenol A, which interferes with hormonal signals and promotes abnormal cell growth. The epigenetic changes induced by exposure to plastic-associated chemicals can have a significant impact on gene expression patterns. Furthermore, MPs can interfere with function of the immune system to detect and eliminate tumor cells.

Conclusion: Nowadays, emerging prevention strategies emphasize multi-faceted approaches. At the environmental level, advanced filtration methods could reduce MPs pollution. Concurrently, the development of truly biodegradable plastics and enhanced recycling techniques aim to curtail the influx of MPs into ecosystems. Additionally, cutting-edge studies are exploring targeted interventions to lessen MPs-induced cellular damage. Additionally, environmental safety measures are evolving rapidly, with stricter regulations on plastic production and disposal being implemented globally. Public awareness campaigns are also crucial in fostering behavioral changes to minimize plastic pollution. Thus, swift and coordinated action across several sectors is vital to safeguard human health and environmental integrity in this pervasive modern challenge.

Keywords: Microplastic; Cancer; Carcinogenesis; Environment, Prevention

24.

Caffeic acid stimulates breast cancer death through Reactive oxygen species (ROS) formation, Caspase activation and mitochondrial membrane potential depletion

(Research Paper)

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Introduction: This study is aimed to evaluate the potential effect of caffeic acid on the growth of breast cancer cells, beside determining the contributing role of caspases, mitochondria and oxidative status

Methods: MCF-7 and MDA-MB-468 breast cancer cells were exposed to varying concentrations of caffeic acid for different periods of time, and the potential cytotoxic effect was measured using the MTT assay. The activity of caspase 3 and caspase 8, as well as the cellular level of reactive oxygen species (ROS) and the level of mitochondrial membrane potential (Δψm), were evaluated in different groups of cells

Results: Our findings showed that caffeic acid decreased the percentage of MCF-7 and MDA- MB-468 cells in a manner that depended on the dose and duration of exposure. The death of breast cancer cells induced by caffeic acid was associated with an increase in ROS level in both cell lines. The decrease in mitochondrial membrane potential (Δψm) following caffeic acid treatment suggests that mitochondria dysfunction may be involved in

the death of breast cancer cells induced by caffeic acid. Importantly, the activity of caspase 8 increased after treatment, indicating the potential involvement of the extrinsic apoptosis pathway in the inhibition of breast cancer cell growth by caffeic acid

Conclusion: Our study highlights the potential pro-apoptotic effect of caffeic acid in both estrogen-positive and estrogen-negative breast cancer cells, which, in conjunction with other evidence, may lead to new insights for more effective therapeutic approaches in breast cancer

Keywords: Caffeic acid, Cytotoxicity, Reactive oxygen species, Caspase 3, Caspase 8, Δψm

25.

Cancer prevention: current advancements and future possibilities (Review)

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Introduction: Cancer presents a significant societal challenge globally, affecting both public health and financial resources. The advent of advanced imaging technologies, diagnostic methods, and targeted therapies has resulted in treatments that are becoming increasingly costly, making them accessible to only a limited number of patients. Focusing on prevention, especially primary prevention, is a crucial strategy in tackling cancer, as it is estimated that one-third to one-half of cancer cases could be avoided based on our understanding of risk factors. Additionally, prevention is a cost-effective approach that benefits the entire population, not just those at high risk, and it is independent of socioeconomic factors. Regulatory initiatives can have a lasting impact, even influencing future generations; by educating individuals, fostering healthy lifestyles, and promoting self-care, these measures can initiate a positive cycle

Methods: In recent years, the field of oncology has transitioned from a reactive stance to a proactive one, leading to the emergence of "P4 medicine," which emphasizes preventive, predictive, personalized, and participatory care. Prevention initiatives play a vital role in cancer control, effectively lowering both cancer incidence and mortality rates. For example, screening programs for colorectal, breast, and cervical cancers have significantly alleviated the burden of these prevalent diseases. Furthermore, both preventive and therapeutic anti-cancer vaccines are essential tools in the prevention arsenal.

Results: Despite advancements, there is still much work to be done. Screening program participation could be enhanced by developing new, more acceptable, and less invasive testing methods, tailoring screening based on personal medical, clinical, radiological, and genetic information (referred to as "population-based personalized cancer screening"), and utilizing modern communication technologies like smartphone apps or personalized messaging (termed "screening 2.0"). Additionally, physicians' advocacy and guidance are crucial, as eligible individuals must feel comfortable discussing their concerns and perceived psychosocial barriers.

Conclusion: New screening initiatives should only be introduced after conducting a thorough health technology assessment within the context of evidence-based medicine, enhancing organized screening programs, and restricting opportunistic or spontaneous programs.

Keywords: Cancer prevention, Organized screening program, Vaccine

26.

Cancer rate in children from ICSI method (Review)

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Introduction: BACKGROUND: The first fertility child was born in the world's laboratory conditions in the 1900s. Since then, more than 8 million children have been created entire the world with reproductive technologies (ART) and a significant portion of them have reached puberty or adulthood. There is increasing evidence that ART methods can disrupt epigenetic processes during the preimplantation period and affect long-term health; And in general, these fertility induction methods can have positive effects and negative aspects in the long run. One of the negative effects can be the increased risk of cancer in children from the ICSI method. We will address this issue in this research. OBJECTIVE: The purpose of this study is whether or not there is a relationship between the occurrence of cancer in children and ICSI infertility treatment method; And if there is, what is the risk of cancer.

Methods: METHODS: In our review article, we searched PubMed, ScienceDirect, Google Scholar, and Scopus for relevant articles published between 2018 and 2024, using keywords like Infertility; Cancer; Assisted reproductive technology (ART); and Intracytoplasmic sperm injection (ICSI).

Results: RESULTS: Recent studies have shown that there is an increasing relationship between the occurrence of various types of cancer in children and ICSI fertility induction method. Alternatively, ICSI has been reported to increase the incidence of chromosomal abnormalities and blood pressure disorders. Also, another study showed that male ICSI offspring had lower HDL levels at 18 years of age than naturally conceived males. But it should be noted that the observed increased risk among children conceived using ICSI must be interpreted with caution owing to the small number of cases. Interestingly, research on mice has shown that assisted reproductive techniques like ICSI can induce morphological and functional defects that may only become evident after germline transmission to subsequent generations.

Conclusion: CONCLUSION: This suggests potential long-term effects that may not be immediately apparent While direct evidence linking ICSI to cancer in offspring is lacking in the provided context, the studies emphasize the need for continued long-term follow-up of ICSI children. The observed increased risks of various health issues, including congenital malformations and chromosomal abnormalities, warrant ongoing monitoring and research to fully understand any potential cancer risks.

Keywords: Cancer, ICSI, ART, Fertility induction method

27.

Cancer therapy by exosomes mediated mRNA delivery (Review)

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Introduction: Exosomes, a subgroup of secretome, secreted from all cells and play a key role in and out of the cells by transferring nucleic acid, proteins, lipids, amino acid and other metabolites as cargos even to distant cells and alter their biological response intrinsically. Although cancer is the hottest field in treatment study, but unfortunately, there is no ideal therapeutic effects. In this position, exosomes can optimise therapeutic strategies due to having a series of useful properties. Despite the existence of many studies based on the ability to transfer multiple cargoes by exosomes, studies directed on the transfer of mRNA by exosomes are very rare. Messenger RNA (mRNA)-based therapeutics involves the delivery of in vitro-transcribed mRNA into the cytoplasm of a target cell, where it is translated into the desired protein and solve the problem of its absence. In this situation, exosomes optimise their transmission. The aim of this review is to review and scrutinise exosomes mediated mRNA delivery studies which were focused on cancer therapy

Methods: All original articles regarding mRNA, exosomes, and cancer treatments were collected, and main findings were summarized in this work.

Results: About colorectal cancer therapy, ALKBH5 mRNA-loaded folic acid-modified exosome-liposome hybrid nanoparticles strategy demonstrated inhibition in the process of tumor formation (1). Besides they showed decrease in expression of inflammation,

angiogenesis and cell proliferation related genes in TCA8113 cell line which were treated with exosomes containing ECRG4 mRNA. Although translated protein detection of ERGC4 mRNA was failed due to ECRG4 is a secretory protein, but inhibition of VEGFA gene expression , CDK4, NF-KB, IL1b, IL6, MCPI genes and dysregulated cell cycle are evidence for ERGC4's role in tumor growth and metastasis.(2) Her2+ human breast cancer is another case which is mRNA-based treatment has been applied on it. Treatment of her2+ cell population with exosomes carrying HChrR6 gene mRNA caused the growth of cancer cells to be inhibited in the presence of CNOB drug and its transformation into cytotoxic drug MCHB.(3)

Conclusion: It can be concluded that exosomes can work well for transfer of mRNA to cancers, and they have the potential to enter clinic in the future.

Keywords: Cancer, exosomes, mRNA, therapy

28.

Cancer treatment method (Review)

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Introduction: Overview of Cancer Types and Their Characteristics Cancer is a complex group of diseases characterized by uncontrolled cell growth and spread to other parts of the body. There are over 100 different types of cancer, typically classified based on the organ or type of cell in which they originate. Common types include breast, lung, prostate, and colorectal cancer, each with its unique characteristics and treatment approaches. The evolving landscape of cancer treatment has seen significant innovations, particularly in immunotherapy, which harnesses the body's immune system to combat malignancies. Since the approval of the first immune checkpoint inhibitor in 2011, various therapies, including monoclonal antibodies and adoptive cell therapies, have shown promising efficacy, enhancing patient survival rates in advanced cases (A. Mishra et al.). Furthermore, advancements in technology, like chemoresistive sensors, offer new opportunities for early cancer detection, potentially transforming patient outcomes through timely interventions (G. Zonta et al.).

Methods: Current Conventional Treatment Methods The landscape of cancer treatment is further enriched by the integration of personalized medicine, which tailors therapies based on an individual's genetic makeup and the specific characteristics of their tumor. This approach allows for a more effective and targeted treatment strategy, minimizing the side effects often associated with traditional therapies such as chemotherapy and radiation. For instance, genomic profiling can identify mutations that drive cancer growth, enabling the use of targeted therapies that specifically inhibit these pathways. Additionally, advancements in precision diagnostics are improving the ability to monitor treatment responses in real time. By leveraging these technologies, healthcare providers can adjust treatment plans proactively, optimizing outcomes and enhancing the overall quality of patient care in oncology. The combination of immunotherapy, personalized medicine, and early detection technologies represents a promising new era in the fight against cancer. Emerging Innovative Cancer Treatments Moreover, innovative cancer treatments are

witnessing a significant shift with the introduction of immunotherapy, which has transformed the landscape of oncology. Recent advances have led to the development of various immunotherapeutic approaches, such as immune checkpoint inhibitors and CAR-T cell therapy, which have shown remarkable effectiveness in treating relapsed or refractory cancers (A. Mishra et al.). These therapies harness the body's immune system to target and eliminate cancer cells more effectively than traditional treatments. As researchers continue to explore the interplay between bacterial biofilms and cancer, new strategies are emerging that could further enhance therapeutic efficacy by targeting shared characteristics between tumors and biofilms (Euna Choi et al.). This evolving field indicates a future where treatment regimens can be personalized even further, promising improved outcomes and quality of life for patients battling cancer. Personalized Medicine and Targeted Therapies The evolution of personalized medicine and targeted therapies represents a paradigm shift in cancer treatment, particularly with the adoption of advanced immunotherapeutic techniques. By leveraging the immune system, therapies such as immune checkpoint inhibitors and CAR-T cell therapy have demonstrated significant success against difficult-to-treat cancers (A. Mishra et al.). This personalized approach not only enhances the specificity of treatment but also minimizes collateral damage to healthy tissues, a common drawback of traditional therapies. Additionally, the potential integration of insights from bacterial biofilms could lead to innovative strategies that target characteristics shared between tumors and these biofilms, further refining treatment personalization (Euna Choi et al.). As ongoing research continues to unveil new connections and strategies, the field is poised for transformative growth, promising improved patient outcomes and a better quality of life for those affected by cancer. Challenges and Limitations in Cancer Treatment The advancements in immunotherapy have sparked hope for more effective cancer treatments, but challenges remain. One significant hurdle is the variability in patient response to these therapies, which can be attributed to differences in tumor biology and immune system interactions. For instance, while immune checkpoint inhibitors have shown remarkable success in certain cancers, others exhibit resistance, limiting their effectiveness (A. Mishra et al.). Furthermore, the complexity of immune mechanisms often means that a one-size-fits-all approach is insufficient; thus, ongoing research is crucial to understand how to tailor treatments to individual patients better. Additionally, identifying biomarkers that predict response to immunotherapy will enhance the personalization of cancer treatment, ultimately leading to improved clinical outcomes for diverse patient populations.

Results: Future Directions and Research in Cancer Therapy Moreover, the integration of novel therapeutic agents holds promise for overcoming current limitations in cancer treatment. For instance, strategies such as combining immune checkpoint inhibitors with other modalities like chemotherapy, targeted therapy, or radiation are being explored to enhance their effectiveness (A. Mishra et al.). This combination approach aims to create a synergistic effect that may reduce resistance and improve patient outcomes. Additionally, advancements in personalized medicine will likely play a pivotal role in the future landscape of cancer therapy. By utilizing genomic profiling and understanding the unique characteristics of each patient's tumor, oncologists can devise tailored treatment plans that maximize efficacy while minimizing adverse effects. As research continues to evolve, the hope is to develop more predictive models to guide clinicians in selecting the most appropriate therapies for individual patients.

Conclusion: Future Directions and Research in Cancer Therapy Moreover, the integration of novel therapeutic agents holds promise for overcoming current limitations in cancer treatment. For instance, strategies such as combining immune checkpoint inhibitors with other modalities like chemotherapy, targeted therapy, or radiation are being explored to enhance their effectiveness (A. Mishra et al.). This combination approach aims to create a synergistic effect that may reduce resistance and improve patient outcomes. Additionally, advancements in personalized medicine will likely play a pivotal role in the future landscape of cancer therapy. By utilizing genomic profiling and understanding the unique characteristics of each patient's tumor, oncologists can devise tailored treatment plans that maximize efficacy while minimizing adverse effects. As research continues to evolve, the hope is to develop more predictive models to guide clinicians in selecting the most appropriate therapies for individual patients.

Keywords: Cancer Treatment Method

29.

Cancer treatment with nanotechnology (Review)

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Introduction: Nanotechnology is a high-application field in basic medicine, relying on the design of various nanostructures used in clinical applications such as early diagnosis or treatment of disease. Cancer treatment strategies are a range of combined chemotherapy drugs, in addition to radiotherapy and auxiliary surgery. Nanomedicine aims to replace chemotherapy drugs that are highly invasive, non-specific and accompanied by unwanted side effects, with specific targeting factors with potential in diagnosis, imaging, targeted delivery and controlled release of therapeutic shipments.

Methods: Because of their ability to have a 'controlled release tank", nanoparticle-based drugs can safely deliver therapeutic agents to specific sites of damage or cells, control drug release, and improve therapeutic effectiveness by increasing the accumulation and release of pharmacologically active agents at the tumor site; nanoparticles also protect the therapeutic agent attached to it, increase drug circulation time, and reduce toxicity and side effects for healthy tissues. The specific properties of nanoparticles allow the Diagnostic and therapeutic agent to be integrated into a nanoparticle. Nanoparticles are able to pass through cell membranes due to their small size and are not detected by the reticuloondothelial system, thus preventing their destruction. Nanoparticles also need to be accumulated in the target tissue for greater effectiveness, which allows the small size of the nanoparticles to pass through the vascular pores of the tissues, avoiding removal by the spleen through penetration into the tissue. The multifunctionality of high-level-to-volume nanoparticles offers high loading capacity for various imaging. It can also improve or reduce its circulation time by changing the surface and load of the nanoparticles.

Results: A range of nanostructures such as liposomes, nanomaterials, quantum dots, peptides, cyclodextrins, carbon nanotubes (CNTs), graphene and metal-based nanoparticles are used for diagnostic or therapeutic purposes. Gold nanoparticles are the main focus of biomedical research due to their specific physical and chemical properties. These nanoparticles have low cell toxicity, increase the lifespan of a drug shipment in the bloodstream, allow easy size control, improve surface chemistry, increase the effects of

the drug on the surface of the cancer cell, and improve pharmacokinetic effects. Also, by loading nanoparticles with RNA such as siRNA and Mirna, the cancer cell gene can be turned off and mRNA translation prevented. Liposomes are used for targeted delivery of natural or synthetic chemotherapy. The encapsulation of drugs in the liposome allows the delivery of therapeutic agents to the target and prevents their absorption by the reticuloandothelial system. Due to the specific stimuli present at the tumor site, liposomes can target tumor cells and release chemotherapy agents enclosed in nanoparticles. Hybrid systems are a mixture of polymer nanoparticles and liposomes. The core of the system, which is a biodegradable hydrophobic polymer, allows the encapsulation of water- soluble drugs and ensures continuous release. To increase circulation time and prevent the immune system from responding, the hybrid system is covered with a hydrophilic shell. Hybrid systems designed from noble metals are promising anticancer agents that play a role in diagnosis and treatment, such as the anti-cancer effect on silver and gold nanoparticles on lung cancer cells, silver and selenium nanoparticles on lymphoma cells, gold and platinum nanoparticles on cervical cancer, and the cytotoxic effects of silver and gold bimetallic nanostructures against breast cancer cells category MCF-7. Dendrimers are nanoscopic macromolecules that play a fundamental role in the emerging field of Nanomedicine and are ideal carriers for pharmaceuticals and targeted applications due to water solubility, biocompatibility, multi-capacitance, and precise molecular weight. Carbon nanotubes can immobilize therapeutic agents such as drugs, proteins, DNA and antibodies on the outer wall or enclose them inside nanotubes and reduce cell toxicity for healthy tissues. Also due to the nanosensor-like structure, carbon nanoparticles are effectively absorbed and transferred to the cytoplasm of the target cell without cell death. Nanoparticles are also used in chemotherapy and imaging, so that nanoparticles enclose the chemotherapy agent and are triggered by specific ligands found in specific molecules on the cancer cell. In imaging, magnetic nanoparticles coated with specific proteins are also used as imaging agents because they can bind to specific tumor tissues.

Conclusion: Overall, nanotechnology in cancer treatment holds great potential for improving the effectiveness and precision of therapies, ultimately benefiting patients by reducing side effects and enhancing treatment outcomes.

Keywords: Nanoparticles Drug delivery Cancer therapy

30.

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

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Introduction: Chimeric Antigen Receptor (CAR) T cell therapy has transformed cancer treatment, especially for blood cancers. This innovative immunotherapy involves modifying a patient's T cells to express receptors that target specific cancer cell antigens, enabling precise identification and destruction of malignant cells. While successful in hematologic cancers, applying CAR T cell therapy to solid tumors like non-small cell lung cancer (NSCLC) presents unique challenges. This article explores these obstacles, highlights promising targets, and discusses current research directions.

Methods: This review synthesizes current literature on CAR T cell therapy, focusing on its application in NSCLC. We analyzed clinical trials, preclinical studies, and recent publications to provide a comprehensive overview of the challenges, advancements, and future directions. The information is sourced from reputable scientific databases and peer-reviewed journals.

Results: Challenges: Solid tumors such as NSCLC create a challenging environment for CAR T cell therapy. The tumor microenvironment (TME) is immunosuppressive, hindering CAR T cell infiltration and survival. Additionally, antigen heterogeneity and immune evasion by tumor cells complicate treatment. Promising Targets: Despite these challenges, several antigens are promising targets for CAR T cell therapy in NSCLC. EGFR, MUC1, and MSLN are particularly attractive due to their overexpression in cancer cells, making them ideal for CAR T cell targeting. Advances and Strategies: Researchers are developing strategies to enhance CAR T cell effectiveness against NSCLC. These include designing multi-targeting CARs to address tumor heterogeneity, combining therapies with checkpoint inhibitors or chemotherapy to boost responses, and exploring direct tumor infusion to overcome the immunosuppressive TME. Clinical Trials and Future Directions: Numerous clinical trials are underway to evaluate various CAR T cell designs and combinations to improve outcomes

for NSCLC patients. These studies aim to optimize dosage, reduce side effects, and enhance CAR T cell persistence and activity within tumors.

Conclusion: While significant challenges remain, ongoing research and innovative strategies offer hope for more effective NSCLC treatments. As our understanding of tumor biology and immunotherapy advances, CAR T cells hold the potential to become a powerful tool in fighting NSCLC, providing new hope for patients battling this complex disease.

Keywords: CAR T Cells, Lung Cancer, NSCLC

31.

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 25 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 CD19 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: CAR-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.

Keywords: CAR-T Cell, Therapy, Hematological Malignancies

32.

Circulating microRNAs as valuable biomarkers for early detection and clinical management of colorectal cancer (Review)

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Introduction: Based on recent studies, new non-invasive approaches by liquid biopsies can be applied for early cancer detection. The analysis of circulating tumor DNA (ctDNA), tumor-derived cells (CTC, circulating tumor cells), or circulating microRNA (miRNA) from body fluids can be applied as valuable biomarkers for cancer monitoring in early diagnosis, prognosis, and therapeutic approaches. According to the restrictions and challenges in diagnostic methods in colorectal cancer (CRC) screening and management, including biopsy-based techniques, liquid biomarkers have been introduced because of several advantages, such as quick and easy extraction from patients, low cost and minimal pain and risk for patients due to its minimal invasiveness. In addition, the biological role of miRNAs in the pathogenesis of CRC can be applied as an important predictive or prognostic biomarker.

Methods: Tumor-specific miRNAs can be found in body fluid circulation, which can be detected in low quantities of samples with high specificity and present in several biofluids, including serum, plasma, saliva, and urine.

Results: Recent studies proposed the members of the MiR-17-92 miRNA cluster, miR-21, miR-23, miR-17/92 Cluster, miR-96, miR-135 family, miR-143, miR-145, miR-150, miR-183, miR-200 family, and miR-203a can be considered as valuable biofluid biomarker for screening of CRC patients.

Conclusion: MiRNAs can be potentially applied as valuable and reliable biofluid markers. However, the most suitable detection method for CRC screening and the application of a precise and definitive diagnostic or prognostic panel comprised of miRNA combinations should be determined in future studies.

Keywords: Colorectal Neoplasms, Circulating MicroRNA, Early Detection of Cancer, Early Diagnosis

33.

Colorectal cancer and Bacteroides fragilis (Review)

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Introduction: Colorectal cancer (CRC) is a common and deadly cancer worldwide. Recent research has identified the gut bacterium Bacteroides fragilis, particularly its enterotoxigenic strain (ETBF), as a significant player in the development of CRC.

Methods: This study reviews existing literature on the relationship between Bacteroides fragilis and colorectal cancer. We searched databases like PubMed and Scopus using keywords such as "colorectal cancer" and "Bacteroides fragilis," and analyzed relevant studies.

Results: The findings suggest a strong link between Bacteroides fragilis and CRC. ETBF produces toxins that cause inflammation and damage the gut lining, contributing to cancer development. The presence of ETBF could also be a potential biomarker for early CRC detection.

Conclusion: The connection between Bacteroides fragilis and colorectal cancer highlights the importance of gut microbiota in cancer. Targeting this bacterium could be key in preventing and treating CRC.

Keywords: Colorectal cancer, Bacteroides fragilis, gut microbiota

34.

Coping Strategies for Sexual Dysfunction in Prostate Cancer Patients: A Systematic Review (Review)

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Introduction: Sexual dysfunction is a common and distressing side effect for patients undergoing treatment for prostate cancer, significantly affecting their quality of life. This systematic review aims to identify and categorize coping strategies used by men with prostate cancer to manage sexual dysfunction, providing insights into adaptive and maladaptive mechanisms.

Methods: A comprehensive search was conducted across multiple databases, including PubMed, Scopus, and Web of Science, to identify relevant studies published between 2000 and 2024. Studies were included if they focused on coping mechanisms related to sexual dysfunction in prostate cancer patients. Data extraction and quality assessment were conducted using standardized protocols, with findings categorized into psychological, behavioral, and social coping strategies.

Results: Twenty-two studies met the inclusion criteria. The most commonly reported coping strategies included: Psychological strategies: Cognitive reframing, mindfulness, emotional regulation, and acceptance. Behavioral strategies: Physical activity, lifestyle modifications (e.g., diet changes), and participation in sexual rehabilitation programs. Social strategies: Seeking support from partners, family, and healthcare providers. In contrast, maladaptive strategies such as avoidance, denial, and withdrawal from social interaction were associated with poorer emotional outcomes. Adaptive coping mechanisms, particularly those involving communication with partners and professional guidance, were found to enhance patients' emotional well-being and improve sexual recovery outcomes.

Conclusion: Prostate cancer patients employ a range of coping strategies to manage sexual dysfunction, with adaptive strategies showing better outcomes in emotional well-

being and recovery. Healthcare providers should prioritize psychological support and tailored interventions to help patients navigate sexual health challenges following treatment.

Keywords: Prostate cancer, sexual dysfunction, coping strategies, systematic review, quality of life

35.

Curcumin-based nanoformulations; a new approach for cancer therapy (Review)

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Introduction: Cancer is responsible for one-fifth of deaths worldwide every year. Cancer is the result of genetic and epigenetic changes that lead to apoptosis, uncontrolled cell proliferation, metastasis, and angiogenesis. In recent years, surgical methods, chemotherapy, and radiotherapy have been used to fight cancer. Still, these methods not only cause pain and discomfort to patients but also require drug resistance and have many side effects. Therefore, researchers have decided to use natural materials that are multifunctional in cancer. In this context, curcumin is a chemical substance extracted from the turmeric plant used to treat many types of cancer due to its anti-inflammatory, antioxidant, and anticarcinogenic properties. However, its efficacy is limited due to rapid metabolism, low bioavailability, and poor solubility in water, and systemic excretion is limited, so researchers have tried to solve these limitations by looking for drug delivery systems such as different nanostructures (polymeric nanoparticles, lipid nanoparticles, etc.).

Methods: This review article is the result of several reviews by the authors, collected from reliable scholarly sources such as Scopus, Web of Science, PubMed.

Results: Curcumin acts on several important targets, including protein kinase C (PKC), thioredoxin reductase, tubulin, 5-lipoxygenase, COX-2, cytokines, transcription factors, enzymes, growth factors and their receptors, and genes involved in cellular proliferation and apoptosis and through different molecular pathways, it can help treat cancer. many studies have shown that Curcumin nanoformulations have the potential to offer several benefits, including improved efficacy and tumor targeting, reduced systemic toxic effects, better compliance, and ease of administration.

Conclusion: Studies have shown that curcumin-based nanoformulations have promising anti-cancer activity in various types of cancer, including breast, lung, prostate, colorectal

cancer and etc. These nanoformulations have been found to inhibit cancer cell proliferation, induce cell death and prevent cancer metastasis. Despite the development of different nanocarriers for curcumin for cancer treatment, side effects such as interactions with other drugs and the toxicity of nanoparticles should be considered. For this reason, further studies should be conducted to prove the clinical efficacy of curcumin nanocarriers and Further research is needed to optimize the design and delivery of these nanoformulations and to evaluate their safety and efficacy in clinical trials.

Keywords: Cancer treatment, Curcumin, Nanotechnology.

36.

Cytotoxic effect of sesquiterpene lactone britannin on colorectal cancer cells in-vitro (Review)

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Introduction: Colorectal cancer (CRC) is the second leading cause of cancer deaths in the United States. Britannin, a sesquiterpene lactone, has demonstrated anticancer properties across various cancers. This study focused on assessing the antiproliferative effects of britannin on the HT29 colorectal cancer cell line.

Methods: The antiproliferative effect of britannin on HT29 cells was assessed using the MTT method. HT29 cells were seeded in 96-well microplates and allowed to adhere for 24 hours. They were then treated with various concentrations of britannin (0-200 µM) for 24, 48, and 72 hours. After discarding the medium, the cells were incubated with MTT solution for 4 hours. The MTT solution was then replaced with a 1% DMSO solution. Finally, absorbance of the formazan crystals was measured at 570 and 630 nm to calculate the proliferation rate of HT29 cells.

Results: Treatment of HT29 cells with various concentrations of britannin for 24 hours significantly reduced the viability percent, yielding an IC50 of 28.6 µM. After 48 hours, britannin treatment further inhibited cell viability, resulting in an IC50 of 20.9 µM compared to controls. Additionally, 72 hours post-treatment, the sesquiterpene lactone showed a notable decrease in HT29 cell viability with an IC50 of 21.3 µM.

Conclusion: The MTT assay results indicated that britannin may exert a significant cytotoxic effect on human HT29 cells through its anti-proliferative activity, suggesting its potential as a natural compound for suppressing colorectal cancer growth.

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

37.

Determining high-risk genotypes 16 and 18 of human papillomavirus by multiplex real-time PCR method in suspected cervical cancer samples (Research Paper)

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1.
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Introduction: Human papilloma virus types 16 and 18 can be mentioned among the main causes of cervical cancer, which is a disease with a high prevalence, especially in developing countries. This study was conducted with the aim of identifying high-risk types 16 and 18 infection in women suspected of having cervical cancer who had referred to medical centers

Methods: After sample collection and DNA extraction, detection was done by Multiplex Real Time PCR molecular method.

Results: The results showed that among the 100 samples suspected of cervical cancer, 52% were positive with genotype 16, 19% were positive with genotype 18, 2% were both genotypes 16 and 18 at the same time, and the rest were negative, of course, this negativity is because we only We examined the two mentioned genotypes

Conclusion: In this study, it was shown that for accurate and specific diagnosis of HPV test and determination of its genotype, instead of using expensive commercial kits that are used in laboratories all over the country, you can use proper primer and probe and Multiplex Real Time PCR method. The use of the probe is as sensitive and accurate as the ready-made kits, but it is more economical and since the lower the cost, the more people are able to use this test for screening, so it is possible to detect the infection in the early stages and before The incidence of cervical cancer was treated.

Keywords: Cervical Cancer, Screening, Human Papilloma Virus, Real-time Multiplex PCR

38.

Development of cellulose-based nanocarriers for drug delivery in prostate cancer treatment (Review)

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Introduction: Despite the important advances made in the diagnosis and treatment of prostate cancer (PC), this disease still causes the death of men in the world Prostate cancer in the advanced stages of the disease is the most lethal male malignancy. Current treatment for advanced-stage PC includes combined chemotherapy, Radiotherapy and surgery. Nevertheless, resistance to therapeutic approaches, including resistance to chemotherapy drugs, is an important challenge in the management of PC. Therefore, new therapeutic strategies based on the development of nanoscale drug delivery systems are necessary for the pharmacokinetics of chemotherapy agents, tissue absorption and improving bioavailability. For this purpose, cellulose-based nanoparticles are non-toxic, biocompatible with the human body, and biodegradable and also the inherent and unique characteristics in accepting the desired modifications such as changing the charge and adding functional groups have been considered and designed by many researchers to deliver drugs to prostate cancer cells. In a study, Ntoutoume et al. designed and synthesized cellulose-based nanocarriers through charge modification of cellulose surfaces, which optimally delivered the loaded curcumin with a low dose to the cytoplasm of prostate cancer cells. The results showed that the induction of cellular apoptosis

increased. This review discusses the prospects, advances and future challenges in the delivery of chemotherapy drugs through cellulose-based nanoparticles and cellulose derivatives with the aim of their importance in the treatment of prostate cancer.

Methods: Original articles published from 2024-2000 on cellulose-based nanocarriers in the field of anticancer drug delivery for prostate cancer treatment were searched from Elsevier and PubMed databases, Google Scholar, Scopus and Web of Science. Using these data, the properties and application of cellulose-based nanoparticles in the treatment of prostate cancer were discussed.

Results: New nanocomplexes are synthesized with structural modifications to change the charge and create functional groups to load chemotherapeutic drugs while leaving the important intrinsic properties of cellulose intact. In this regard, the delivery platform based on cellulose nanocrystals was performed using charge modification. Cellulose nanocrystals were attracted to the positive charge of cationic cyclodextrins through electrostatic bonding, and stable complexes were designed that could load non-polar drugs into hydrophobic cavities. High release loading of hydrophobic drug in the cytoplasmic environment of prostate cancer cell was optimally reported. The results introduced cellulose nanocarrier as a suitable tool for the optimal delivery of chemotherapy drugs to cancer cells for the treatment of prostate cancer.

Conclusion: Cellulose nanoparticles are of significant importance in overcoming drug resistance, reducing side effects and treating prostate cancer by transferring chemotherapy drugs to the target tissue.

Keywords: Cellulose nanocarriers, Modified cellulose nanoparticles, drug delivery, prostate cancer therapy

39.

Development of Hyaluronic acid (HA)-based nanocarriers for delivery of miRNAs in breast cancer therapy (Review)

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Introduction: Breast cancer is very common in the world and is considered as first rank deadly cancer in woman. In recent years, gene therapy based on miRNAs as important pathological regulators of cancer has been gained more attention for developing advanced therapeutics. However, direct administration of miRNAs has a very low and unrealistic effect due to low stability and reduced penetration along the cell membrane. High efficiency delivery carriers are required for targeted miRNA delivery. Hyaluronic acid (HA) is a polysaccharide and because of its natural affinity to bind to CD44 expressed on tumor cells surface it has been used in the delivery of miRNA and drugs. Also, HA has unique biological and chemical properties including biocompatibility and having multiple functional groups for chemical composition with polymers to be utilized in breast cancer targeting. This review discusses the recent progress and future prospects in HA-mediated delivery of miRNAs with significance in breast cancer therapy.

Methods: Original articles published since 2008 on HA nanocarriers in the field of RNA carrier for breast cancer treatment were searched from Google Scholar, Scopus, and

PubMed databases. Using these information, the application and properties of HA-based nanocarriers were discussed.

Results: About 18 different microRNAs were tested to evaluate their efficacy and the safety in triple-negative mice models. Among all founded miR-based therapeutics, miR-21 was the most studies miRNA and miR-205a showed proper antitumor and antimetastatic effects. Recently, a hyaluronic acid (HA)-decorated polyethyleneimine poly (D, L-lactide-co-glycolide) (PEI-PLGA) nanoparticle system was developed, which enabled active targeted co-administration of miR-542-3p and doxorubicin (DOX) for Treatment of triple negative breast cancer (TNBC). HA/PEI-PLGA nanoparticles increased drug uptake in MDA-MB cells and miR-542-3p induced apoptosis in breast cancer cells through p53 activation. Moreover, in another study miR-34a was delivered in combination with DOX in TNBC by HA-chitosan nanoparticles.

Conclusion: Regarding the biocompatibility and excellent targeting efficiency of HA mediated delivery of miRNAs in published breast cancer studies, the use of HA-based nanocarriers is highly recommended for future breast cancer therapies.

Keywords: Hyaluronic acid (HA), delivery of miRNAs, breast cancer therapy

40.

development of nanofibrous scaffold incorporated with ZnO NPs against human melanoma A357 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 A375 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 A357 cell line was conducted through the MTT assay. Upon achieving the IC50 concentration, the A357 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 whenexposed to the IC50 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

41.

Diagnostic value of HOXB-AS1 in breast cancer: a promising regulator of key signaling pathways (Review)

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Introduction: Antisense long non-coding RNAs (AS-lncRNAs) are transcribed from the opposite DNA strands of coding or non-coding genes and play crucial roles in cancer development and progression. AS-lncRNAs can either inhibit or promote tumor growth and metastasis, influencing gene expression regulation at both nucleic and cytoplasmic levels through cis and trans mechanisms. Aberrant AS-lncRNA expression in cancer cells is linked to alterations in various signaling pathways, making them promising targets for cancer research and potential clinical applications. The HOXB cluster antisense RNA 1 (HOXB-AS1), located on chromosome 17, has been associated with several cancers, including glioblastoma and endometrial cancer. This study aims to investigate the expression and role of HOXB-AS1 in breast cancer (BC), given its potential as a therapeutic target or biomarker.

Methods: We conducted an in-silico analysis of HOXB-AS1 expression using microarray data from the GEO database, followed by experimental validation using BC and normal tissue samples from Iranian patients. RNA was extracted, and quantitative real-time PCR (qPCR) was performed to measure HOXB-AS1 expression. Results were verified with data from The Cancer Genome Atlas (TCGA). Differentially expressed genes (DE genes) were

identified, and their correlation with HOXB-AS1 was analyzed. Additionally, protein-protein interaction (PPI) networks and hub genes were explored using bioinformatics tools.

Results: qPCR results showed a significant downregulation of HOXB-AS1 in BC tissues compared to normal tissues. TCGA data corroborated these findings. Lower HOXB-AS1 levels were associated with decreased relapse-free survival (RFS) but not overall survival (OS) in BC patients. Receiver Operating Characteristic (ROC) curve analysis indicated that HOXB-AS1 could serve as a diagnostic marker for BC. Correlation and pathway analyses revealed that HOXB-AS1 expression negatively correlated with several oncogenic genes, suggesting its potential role as a tumor suppressor.

Conclusion: HOXB-AS1 is significantly downregulated in breast cancer tissues, and its reduced expression is linked to poorer relapse-free survival. These findings suggest that HOXB-AS1 might function as a tumor suppressor in BC and highlight its potential as a diagnostic biomarker. Further research is needed to fully elucidate its role and therapeutic applicability in breast cancer.

Keywords: Antisense RNAs Breast cancer noncoding RNA Bioinformatics Biomarker

42.

effect of pomegranate extract on mcf-7 and lymphocyte (Research Paper)

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Introduction: Breast cancer is one of the problems of today's world, which has caused many deaths, and these deaths often occur due to the drug resistance of cancer cells to common breast cancer treatments. The use of an efficient auxiliary drug along with common cancer treatments can break this drug resistance and reduce its effects. One of the accessible and harmless suggestions are herbal medicines. Iran can improve in this field due to its favorable climate. Pomegranate, which is a fruit with antioxidant properties, is one of the suggestions. This fruit seems to be effective in the more effective treatment of cancer cells due to the presence of allagitanin, which has apoptotic properties. In these studies, we investigated the effects of pomegranate extract on breast cancer in mcf-7 cell line and also its effects on lymphocyte cells.

Methods: The MCF7 cells were cultured in DMEM, supplemented with 10% FBS, 100 units/ml penicillin, and 100 µg/ml streptomycin. Cells were maintained in a humidified incubator at 37°C with 5% CO2. Then the cells were treated with different concentrations and mtt test was performed for them. The best drug concentrations were extracted using the kit, their RNA was extracted, and then cDNA was made, and real time was performed by designed primers. Lymphocyte cells, after being extracted from fresh blood, were poured into the plate using Ficoll and then treated with specific concentrations. After 24 hours, mtt test was performed and the best concentrations were analyzed after rna extraction and cDNA production by real time and designed primers. In the end, all the results obtained from mcf7 cells and lymphocytes were examined and analyzed using Linerg and Genex software.

Results: The real time results of mcf-7 cells showed that the ratio of bax/bcl2 has increased significantly, which indicates the good effect of this extract. Also, the mtt results

of lymphocyte cells showed that these cells multiplied when exposed to pomegranate extract, as well as the expression level bcl2 was increased compared to bax in these cells.

Conclusion: Pomegranate extract seems to have a good effect on this type of cancer cell and can act as a treatment aid along with other treatments. Also, this extract has a good effect on lymphocyte cells and acts as a lymphocyte cell booster. Further research on other cancer cell lines needs to be investigated.

Keywords: breast cancer/ pomegranate extract/ mcf7/ bax/ bcl2

43.

Emerging Role of CRISPR/Cas9 Technology for Targeting microRNAs in breast cancer (Review)

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Introduction: Introduction: Breast cancer is an aggressive disease that has a high prevalence in women all over the world. This heterogeneous type of cancer includes many oncogenic pathways and many genetic and epigenetic changes. Currently, the main treatments for breast cancer are radiotherapy, chemotherapy, and surgery. Also, early breast cancer screening is heavily dependent on tissue biopsies, which are invasive and limited. Therefore, in recent years, to improve the results of breast cancer diagnosis and treatment, liquid biopsy containing free circulating and exosomal microRNAs(miRNAs) has been increasingly revealed as a potential minimally invasive alternative to tissue biopsy.

Methods: Methods: Google Scholar and PubMed were used as search engines. Search was performed with the following terms: CRISPR/Cas9 technology, microRNAs, and breast cancer. Finally, 40 related articles were selected and reviewed from studies of the last five years.

Results: Discussion: MiRNAs are endogenous single-stranded RNAs that pair with the 3' untranslated region of target mRNAs to regulate mRNA target gene expression. These types of non-coding RNAs are involved in various cellular processes including proliferation, differentiation, apoptosis, migration, metabolism, and stress response. MiRNAs are stable under different conditions, including exposure to RNases, multiple thawing and freezing cycles, and extreme pH. This stability has led to identifying these types of circulating RNAs as robust biomarkers in the diagnosis of various cancers. In the past decade, some miRNAs have been used as breast cancer biomarkers for diagnosis (miR-9, miR-10b, and miR-17-5p), prognosis (miR-148a and miR-335), and prediction of treatment outcomes (miR-30c, miR-187 and miR-339-5p) have been used. Targeting miRNA to stimulate or suppress gene expression has a significant impact on the study of cancer biology as a prognostic and therapeutic tool. There is increasing evidence that small non-coding RNAs, including miRNAs, can be targeted by the CRISPR/Cas9 system for loss-of-function assays while lacking an open reading frame. Therefore, CRISPR/Cas9 technology represents a

novel gene editing strategy with compelling robustness, specificity, and stability to modulate miRNA expression.

Conclusion: Conclusion: CRISPR/CAS9 technology is a promising therapeutic approach for miRNA targeting. This technique is a more effective, accurate, and stable method to activate and deactivate miRNA in cancer cells than recent methods. The main advantage of this method is that it integrates the inserted mutation into the genome and transmits it to the next generation. The ability of CRISPR/CAS9 technology to modify the genome has started a new phase in human evolution. This advanced genome editing technology has made it possible to adopt a modern approach to studying the role of different molecules in the development of cancer.

Keywords: Keywords: CRISPR/Cas9, microRNAs, Breast Cancer

44.

Evaluating combinatorial effects of stylosin and radiotherapy on human glioblastoma cells (Review)

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Introduction: Stylosin, a monoterpene compound extracted from Ferula species, exhibits valuable pharmaceutical effects, such as anticancer properties. Glioblastoma is the most aggressive and common type of malignant brain tumor that originates from glial cells. Despite the routine use of surgery, chemotherapy and radiotherapy for treating glioblastoma, the survival rate remains low.

Methods: The aim of present study was to study toxic effects of stylosin and radiotherapy on human glioblastoma cells for the first time. In this regard, U87 cells were treated with increasing concentrations of stylosin (20, 40, 60, 80 and 100 µM) during five consecutive days and viability was evaluated by alamarBlue assay. Upon determining the optimum concentrations of stylosin, cells were treated with 60 and 80 µM stylosin for 48 h, then exposed to 4, 6 and 8 Gy ionizing radiation (IR) and recovered for 72 h. To note, cells only exposed to IR and recovered for 72 h were also considered as relevant controls.

Results: Findings revealed 84% and 42% viability for U87 cells upon 120 h treatment with 60 and 80 µM stylosin, respectively. Cotreatment of glioblastoma cells with 60 µM stylosin and 8 Gy IR decreased viability down to 76%. Intriguingly, effects of 80 µM stylosin were more considerable, as viability of cells was reduced to 10%, 11% and 10% after irradiation at 4, 6 and 8 Gy, respectively.

Conclusion: Current findings suggest that stylosin could be considered as a potent agent for combinatorial treatment of glioblastoma.

Keywords: Stylosin, Radiotherapy, Glioblastoma, Combination.

45.

Evaluation and Bioinformatics Analysis of Cervical Cancer Genetic Origin of Cervical Cancer among Patients and Feedback To Generation Drugs **(Research Paper)**

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Introduction: Cervical cancer is seen as a common disease among Iranian women. This study examines the genetic origin of cervical cancer and related chemotherapy drugs, which is one of the main methods in the cancer treatment protocol. We hope to improve cancer treatment using NGS technology and cancer genomic knowledge.

Methods: This study was conducted through the NCBI database to classify several SNP-associated with genes based on population and most citations. Also, side effects caused by chemotherapy drugs used to treat cervical cancer in Iran were collected. The obtained information was analyzed by pharmacogenomics software (MEGA GENE) to analyze polymorphism information and identify side effects related to patients' genetics.

Results: Analyzes based on MEGA GENE software show that RS1799966, RS28897672, RS1799950, RS144848, RS80359550, RS28897728,1800734, RS1799977, RS35502513 polymorphisms can be involved in the occurrence of cervical cancer with genetic origin. These SNPs can cause other phenotypes such as thalassemia, leukemia, Fanconi anemia, breast-ovarian cancer, and colorectal cancer.

Conclusion: Based on our findings, we recommend that oncologists perform genetic testing to identify polymorphisms before prescribing chemotherapy to treat cervical cancer patients. This method allows specialists to prescribe drugs whose side effects are not the same as the possible phenotypes caused by the polymorphism detected in the patient's sample so that chemotherapy treatment can be performed with the least complications for the patient.

Keywords: NGS, Cancer Genomics, Pharmacogenomics, Cervical Cancer, MEGA GENE

46.

Evaluation of the Effect of Radiotherapy on CCL5/miR-214 -3p/MALAT1 Genes Expression in Blood Samples of Breast Cancer Patients (Research Paper)

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Introduction: Current cancer therapies include chemotherapy, radiation therapy, immunotherapy, and surgery. Despite these treatment methods, a major point in cancer treatment is early detection. RNAs (mRNA, miRNAs, and LncRNA) can be used as markers to improve cancer diagnosis and treatment. This research examined how radiotherapy affected CCL5, miR-214, and MALAT-1 gene expression in the immune pathway in peripheral blood samples from radiation therapy-treated breast cancer patients.

Methods: Before and after radiotherapy, peripheral blood was collected from 15 patients in four steps. Blood samples were collected in an outpatient facility from 20 healthy female volunteers with no history of malignant or inflammatory conditions. RNA was extracted from the blood samples and cDNA was synthesized. CCL5, miR-214, and MALAT-1 gene expression were determined by real-time polymerase chain reaction (RT-PCR). CCL5 protein levels in the serum were determined in 80 samples (60 BC and 20 healthy controls) using Quantikine Enzyme-Linked Immunosorbent Assay (ELISA) kits (R&D Systems). The data were then statistically evaluated.

Results: here was a significant difference between CCL5 levels in tumoral and adjacent normal blood samples ($p < 0.05$). The results also show that the level of gene expression and serum concentration of CCL5 protein in different phases of radiotherapy is significantly different. On the other hand, the expression level of the miR-214 gene was significantly decreased in patients compared to the control group, but this decrease was not significant for the MALAT-1 gene ($p< 0.05$). Also, after each stage of radiotherapy, the expression level of these two genes showed a decrease, but in the fourth week after radiotherapy, this

decrease was significant ($p< 0.05$). Radiotherapy is associated with a decrease in the expression of miR-214 and MALAT-1, as a result, an increase in the expression of CCL5.

Conclusion: An increase in the concentration of CCL5 protein is accompanied by an increase in the level of monocytes, which ultimately causes the infiltration of macrophages and can ultimately cause cancer recurrence. It is suggested that these genes can probably be used as diagnostic and therapeutic radiotherapy markers in breast cancer.

Keywords: Breast cancer, radiotherapy, ELISA, miR-214, CCL5, MALAT-1

47.

Evaluation of the expression of two circular non-coding transcripts involved in pluripotency and cell proliferation, CircBIRC6 and CircFOXP1, in esophageal cancer cell lines and stem cells. (Research Paper)

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Introduction: Background and Objective Esophageal cancer is one of the rare types of cancer, characterized by a significant increase in mortality rates. This disease is often diagnosed at advanced stages, highlighting the need for new and effective diagnostic and therapeutic methods. In recent years, extensive research has been conducted on non-coding molecules such as circular RNAs (circRNAs), which play important roles in gene expression regulation and biological processes. CircRNAs have been proposed as potential biomarkers for the identification and prediction of cancer, and they can aid in understanding the molecular mechanisms of the disease. The objective of this study is to investigate the expression of circRNAs in esophageal cancer cell lines and compare them with mesenchymal stem cells and embryonal carcinoma. Through this research, we aim to identify specific circRNAs that may serve as new biomarkers for esophageal cancer. This information could lay the groundwork for future research in this area and contribute to the development of novel diagnostic and therapeutic approaches. Overall, this study explores the relationship between circRNAs and esophageal cancer, emphasizing the importance of these molecules in disease detection and prediction.

Methods: In this study, several cell lines were selected, including esophageal cancer cell lines, embryonal carcinoma (NT2), mesenchymal stem cells (MSCs), and induced pluripotent stem cells (iPSCs) (NP40-8 and NP41-17), and cultured under appropriate conditions. RNA was extracted from these cell lines at a density of 70 to 80 percent, and the quality and concentration of the RNA were measured using a Nanodrop c2000 device. For cDNA synthesis, 1 microgram of RNA was utilized with the SMOBIO kit. Subsequently, the concentration of primers and annealing temperature for the Real-Time PCR reaction were optimized, and the expression of circular RNAs was investigated in the iPSC cell line.

Finally, the expression levels of the RNAs were normalized against a reference gene, and statistical analysis was performed using the Kruskal-Wallis test.

Results: In this study, the cell lines were successfully cultured, and their quality was confirmed. The concentration of the extracted RNA ranged from 460 to 2300 ng/µl, with 260/280 and 260/230 ratios indicating acceptable RNA quality. Additionally, cDNA synthesis was successfully achieved, and the expression of circRNAs was confirmed, as the melt curves demonstrated the specificity of the products. Ultimately, circBIRC6 and circFOXP1 showed significant expression in MSC and NT2 cell lines compared to certain esophageal cancer cell lines, confirming their potential as biomarkers for esophageal cancer.

Conclusion: This study investigates circular RNAs (circRNAs) in esophageal cancer, focusing on two key circRNAs, circBIRC6 and circFOXP1. This disease is associated with recurrence and resistance to treatment, making the identification of molecular mechanisms for early detection essential. CircBIRC6 enhances the stemness of cancer cells by sequestering miR-34a and miR-145, potentially leading to tumor recurrence. CircFOXP1 supports WNT signaling pathways, and its disruption can contribute to oncogenesis. CircRNAs could serve as new biomarkers for the early detection of esophageal cancer. Further research is necessary to explore the mechanisms of circRNAs and their therapeutic potential. Ultimately, circRNAs offer new opportunities for the diagnosis and treatment of esophageal cancer, aiding in a better understanding of this disease.

Keywords: Circular RNAs (circRNAs), esophageal cancer, cell lines, stem cells, Real-Time PCR.

48.

Examining the expression of Circ_0000745 and its relationship with hsa-miR-335-5p in the pathogenesis of breast cancer through the study of tissue samples from women in hospitals in Qazvin province. (Research Paper)

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Introduction: Breast cancer is one of the most common cancers among women, and early diagnosis of this disease plays an essential role in improving its prognosis. In recent years, non-coding RNAs such as circRNAs and miRNAs have been recognized as possible biomarkers for cancer diagnosis and prognosis. Circ_0000745 (SPECC1) and hsa-miR-335-5p are two key molecules involved in the regulation of genes related to breast cancer and may be involved in cell proliferation and cancer progression.

Methods: In this study, tumor and normal tissue samples were collected from patients with breast adenocarcinoma. After extracting total RNA from tissue samples, cDNA synthesis was performed. The expression level of circ_0000745 (SPECC1) and hsa-miR-335-5p was evaluated using qRT-PCR technique. Also, the relationship between the expression of these RNAs and the clinical characteristics of the patients was investigated.

Results: The results showed that the expression of circ_0000745 (SPECC1) was significantly increased in cancer tissues, while hsa-miR-335-5p was significantly decreased in tumor tissues. These results indicate the possible role of these two molecules in regulating the processes of cell proliferation and migration in breast cancer.

Conclusion: Increased expression of circ_0000745 (SPECC1) and decreased expression of hsa-miR-335-5p can be proposed as a new biomarker pattern for breast cancer diagnosis and prognosis. These findings suggest that the circRNA-miRNA axis may be a potential therapeutic target in the treatment of breast cancer and needs further research.

Keywords: breast cancer Circular RNA microRNA Gene expression Non-coding RNA (ncRNA)

49.

Exosomes derived from stem cells in cancer treatment Review article (Review)

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Introduction: Stem cell-derived exosomes have emerged as a promising approach in cancer therapy, offering a unique combination of targeted delivery and therapeutic potential. This review explores the latest advancements in utilizing exosomes from various stem cell sources for cancer treatment. Mesenchymal stem cells (MSCs) have been the primary focus, with their exosomes demonstrating remarkable anti-tumor properties. Recent studies have shown that MSC-derived exosomes can inhibit tumor growth, reduce metastasis, and enhance drug sensitivity in multiple cancer types, including breast, lung, and colorectal cancers. The mechanisms underlying these effects involve the transfer of specific miRNAs, proteins, and lipids that modulate vital oncogenic pathways. Importantly, stem cell-derived exosomes exhibit natural tumor-homing abilities, allowing for targeted delivery of therapeutic cargo. Research has successfully loaded these exosomes with chemotherapeutic drugs, siRNAs, and CRISPR-Cas9 components, enhancing their therapeutic efficacy while reducing systemic toxicity. Stem cell-derived exosomes represent a versatile and potent tool in cancer therapy, offering new possibilities for targeted treatment and overcoming the limitations of conventional approaches. As research progresses, these nanovesicles may play a pivotal role in the future of personalized cancer medicine.

Methods: Stem cell-derived exosomes (SC-expos) are emerging as a promising avenue for cancer therapy. Scientists are actively investigating their potential using a multi-pronged approach. Researchers first need to isolate SC exosomes from stem cells. Several techniques exist, each with strengths and weaknesses. Once isolated, scientists use electron microscopy, protein analysis, and other methods to confirm the identity and properties of the exosomes. In the lab, scientists use cancer cell lines and co-culture models to evaluate the anti-tumor effects of SC exosomes. They assess how exosomes influence cancer cell growth, movement, and invasion. Additionally, researchers analyze the cargo carried by SC exosomes to understand their potential mechanisms of action.

Studies in mice with implanted tumors or spontaneous cancers help assess SC-exosome efficacy in a more complex setting. These models allow researchers to evaluate tumor growth, metastasis, and animal survival after exosome treatment. Different methods for delivering SC exosomes, such as intravenous or local delivery, are being explored. Researchers are also carefully evaluating the safety profile of SC-exosome therapy, monitoring for potential side effects and unintended consequences. By employing these rigorous methods, scientists build a solid foundation for future clinical trials. This research holds promise for translating SC-exosome therapy into a safe and effective approach to cancer treatment.

Results: Stem cell-derived exosomes (SC-exosomes) are exciting contenders in the fight against cancer. Research suggests they hold immense therapeutic potential. Scientists are isolating and characterizing SC-exosomes using various techniques, ensuring their identity and purity. Lab studies using cancer cell lines delve into how these exosomes impede tumor growth, spread, and invasion. Additionally, researchers are analyzing the exosomal cargo to understand their precise attack mode. Animal models with implanted or spontaneous cancers provide a more realistic picture of SC-exosome efficacy. These studies assess tumor response and animal survival after exosome treatment. Different delivery methods, like intravenous injection, are being explored to optimize how these exosomes reach cancer cells.

Conclusion: Stem cell-derived exosomes (SC-exosomes) have emerged as a revolutionary frontier in cancer treatment. Their unique properties, including the ability to deliver therapeutic molecules and modulate the tumor microenvironment, offer a powerful weapon against this devastating disease. While research is still in its early stages, pre-clinical studies utilizing sophisticated methods like characterization techniques, cell line models, and animal studies have yielded promising results. These studies unravel the mechanisms by which SC-exosomes combat cancer and pave the way for optimizing delivery methods and ensuring safety. The future of SC-exosome therapy appears bright. Continued research holds the potential to translate this innovative approach into a clinical reality, offering new hope for improved outcomes and effective cancer treatment strategies.

Keywords: Exosomes, Treatment, stem cells, cancer

50.

Exploring Natural Flavonoids as Potential Inhibitors of ABC Transporters in Human Renal Cell Carcinoma (Review)

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Introduction: Renal cell carcinoma (RCC) is a significant global health concern, ranking as the sixth most frequently diagnosed cancer in males and the tenth in females worldwide. The increasing incidence of RCC, with an annual rise of approximately 2%, underscores the urgent need for innovative therapeutic strategies to combat this malignancy. Drug resistance in RCC poses a substantial obstacle to effective treatment, The objective of present study was to determine whether natural flavonoids Hesperetin, Luteolin and Ampelopsin have the potential to target drug resistance mediators, ABCB1 and ABCC1.

Methods: The analysis of ABCB1 and ABCC1 expression in RCC was conducted via GEPIA2 web-tool, which uses RNA sequencing data from the cancer genome atlas. The SMILE codes of natural flavonoids were retrieved from PubChem database, and then subjected to SwissTargetPrediction to predict the most probable protein targets of our bioactive small molecules.

Results: Gene expression analysis revealed significant ($p<0.01$) up-regulation of ABCB1 in RCC patients (286 samples) in comparison with normal tissues (60 samples). Elevated expression of ABCC1 was also detected in RCC samples, although not significant ($p>0.05$). Investigating the probability of Hesperetin to target ABCB1 and ABCC1 was as 0.111 and 0.127, respectively. Regarding Luteolin, probability was as 0.534 and 0.658 for ABCB1 and ABCC1, respectively. In addition, the predicted probability of Ampelopsin to target both ABCB1 and ABCC1 was as 0.109.

Conclusion: According to the current computational analysis, Luteolin has the highest probability to target ABC transporters, and thus, could be considered as a potent small molecule to combat drug resistance in RCC.

Keywords: Renal cell carcinoma, Drug resistance, ABC transporters, Natural flavonoids, Luteolin.

51.

Exploring Single-Cell RNA Sequencing as a New Frontier in Cancer Diagnosis (Review)

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Introduction: Cancer is a complex disease, with each tumor containing a diverse mix of cells. Traditional diagnostic methods, such as bulk RNA sequencing, measure the average gene expression across all cells in a sample, which can mask critical differences between individual cells. These differences, or cellular heterogeneity, can provide crucial insights into tumor behavior, including growth patterns, treatment responses, and the potential for metastasis. Single-cell RNA sequencing (scRNA-seq) is a cutting-edge technology that allows researchers to analyze the gene expression of individual cells within a tumor. This method is revolutionizing cancer diagnosis by revealing the unique characteristics of different cell populations within a tumor, which could lead to more precise and personalized treatment strategies. This review explores the technology of scRNA-seq, its applications in cancer diagnosis, and its potential to transform how we detect and treat cancer.

Methods: To compile this review, we conducted a thorough analysis of recent studies that utilized scRNA-seq for cancer diagnosis. The focus was on understanding the methodology of scRNA-seq, including the various techniques used to isolate and analyze individual cells, such as droplet-based and plate-based methods. We also reviewed the bioinformatics tools used to process scRNA-seq data, which help identify distinct cell types, understand their roles in cancer progression, and track cellular changes over time. The challenges associated with scRNA-seq, such as technical variability and data interpretation, were also discussed.

Results: The application of scRNA-seq in cancer diagnosis has yielded significant findings. Researchers have discovered that tumors consist of multiple subpopulations of cells, each with its own unique gene expression profile. Some of these subpopulations are associated with drug resistance, while others may drive tumor growth or metastasis. scRNA-seq has also been used to identify rare cell types within tumors, such as cancer stem cells, which may be critical targets for new therapies. Additionally, the integration of scRNA-seq data with other types of molecular data has provided a more comprehensive understanding of

tumor biology, leading to the identification of new biomarkers for early detection and treatment.

Conclusion: Single-cell RNA sequencing is emerging as a powerful tool in cancer diagnosis, offering a detailed view of the molecular landscape of tumors at the single-cell level. This technology has the potential to significantly improve the accuracy and precision of cancer diagnostics, leading to more personalized and effective treatment strategies. As scRNA-seq technology continues to advance, it is expected to play an increasingly important role in clinical oncology, ultimately improving outcomes for cancer patients. Future research should focus on overcoming the current limitations of scRNA-seq, such as data complexity and cost, to fully harness its potential in cancer diagnosis.

Keywords: Single-cell RNA sequencing, cancer diagnosis, tumor heterogeneity, personalized medicine, biomarkers

52.

Exploring the Anti-Cancer Potential of Probiotics: EGFR Pathway Modulation in Colorectal Cancer (Review)

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Introduction: The epidermal growth factor receptor (EGFR) pathway plays a crucial role in colorectal cancer (CRC) and can be affected by specific probiotics. The EGFR family consists of four members: EGFR/ErbB1, HER1, HER2/ErbB2/Neu, HER3/ErbB3, and HER4/ErbB4. When ligands bind to these receptors, they dimerize, activating their tyrosine kinase domains, which triggers various cell responses, such as growth and differentiation. In the context of CRC, the overexpression of EGFR and HER2 interferes with this pathway, leading to heightened cell growth, survival, and the potential for metastasis. As a result, both EGFR and HER2 have become important targets for treatment, with cetuximab and trastuzumab being among the available therapies.

Methods: The anticancer effects of potential probiotic groups were examined in LS174T cancer cells compared to IEC-18 normal cells. The groups included: 1. a single strain of Bifidobacterium breve, 2. a single strain of Lactobacillus reuteri, 3. a cocktail of 5 Lactobacillus strains (LC), 4. a cocktail of 5 Bifidobacteria strains (BC), and 5. a cocktail of 10 strains combining Lactobacillus and Bifidobacterium (L+B). Apoptosis rates and expression levels of EGFR, HER-2, and PTGS-2 (COX-2 protein) were measured to evaluate anticancer properties. The BC group, identified as the most effective in vitro, was further tested in mouse models.

Results: BC induced approximately 21% apoptosis in LS174T cells, while only about 3% in IEC-18 cells. BC reduced the expression of EGFR by 4.4 times, HER-2 by 6.7 times, and PTGS-2 by 20 times in LS174T cells. In contrast, BC had minimal impact on gene expression in IEC-18 cells, resulting in only a 1.1-fold decrease, a 1.8-fold increase, and a 1.7-fold decrease in EGFR, HER-2, and PTGS-2 expression, respectively. Western blot analysis corroborated these findings at the protein level. Additionally, BC significantly improved the disease activity index, restored colon length, and prevented the increase in tumor incidence and progression to more advanced stages and grades.

Conclusion: Overall, taking into account the impact on both cancer and normal cell lines, the Bifidobacteria cocktail proves to be the most effective treatment compared to the other bacterial combinations tested in this study. This promising probiotic demonstrates significant “protective” anti-cancer effects similar to the established drugs cetuximab and trastuzumab, capable of downregulating onco-markers such as EGFR, HER-2, and PTGS-2 (COX-2). It notably improves the disease activity index, restores colon length, reduces tumor incidence, and prevents tumors from advancing to more severe stages. In general, this probiotic could be a beneficial nutritional supplement to use alongside cetuximab and trastuzumab for treating and preventing colorectal cancer (CRC). As the findings of this study may vary by strain and cell type, further research on different Bifidobacterial strains and cell types is advisable to gain a deeper understanding of this bacterium’s anti-CRC mechanisms.

Keywords: Colorectal Cancer, EGFR Pathway, Probiotics, HER-2

53.

Exploring the Correlation of Key Breast Cancer Biomarkers with BCL2, GRB7, and BIRC5 Gene Expression: Advancing Personalized Treatment Strategies (Research Paper)

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Introduction: Breast cancer is a heterogeneous disease characterized by a diverse range of molecular alterations. The assessment of key biomarkers such as estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), and Ki67 at the primary stage, using molecular techniques like immunohistochemistry and reverse transcriptase quantitative PCR (RT-qPCR), plays a crucial role in determining intrinsic tumor subtypes. Furthermore, the expression levels of these essential biomarkers in individual patients can enable personalized treatment approaches, mitigate the likelihood of inappropriate therapy, and provide insights into the potential risk of tumor recurrence post-surgery. Certain multigene RT-qPCR assays focused on pretreatment tissue samples evaluate a specific set of hormone receptor genes linked to breast tumor invasion and proliferation, alongside traditional biomarkers. These assays are vital for selecting appropriate therapies and predicting the likelihood of tumor recurrence. Among

these important biomarkers are BCL2, GRB7, and BIRC5 (Survivin), which exhibit a strong correlation with primary biomarkers such as ER, PR, HER2, and Ki67. Investigating BCL2 expression is critical in cases of ER-positive tumors that are resistant to hormone therapy, as it can guide the implementation of supplementary hormonal treatments aimed at reducing tumor size. Additionally, elevated GRB7 expression in HER2-positive tumors is associated with an increased risk of tumor recurrence; hence, GRB7 antagonist peptides in HER2+/GRB7+ cases may enhance survival rates. Furthermore, a high co-expression of Ki67 and BIRC5 is indicative of a greater likelihood of tumor recurrence and metastasis, suggesting that more aggressive treatment strategies may be necessary to extend patient survival. In this study, we aimed to evaluate the correlation between BCL2, GRB7, and BIRC5 biomarkers and major breast cancer biomarkers, with the goal of optimizing personalized treatment strategies for breast cancer patients.

Methods: Firstly, RNA of formalin-fixed paraffin-embedded (FFPE) tumor tissues from 100 patients with infiltrative, primary stage, and untreated breast cancer and 12 normal margin samples were extracted. In addition, immunohistochemistry (IHC) results of key biomarkers for breast tumor tissues were available. After that, RNA-extracted samples were examined by TaqMan probe RT-qPCR for quantification of BCL2, GRB7, and BIRC5 expression. Then, the relative fold change (RFC) of each sample was calculated by the Livak formula. Next, the qualitative expression of biomarkers BCL2, GRB7, and BIRC5, obtained from RT-qPCR testing, was evaluated in relation to the qualitative expression of the four main biomarkers, ER, PR, HER2, and Ki67, obtained from IHC testing, using the Chi-square statistical test. Finally, using the non-parametric Spearman statistical test, the correlation of expression between the three biomarkers BCL2, GRB7, and BIRC5 was examined across the entire study population.

Results: The statistical analysis revealed significant correlation between the expression of BCL2 with ER (p-value = 0.025) and PR (p-value = 0.008). GRB7 was significantly correlated with HER2 (p-value = 0.000), and BIRC5 with Ki67 (p-value = 0.001). There was a significant inverse correlation between the relative expression of BCL2 and BIRC5 (p-value = 0.000). Conversely, there was a significant direct correlation between BCL2 and GRB7 (p-value = 0.000). However, the analysis did not reveal a significant correlation between BIRC5 and GRB7 (p-value = 0.054)

Conclusion: A significant correlation was identified between the expression levels of BCL2 with ER and PR, GRB7 with HER2, and BIRC5 with Ki67. This interrelationship is crucial not

only for guiding treatment decisions tailored to specific breast cancer subtypes but also for offering reliable prognostic insights. Such insights can aid in predicting the duration of tumor recurrence post-treatment, assessing survival probabilities, and evaluating the risk of metastasis. The correlation between BCL2 and GRB7 supports the hypothesis that increased expression of these biomarkers may lead to the inhibition of apoptotic pathways across various breast cancer subtypes. In contrast, the negative correlation observed between BCL2 and BIRC5 indicates that, in advanced stages of the disease, high levels of BCL2 expression may be viewed as a negative prognostic factor. This interplay among the biomarkers highlights the complexity of breast cancer biology and underscores the importance of tailored therapeutic approaches based on biomarker profiles.

Keywords: Breast cancer; Biomarkers; Personalized medicine; BCL2; GRB7; BIRC5

54.

Exploring the Promising Role of Echinococcus granulosus and Nanotechnology in Cancer Immunotherapy: A Prospective Review (Review)

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Introduction: Several approaches to cancer treatment using immunotherapy have been developed to treat cancer in recent decades. It has been shown that immunotherapy stimulates the immune system, which, in turn, identifies and destroys cancer cells. Additionally, nanocoatings can deliver immunostimulating molecules precisely and efficiently to minimize side effects. Research has shown that Echinococcus granulosus (E. granulosus) can modulate and strengthen the body's immune system, offering a possible new way to treat cancer. Some studies have shown parasites combined with nanotechnology and nanocoatings can significantly improve cancer treatment results. However, they require refinement and strengthening to treat patients despite their limited effectiveness and variable responses effectively. This review aims to discuss some of the critical characteristics of E. granulosus and how parasites and nanotechnology are combined to improve cancer treatment outcomes significantly.

Methods: From 2015 to 2024, research data from several databases, such as PubMed, Scopus, Science Direct, and Google Scholar, were collected. The search strategy aimed to download and retrieve published articles on cancer treatment using parasites, especially E. granulosus. Several keywords were used, such as "nanomedicine," "nanocoating," "drug delivery, "nanotechnology," "Echinococcus granulosus," " immunotherapy," and "cancer"

were used. Our comprehensive search identified 10,000 studies. With the development of nanotechnology, several innovative treatments and drug delivery systems have been developed to fight cancer.

Results: Several studies have shown that E. granulosus antigens can activate and stimulate T cells, thereby increasing their proliferation and fight against several cancers, such as colon cancer, lung cancer, breast cancer, melanoma, and hepatic cancer. Echinococcus granulosus antigen B (EgAgB) was one of the markers that stimulate the immune response against cancer by enhancing the production of interleukin-12 and interferon-gamma. An experiment on mice with melanoma indicated that injections of E. granulosus antigens could activate killer T cells, leading to smaller tumors in mice with melanoma. Some studies suggested that these nanocoating can coat this antigen and exhibit better properties. Through the use of nanocoatings, immunostimulating molecules can be delivered precisely and effectively in order to minimize side effects and optimize therapeutic outcomes; as a result of their unique properties, these nanocoatings and their specific structure have become valuable tools for enhancing biological functions and drug delivery. Through nanotechnology, effective molecules can be delivered to the desired parts of the body in a more precise way. So, as a consequence, fewer drugs are needed, and adverse side effects in other areas of the body are reduced, increasing the patient's quality of life and the effectiveness of treatment even though combinations of parasites and nanocoatings can significantly improve cancer treatment results.

Conclusion: Multiple antigens associated with E. granulosus have demonstrated antitumor properties. Despite their capabilities, delivering them effectively and strategically remains the main challenge. Using nanocoatings to deliver parasite antigens improves cancer treatment side effects and effectiveness. Several challenges remain, including immune reactions, nanocoating stability, and production costs. Nanocoating technologies need to be optimized, and the mechanism of parasite antigen action needs to be studied.

Keywords: E. granulosus, Nanocoating, Immunotherapy, Cancer, Nanotechnology

55.

From Discovery to Therapeutic Frontiers: The Multifunctional Role of Exosomes

(Review)

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Introduction: Extracellular vesicles (EVs) are membranous structures enclosed by lipid bilayers that are secreted by various cell types under normal physiological conditions or in response to specific biological signals. These vesicles consist of heterogenous populations differing in size and the subcellular origin of their membranes. The term "exosome" was first introduced in the 1980s., following by discovery that these vesicles are released upon the fusion of multicellular bodies (MVBs) with the plasma membrane during the maturation of reticulocytes.

Methods: Exosomes play crucial roles in a variety of biological processes, including viral infections, immune responses, mammalian development, and reproduction. Notably, their functions can differ based on the originating cell type and biological context; for instance, exosomes from leukocytes containing IFNa can inhibit viral replication, while those released from infected cells may facilitate it. They also present new opportunities for drug delivery, offering advantages over conventional carriers such as liposomes. Key features that enhance their potential include the presence of membrane-anchored proteins that promote endocytosis and effective payload delivery, as well as their bioengineered surfaces, which are less prone to protein corona formation. Certain exosomes can influence immune responses by modulating phagocytosis, as demonstrated by exosomes derived from CD47-overexpressing fibroblasts, which reduce clearance by monocytes and macrophages while enhancing uptake by neoplastic cells. Advances technologies like microfluidics and nanopore sequencing are improving the isolation and characterization of exosomes, enhancing their potential in personalized medicine. By utilizing exosomes-based diagnostics and therapies, researchers aim to deepen the understanding of disease mechanisms and develop targeted treatment strategies that could significantly improve cancer therapy and patient outcomes.

Results: As our understanding of cell-to-cell communication evolves, it is now recognized that EVs, especially exosomes, can transfer diverse molecular cargos_ such as microRNAs, messenger RNAs and proteins_ both locally and to distant target cells. They are implicated in critical processes like angiogenesis, metastasis, and modulation of immune responses, highlighting their significance as both biomarkers and therapeutic agents in cancer.

Conclusion: Extracellular vesicles (EVs), particularly exosomes, are pivotal in mediating intercellular communication and influence a variety of biological processes, including immune modulation, viral response, and cancer progression. Their capacity to encapsulate and transport bioactive molecules makes them valuable as biomarkers and therapeutic agents. Furthermore, the engineering of exosomes for enhanced drug delivery presents innovative opportunities in targeted therapies. Further research should focus on elucidating the specific molecular mechanism of exosome-mediated their utility in regenerative medicine and personalized therapies.

Keywords: Extracellular vesicles (EVs)- Exosomes- Drug delivery- Biomarker

56.

Garlic consumption has a potentially favorable effect against colorectal cancer (CRC) (Review)

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Introduction: Colorectal cancer (CRC) is the most common cancer of the gastrointestinal tract and is one of the most frequently diagnosed malignancies in adults. Colorectal cancer is common, accounting for 15% of all newly diagnosed cancers, and tends to be a disease of the elderly, with the median age of diagnosis between 60 and 80 years of age, slightly younger for rectal cancer. There is also a slight male predilection for rectal cancers, not found in tumors elsewhere in the colon. Garlic (Allium sativum) has been used medicinally for over 5000 years, but in the last 30 years, a considerable body of evidence has sought to link extracts of the vegetable or its active ingredients to physiological processes and to a role in the prevention or management of human disease. Claims have been and are being made for a role of garlic in antibacterial, antiviral, antiinflammatory, and antineoplastic activities. Moreover, some evidence exists that it may prevent colorectal tumor formation, reduce cholesterol, reduce blood pressure (BP), provide anticoagulation, and provide broad antioxidant activity to limit free radical damage. Garlic has been used globally in numerous ways. Some evidence has suggested that garlic consumption can lower CRC risk. The purpose of this review study is to focus on the Garlic is used to prevent colorectal 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 " Colorectal cancer " " Garlic " " Diet " . The search was restricted to studies published in English with accessible full texts. Review articles, duplicates, and non-relevant studies were excluded

Results: Based on the existing evidence, garlic intake could reduce the risk of CRC. The cancer-prevention mechanism of garlic remains unclear. S-allylmercaptocysteine, the

water-soluble derivative of garlic, has been found to display anti-proliferative capacity in numerous cancer cell lines, and it has also shown tumor-inhibiting effects in in vivo conditions. Garlic can enhance the anticancer ability by activating the antioxidant transcription expression of Nrf2 and the downstream gene NQ01. Aged black garlic (ABG) can modify the mRNA expression of neuropeptides and proteins in the case of inflammation. Alternatively, ABG can exert its anticancer function by suppressing the proliferation of cells. Garlic is potentially potent against some types of cancers; importantly, it is a universal anticancer drug that is potent against different cancers; this effect is achieved by suppressing the growth of cancer cells and effectively suppressing the proliferation of infiltrative macrophages within the tumor-like microenvironment. A large amount of preclinical data suggests that garlic has a certain effect on modulating the metabolism of carcinogens, inhibiting the progression of the cell cycle, inducing apoptosis and histone modification, and inhibiting angiogenesis.

Conclusion: 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 " Colorectal cancer " " Garlic " " Diet " . The search was restricted to studies published in English with accessible full texts. Review articles, duplicates, and non-relevant studies were excluded

Keywords: Colorectal cancer, Garlic, Diet

57.

Genetic and Epidemiological Factors in Breast Cancer Incidence Among Women with a Family History (Review)

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Introduction: Breast cancer remains one of the most prevalent cancers among women worldwide. This study aims to investigate the genetic and epidemiological factors contributing to breast cancer in women with a family history of the disease. Specifically, we compare the frequency of breast cancer-related gene mutations (such as BRCA1 and BRCA2) in women with and without a family history of breast cancer. Additionally, we examine environmental and lifestyle factors that may influence breast cancer risk in women with a familial predisposition regarding questioner.

Methods: This study involved a cohort of 500 women diagnosed with breast cancer, divided into two groups: those with a family history of breast cancer (250 women) and those without (250 women). The sample included 0 men and 500 women, with a mean age of 52.3 years. Genetic testing for BRCA1 and BRCA2 mutations was conducted, and data on environmental and lifestyle factors were collected through structured interviews and questionnaires.

Results: Among the women with a family history of breast cancer, 125 (50%) tested positive for BRCA1 mutations, and 75 (30%) tested positive for BRCA2 mutations. In contrast, among the women without a family history, 25 (10%) tested positive for BRCA1 mutations, and 15 (6%) tested positive for BRCA2 mutations. Analysis of environmental and lifestyle factors indicated that women with a family history who engaged in regular

physical activity had a 20% lower incidence of breast cancer, while those with high alcohol consumption had a 15% higher incidence.

Conclusion: The findings suggest a significantly higher prevalence of BRCA1 and BRCA2 mutations in women with a family history of breast cancer compared to those without. Additionally, environmental and lifestyle factors play a crucial role in modulating breast cancer risk among genetically predisposed individuals. These results underscore the importance of genetic screening and lifestyle modifications in managing breast cancer risk in women with a family history of the disease.

Keywords: Breast cancer, BRCA1, BRCA2, family history, genetic mutations, epidemiology, environmental factors,

58.

Genetic Influences on Pregnancy Maintenance and Cancer Risks (Review)

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Introduction: Cancer can develop in conjunction with various conditions and physiological states, such as obesity, aging, and pregnancy. The incidence of cancer during pregnancy is approximately 1 in 1,000 to 2,000 pregnancies, with the most common types being breast cancer, melanoma, cervical cancer, lymphoma, and acute leukemia. Cancer during pregnancy is typically defined as a diagnosis made either during the pregnancy or within one year post-delivery. As the trend of delaying pregnancy continues, the incidence of cancer associated with pregnancy is on the rise. Telomerase activity, which is usually minimal in normal somatic cells, is significantly elevated in 85% of human cancers. The intracellular levels of telomerase are strongly correlated with a cell's proliferative potential. During human pregnancy, telomerase activity peaks in the first trimester and gradually decreases as the placenta matures. Additionally, survivin—a protein known to promote cell proliferation and inhibit apoptosis—is overexpressed in various cancers and is similarly upregulated by trophoblast cells during pregnancy. Also HLA molecules regulate the immune system by presenting peptides that allow immune cells to distinguish between healthy and abnormal cells. While the immune system relies on HLA for recovery, it can also promote immune tolerance, increasing disease susceptibility or supporting fetal survival during pregnancy. Both cancer and pregnancy share mechanisms of immune tolerance, involving irregular peptides and abnormal HLA expression. Early fetal development and tumor growth are similar in their ability to evade immune detection. Understanding these parallels could lead to new treatments for pregnancy complications

and cancer by targeting shared pathways. The purpose of this review is to investigate genetic influences on pregnancy retention and cancer risks.

Methods: Twenty relevant articles investigating the relationship between genetic influences on pregnancy retention and cancer risks were identified through searches of PubMed and Google Scholar databases using predefined keywords. These articles were then selected for review and analysis.

Results: The early development of a fetus in the first trimester shares similarities with the growth of tumor cells. Both entities possess genetic differences from the host, which should trigger recognition by the immune system. However, each employs mechanisms to create a tolerogenic immune environment, allowing for survival. ERAP1 and ERAP2 trim peptides for antigen presentation on HLA class I molecules in the endoplasmic reticulum, a key process for tumor cell-immune system interactions. These proteins are potential anti-cancer targets, enhancing immune responses through T and NK cell-mediated cytotoxicity. Abnormal HLA peptides linked to ERAP2 expression are found in both pregnancy and cancer. ERAP enzymes and HLA class I peptides also contribute to genetic risk for Hodgkin's Lymphoma, with significant interactions observed between HLA-A11 and ERAP1 SNP rs27038, as well as ERAP1 SNP rs26618 and HLA-Cw2. Risk alleles can further influence ERAP expression. Trophoblast cells secrete various immunomodulatory proteins, including soluble HLA-G, which disrupts NK/DC interactions, promotes proinflammatory cytokine release, and induces CD8+ cell apoptosis. Soluble HLA-G is commonly observed in cancers such as leukemia, multiple myeloma, breast and ovarian carcinoma, and lung cancer. Cancer cells also induce monocytes to release HLA-G, further suppressing antitumor immunity. Tumors diagnosed during pregnancy show high levels of RANKL, indicating pregnancy's influence on breast tumor biology. Genomic analysis reveals similar common mutations (e.g., TP53, PIK3CA) between pregnant and non-pregnant breast cancer patients, but pregnant patients display a higher frequency of non-silent mutations, mucin gene mutations, and mismatch repair deficiency signatures. Trophoblast and tumor cells share invasion-related proteins. Heat shock protein 27 (HSP27) is elevated in both, promoting metastasis and inhibiting apoptosis. Matrix metalloproteinases (MMPs) aid in neovascularization and tissue remodeling, while Ras homolog family member A (RhoA) and its signaling pathway regulate migration and proliferation. Galectin-1 contributes to tumor and trophoblast invasion, immune regulation, and angiogenesis.

Conclusion: Current research on the immune effects of pregnancy and cancer remains incomplete, warranting further investigation into how these conditions impact the immune environment. A deeper understanding of these immune interactions in the context of pregnancy disorders and cancer could pave the way for novel therapeutic approaches for both conditions. Identifying key factors in pregnancy maintenance and their association with cancer incidence could pave the way for preventive measures against cancer and the development of personalized, targeted treatments for women.

Keywords: Cancer, Genetics, Fetus, Pregnancy

59.

Genomic Instability and Cancer Stem Cells: Implications for Cancer Progression and Therapeutic Resistance (Review)

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Introduction: Genomic instability, characterized by an increased frequency of mutations, chromosomal aberrations, and DNA damage, is a hallmark of cancer. Cancer stem cells (CSCs), a subpopulation within tumors with self-renewal and differentiation capabilities, have been implicated in tumor initiation, progression, and resistance to conventional therapies. The interplay between genomic instability and CSCs is emerging as a critical factor in driving cancer heterogeneity, metastasis, and treatment failure. This review aims to provide a comprehensive analysis of the role of genomic instability in the maintenance and function of CSCs, highlighting the underlying molecular mechanisms. We will explore how genomic instability contributes to the emergence and evolution of CSCs and discuss the therapeutic challenges posed by this relationship.

Methods: A systematic literature review was conducted, focusing on studies investigating the relationship between genomic instability and CSCs across various cancer types. Key findings were synthesized to identify common pathways and potential therapeutic targets.

Results: Genomic instability in CSCs arises from a variety of genetic and epigenetic alterations that disrupt critical cellular processes, such as DNA repair, cell cycle regulation, and chromosomal segregation. These disruptions not only contribute to the maintenance and survival of CSCs but also endow them with adaptive capabilities that promote tumor progression and therapeutic resistance.Key Findings:Defective DNA Damage Response (DDR) Pathways: CSCs frequently exhibit deficiencies in DNA damage response (DDR) pathways, including homologous recombination (HR) and non-homologous end joining (NHEJ). For instance, mutations in BRCA1/2 genes, which are commonly associated with breast and ovarian cancers, lead to defective HR repair, resulting in the accumulation of DNA double-strand breaks. In response to these deficiencies, CSCs often activate alternative repair mechanisms, such as error-prone NHEJ, which increases genomic instability. This ongoing accumulation of genetic damage

generates a diverse pool of CSCs with varying resistance profiles, enabling the selection of subclones that can survive and proliferate under therapeutic pressures. Such genetic diversity within CSCs is a key factor driving relapse and metastasis in cancer patients.Chromosomal Instability (CIN) and Aneuploidy: Chromosomal instability (CIN), characterized by frequent gains and losses of whole chromosomes or large chromosomal regions, is another hallmark of CSCs. This form of genomic instability is particularly prominent in colorectal cancer, where CSCs have been shown to exhibit high levels of CIN. The resulting aneuploidy, or abnormal number of chromosomes, leads to the dysregulation of oncogenes and tumor suppressor genes, further enhancing tumor heterogeneity. This chromosomal missegregation not only allows CSCs to adapt to changing microenvironments but also enables them to evade immune surveillance. Importantly, the ongoing chromosomal reshuffling in CSCs generates novel karyotypes that can confer resistance to targeted therapies, posing a significant challenge to effective cancer treatment.Epigenetic Modifications: Epigenetic alterations, such as DNA methylation and histone modifications, play a crucial role in regulating gene expression in CSCs. Aberrant methylation of tumor suppressor genes, like CDKN2A, has been observed in glioblastoma stem cells, leading to their silencing and promoting unchecked cell cycle progression. These epigenetic changes can induce genomic instability by altering the expression of key genes involved in DNA repair and chromosome stability. Furthermore, the reversible nature of epigenetic modifications allows CSCs to dynamically respond to therapeutic interventions, switching between different states that confer survival advantages under stress.Telomere Dysfunction: Telomere maintenance is another critical factor contributing to the genomic instability of CSCs. CSCs often display altered telomerase activity, leading to telomere shortening or elongation. In pancreatic cancer, CSCs with critically short telomeres undergo telomere crisis, resulting in chromosomal fusions and breakage-fusion-bridge cycles. These cycles generate extensive genomic rearrangements, creating a population of CSCs with enhanced metastatic potential and resistance to therapy. Conversely, some CSCs upregulate telomerase to maintain telomere length, thereby sustaining their immortality and promoting tumor growth.Microenvironment-Induced Instability: The tumor microenvironment (TME) plays a pivotal role in inducing genomic instability in CSCs. Hypoxia, a common feature of the TME, has been shown to downregulate key DNA repair genes in CSCs, such as RAD51 and MRE11, leading to the accumulation of DNA damage. Additionally, interactions between CSCs and stromal cells can trigger the secretion of reactive oxygen species (ROS), further promoting genomic

instability. This dynamic crosstalk between CSCs and the TME not only enhances the adaptability of CSCs but also drives their evolution towards more aggressive phenotypes.

Conclusion: Genomic instability plays a pivotal role in the biology of CSCs, contributing to their maintenance, evolution, and resistance to treatment. Understanding the molecular mechanisms linking genomic instability and CSCs is crucial for the development of targeted therapies that can effectively eliminate these cells and improve patient outcomes. Future research should focus on identifying novel biomarkers and therapeutic targets within this context to overcome the challenges posed by CSC-driven tumor heterogeneity and resistance. The integration of advanced genomic technologies and epigenetic therapies holds promise in unraveling the complexities of CSCs, offering hope for more effective and lasting cancer treatments.

Keywords: Genomic Instability, Cancer Stem Cells, Therapeutic Resistance, Tumor Heterogeneity, DNA Damage.

60.

HIF targeting in cancer therapy (Review)

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Introduction: Cancer is a heterogeneous disease influenced by intrinsic mutation burden and factors within the tumor microenvironment (TME) that are involved in its initiation, progression, and responses to therapy. None of the current cancer treatment modalities utilized for cancer management are entirely efficacious, and their efficacy is limited by drug resistance, non-specific targeting, tumor heterogeneity, TME factors, and metastasis. Addressing these challenges requires the development of innovative therapeutic strategies capable of overcoming these barriers. Numerous endeavors have been undertaken to enhance treatment efficacy and ameliorate patient outcomes.

Methods: Accumulating evidence suggests that both cellular and acellular components of the TME can influence tumor initiation, growth, invasion, metastasis, and response to therapies. The increasing recognition of the TME's role in cancer progression and therapy resistance has led to a paradigm shift in cancer research and treatment. Rather than solely targeting tumor cells, a broader strategy is being developed, including the indirect targeting of the TME to enhance anti-tumor responses. This shift acknowledges the multifaceted nature of primary and secondary resistance to therapies, which arise not only from tumor intrinsic factors but also from the complex crosstalk between cancer cells and their intermingled TME. As a result, emerging approaches integrate TME-targeted therapies, immunotherapy, and combination treatments, to enhance the therapeutic landscape and hold promise for improving outcomes for cancer patients. While immunotherapy exerts durable and effective responses, only a minority of patients respond at present. Combining various treatment modalities with targeted TME agents has considerable potential to significantly enhance treatment efficacy and improve outcomes for cancer patients.

Results: In this context, several agents and approaches have been developed to target both cellular components, such as chemokines (CCL2/CCR2), and immune checkpoints (PD-1 and CTLA4), and non-cellular components like collagen and metalloproteinase in the extracellular matrix (ECM), as well as hypoxia-induced factor (HIF) and vascular endothelial growth factor (VEGF) within the TME.

Conclusion: Targeting HIF, in particular, has demonstrated remarkable anti-cancer responses in both preclinical and clinical studies. This review explores therapeutic interventions targeting HIF and their impact on anti-cancer responses, with a special emphasis on lung cancer, the leading cause of cancer death, without disregarding valuable insights from other oncological fields.

Keywords: HIF, Therapy, Targeting, Tumor microenvironment (TME)

61.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8847166/ **(Review)**

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2.

Introduction: Although great research has been done to clarify the pathogenesis of colorectal cancer (CRC), it is still the third common cancer worldwide. Pathogenesis of CRC as a heterogeneous disease is correlated with mutations and epigenetic alterations that result in the inactivation of tumor-suppressive and activation of an oncogene. Small non-coding RNAs (sncRNAs), emerging as a key player in regulating the genes and protein expression, with a length less than 200 nucleotide (nt). In this review, we aimed to focus on the role and the biogenesis of PIWI interacting RNA (piRNAs), and tRNA-derived small RNA (tRFs) and PIWI proteins in the initiation, progression, and metastasis of CRC and their molecular mechanisms to understand their function in cancers and to provide better therapeutic strategies for CRC.

Methods: Recently with the help of new sequencing a huge number of snRNAs have been discovered and many of them are indicated as biomarkers and prognostic factors based on their gene regulatory function both in the nucleus and in the cytoplasm. However, only a small number of them are available as therapeutic tools. Previous have uncovered the important roles of sncRNAs in gene regulation and other cellular processes related to initiation, progression of tumors and different response to chemo therapy and radiotherapy treatments. The expression patterns of sncRNAs are very in different tumor tissues compared to the corre sponding normal tissue and some of them have show a close association with tumor stages and metastasis. For examole, piR-5937 and piR 28,876 expression were decreased significantly in serum of patients with colorectal cancer and correlating with clinical stage I, suggesting as promising biomarkers for early CRC detection [50,51]. PIWIL2 expres sion was positively associated with CRC and was related to various clinic-pathologic parameters and a poor prognosis [35]. Therefore small non-coding RNAs can be used as new biological markers for the early detection of CRC due to their stability abundance tissues, nominated as an attractive prognostic and diagnostic biomarker candidate [26,31,32]. However our understanding of this field remains incomplete and their mechanism in cellular signaling pathways and animal models needs

more investigations. New studies have aimed into the employment of ncRNA in lipid nano-particles as new therapeutic strategies for delivery. The application for novel sncRNAs is so rare and there are many new challenges to overcome before their widely applications. The reason might be due to several factors. First, is based on the difficulty of tar geting specific genes due to their short sequence, they might regulate several target genes non-specifically. Second, the optimal system for delivering sncRNAs has not been fully established yet, therefore better understanding about the role of sncRNAs will pave a new ways in their therapeutic application in CRC treatment.

Results: Not applicable Ethics approval and consent to participate Not applicable Consent for publication Not applicable Availability of data and materials Not applicable CRediT authorship contribution statement Mandana AmeliMojarad: Writing – original draft. Melika Ameli Mojarad: Writing – review & editing. Jian Wang: Writing – original draft.

Conclusion: With the development of bioinformatics and sequencing technolo gies, more discoveries have been done on the crucial roles of non-coding RNA (ncRNAs) in cellular biology. piRNAs and tRFS as a novel members of small non-coding RNAs and PIWI proteins found to play different regulatory functions and new strategies have focused on their thera peutics roles in cancer because of their role in the development of human cancers in a tissue-specific manner in both tissue and blood emerging as a highly promising biomarker in different cancers including CRC. However, research on their function and biosynthesis is not fully explored yet and needs more investigation for its potential therapeutic applications and further studies have to be done to uncover sncRNAs roles as important regulators in CRC in development.

Keywords: piRNA tRFs PIWI Colorectal cancer

62.

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 1935, and the incidence of the syndrome is estimated at 15-20% of women in the world of reproductive age, (15-20%) of women in the world of reproductive age (12-45) years. It is the leading cause of infertility. Whether it is primary or secondary in women. About 26% of women with cysts are within primary infertility, 14% of them are within secondary infertility, 30% include a regular menstrual cycle, 50% suffer from infrequent menstruation, and 20% 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-1, 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

63.

Investigating different stages of esophageal cancer differentiation using histochemical technique (Review)

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Introduction: Esophageal Squamous Cell Carcinoma (ESCC) is the seventh most common and lethal malignancy worldwide with a high incidence in Iran. Esophageal cancer has a poor prognosis and low 5-years survival rate. Despite several studies on esophageal cancer, its underlying mechanism remains unclear. This study was conducted in order to investigate histochemistry and its relationship with tumor differentiation in esophageal carcinoma.

Methods: Tissue samples of esophageal carcinoma of 40 patients with different differentiations (well, moderate, poorly and undifferentiated) along with healthy esophageal samples were selected from the pathology department of Imam Reza Hospital (AS) in Mashhad after studying hematoxylin and eosin slides. To ensure the previous diagnosis, 5 micrometer thick sections were prepared and stained with Alcin Blue with PH 1 and 2.5 (to identify sulfated and carboxylated acid glycoproteins) and examined microscopically. The results were analyzed and evaluated by color intensity table (according to Gong method) and Kruskal-Wallis statistical analysis.

Results: The results showed that sulfated and carboxylated acidic mucous compounds are not present in any of the different stages of esophageal squamous cell carcinoma

differentiation, similar to normal tissue, while the reaction of tumor stroma and esophageal mucous glands was positive for the above compounds.

Conclusion: It seems that in the cancerous process, changes in the function of esophageal lining cells that lead to changes in the production of sulfated and carboxylated mucous compounds do not occur.

Keywords: esophageal carcinoma, histochemistry, cell differentiation, Alcin blue

64.

Investigating different stages of esophageal carcinoma differentiation using lectin histochemistry method (Review)

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Introduction: Sugar compounds (Glycoconjugates) of cell surface and cell matrix play an important role in the normal physiology of cells and regulation between cell-cell and cell-matrix actions. The change of cellular glycoconjugates is one of the most important phenomena in the course of neoplastic changes and indicates abnormal biological behaviors of tumoral cells. The terminal sugar of the above compounds shows a special temporal and spatial pattern in different stages of the process of neoplastic differentiation of tissues. Despite the progress of endoscopic and surgical techniques, esophageal cancer, which is the third most common cancer of the digestive tract, is still one of the main causes of cancer-related deaths in the world. Therefore, the aim of this research was to study the changes of some sugar compounds in different stages of differentiation of esophageal carcinoma tissue (SCC) in humans by histochemical lectin method

Methods: Tissue samples of esophageal carcinoma of 40 patients with different differentiations (well, moderate, poorly and undifferentiated) along with healthy esophageal samples were selected from the pathology department of Imam Reza Hospital (AS) in Mashhad after studying hematoxylin and eosin slides. To ensure the previous diagnosis, 5 micrometer thick sections were prepared and stained with by histochemical lectin method with SBA and MAA lectins (conjugated with HRP enzyme) and were examined

microscopically. The results were analyzed and evaluated by Kruskal-Wallis statistical analysis

Results: The results of MAA lectin investigation showed the absence of sugar terminal in normal lining and different stages of differentiation of SCC cells, stroma and esophageal mucous glands in normal and cancerous tissue. But the results of SBA lectin showed that the pattern of reaction in normal and tumoral cells was different in different areas and increased with the decrease in the degree of differentiation except for the undifferentiated stage

Conclusion: According to the research done, it seems that in the cancerous process, changes in the function of the esophageal lining cells that lead to changes in the MAA sugar terminal do not occur, while the difference in the presence of the SBA sugar terminal in tumoral cells probably indicates changes. Glycosylation of cellular proteins is obvious and unusual in the cancerous process of the esophagus lining.

Keywords: esophageal carcinoma, lectin histochemistry, SBA, MAA

65.

Investigating different stages of gastric carcinoma differentiation using lectin histochemistry method (Review)

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Introduction: Cell surface glycoconjugates play an important role in intercellular reactions, cell with extracellular matrix and cell recognition. The changes of these glycoconjugates in cancer cells are related to the change in the adhesion of these cells and the development of aggressive tumor types. Gastric carcinoma is the second most common cancer in Iran and one of the main causes of cancer-related deaths in the world, in which the cells of the gastric glands undergo genetic and morphological changes. In this study, we discussed the changes of some sugar terminals in the stages of tumor differentiation, as well as the quantitative and qualitative changes of mucous compounds in different differentiations of gastric carcinoma cancer.

Methods: Tissue samples of gastric carcinoma of 40 patients with different differentiations (well, moderate, poorly and undifferentiated) along with healthy gastric samples were selected from the pathology department of Imam Reza Hospital (AS) in Mashhad after studying hematoxylin and eosin slides. To ensure the previous diagnosis, 5 micrometer thick sections were prepared and stained with by histochemical lectin method with SBA and MAA lectins (conjugated with HRP enzyme) and were examined microscopically. The results were analyzed and evaluated by Kruskal-Wallis statistical analysis

Results: Changes in the response of stroma and tumor cells compared to healthy tissue in the reaction with SBA lectin were not significant, and the response of healthy and cancerous tissues to MAA lectin was negative.

Conclusion: It seems that sugar terminals attached to SBA and MAA lectins do not play an important and essential role in cell interactions and creating special behaviors resulting from neoplastic changes in gastric glandular cells. It seems that each sugar compound follows a specific release pattern due to its specific role in different stages of differentiation.

Keywords: Gastric carcinoma, lectin histochemistry, SBA, MAA

66.

Investigating the anticancer effect of antibiotics in ITM and microbiome (Review)

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Introduction: The essay investigates the complex relationship between antibiotics, the microbiome, and cancer treatment, highlighting the potential benefits and risks of antibiotic use in oncology. 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 (1). 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 (2). 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 (3). 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 (3). 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 (4). Intratumoral Microbiome and Its Impact on Treatment In addition to the gut microbiome, the essay explores the role of the intratumoral microbiome, which refers to the bacterial communities found within tumors. Although research in this area is still emerging, there is growing evidence that intratumoral bacteria can influence cancer progression and response to treatment. Some bacteria found in tumors can metabolize chemotherapeutic agents, reducing their effectiveness. For instance, intratumoral bacteria have been shown to inactivate gemcitabine, a common chemotherapy drug, thereby leading to drug resistance (5). The presence of intratumoral 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 (6). Thus, understanding the role of intratumoral microbiota offers new opportunities to optimize cancer treatments by potentially targeting these bacteria to improve therapeutic outcomes.

Methods: Research suggests that the 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 35 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 16S 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 (2). 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 (7).

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, microbiome, anticancer, intra-tumoral microbiome

67.

Investigating the effect of jujube (high TPC) and cedar honey (low TPC) on the expression of cyclin D1 gene in MCF-7 breast cancer cell line **(Research Paper)**

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Introduction: Breast cancer is one of the most common cancers in women. Honey is an essential natural ingredient used in traditional medicine to cure a number of disorders. It possesses several antioxidants, anti-inflammatory, antibacterial, anti-cancer, and immune system regulating effects. This work used two distinct types of honey, (honey with high TPC (Total Phenolic Content) (jujube honey) and honey with low TPC (cedar honey)) to evaluate cyclin D1 gene expression in MCF-7 cell line. Cyclin D1 gene is activated in the G1 phase and is involved in tumorigenesis. This study was carried out to investigate the effect of jujube (high TPC) and cedar honey (low TPC) on the expression of cyclin d1 in the MCF-7 breast cancer cell line.

Methods: MCF-7 cell line was cultured at RPMI-1640 supplemented with 10% FBS. After the MTT was determined. 104 cells were seeded into the each well of 96-well plate in RPMI-1640 under 37 °C and 5% CO2. Cells were treated with different concentrations of honey (0, 3, 6.25, 8, 10, 12.5, 15, 20 and 25 %) for 24 hours. Finally, cell mortality was assessed using MTT colorimetric assay. Also, 105 cells were seeded into a 12-well plate and treated with honey (0, 3% and 5%) for 24 hours. Then, all samples have gathered for extraction of RNA and were reverse transcripted to cDNA; after that, analyzing gene expression using the SYBR Green method and Real Time-PCR thermocycler (ABI-USA). The 2-ΔΔct was entered into the SPSS software for one-way ANOVA analysis.

Results: The results of the MTT assay showed that the IC50 of high-TPC honey was in lower concentration of low-TPC honey on MCF-7 cells (5% and 9%, respectively). Real-time PCR results showed a significant decrease in mRNA levels at all concentrations (3%, and 5%) of high TPC honey while there was no significant decrease in the expression of the cyclin D1 gene in Low TPC honey. Data distribution in this process was downward (concentration-dependent manner) and data distribution was normal (P-Value ≤ 0.05 was approved).

Conclusion: Previous researches have shown that honey's cytotoxicity can be attributed to phenolic and flavonoid compounds, as well as their antioxidant capabilities. Honey can cause cytotoxicity by raising caspase 3, caspase 8, caspase 9, and the proapoptotic protein Bax while lowering the anti-apoptotic protein Bcl2. Previous studies have shown that honey reduces ER activity in an ERE-dependent pathway, it may also exert its effect through the SP1 and cAMP-PKA pathways. This claim requires more empirical studies.

Keywords: Honey,cyclin d1 ,breast cancer

68.

Investigating the effect of Sinopharm and AstraZeneca vaccine injection on intra-tumoral microbiome of TNBC mice model (Research Paper)

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Introduction: SARS-CoV-2 virus has a single-stranded, globular RNA. Infection with SARS-CoV-2 virus is mainly associated with fever, dry cough, fatigue, lethargy and loss of appetite[1]. People with cancer were 75% more susceptible to the most severe form of this virus than other people[2,3] (figure1). The most common type of cancer in women is breast cancer, the most metastatic molecular subtype of that is triple negative breast cancer [4]. Recent studies since 2019 have shown that the microbiota can influence the progression of cancer suppression[5].Microbiota refers to a collection of microbes living in the body and microbiome is defined as all the genomes of this microbiota[6]. Our main goal in this study was to investigate the effect of injecting Sinopharm and AstraZeneca vaccines on the amount of intra-tumoral bacteria in a triple-negative breast cancer mouse model. The effect of Sinopharm and AstraZeneca vaccine in increasing anti-tumor properties, i.e. reducing metastasis and tumor size, has been proven [7] (figure 2), and the mechanism of effect of Sinopharm and AstraZeneca vaccines on increasing anti-tumor properties has been investigated in this article

Methods: 4T1 mouse cells (TNBC) was cultured in vitro, and these cells was subsequently used to produce TNBC mice models. The mouse model was injected with Sinopharm vaccines in one dose (S1) and two dose (S2) and AstraZeneca vaccine in one dose (A1) and two dose (A2). After 30 days, tumor samples from all mice were dissected. Total RNA extracted from these tumors, and real-time PCR test was performed to measure the expression of 16s rRNA gene based on realQ Plus 2x Master Mix SYBR Green protocol (figure 3). Data analysis performed according to the obtained Cts and using the formula 2^-

dct. Statistical analysis: Data analysis and graphs were done with the help of Graph pad prism statistical software. The t-test was used to check the difference between the means between the two groups, and p-value less than 0.05 was considered significant.

Results: Real-time PCR results showed that the average relative expression of the 16S rRNA gene of the mouse tumor sample that received the first dose of Sinopharm vaccine (S1 = 0.092), the second dose of Sinopharm vaccine (S2 = 0.0087) and after the injection of the first dose of AstraZeneca vaccine (A1 equal to 0.3) compared to the control sample in which no vaccine was injected, had a decrease in expression, but in the sample that was injected with the second dose of AstraZeneca vaccine (A2 equal to 0.78), no significant difference was observed compared to the control sample (figures 4-6).

Conclusion: Real-time PCR results showed that the injection of Sinopharm and AstraZeneca vaccines led to a decrease in the relative expression of the 16S rRNA gene compared to the control sample, which proves the decrease in the population of bacteria inside the tumor after the injection of the mentioned vaccines. On the other hand, AstraZeneca and Sinopharm vaccines lead to an increase in anti-tumor properties; hence, one of the mechanisms of which can be proposed for the seen anti-cancer effect of the vaccination might be through affecting the intra-tumoral microbiota

Keywords: Triple-negative breast cancer, covid-19 vaccines, Sinopharm vaccine, AstraZeneca vaccine

69.

Investigating the expression changes of PI3k/Akt and miR-181a-5p in Jurket cell line after treatment with Cassiopeia andromeda toxin (Research Paper)

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Introduction: Nowadays, the use of drugs of natural resources is being considered. Cassiopea andromeda is a member of the family of jellyfish called upside-down jellyfish. The anticancer capabilities of Cassiopea andromeda venom have been displayed in several studies. On the other hand, miR-181a-5p acts as an oncomiR or tumor suppressor in various cancer types by affecting multiple hallmarks of tumors. It causes the activation and increase in the expression level of PI3k/Akt pathway genes. Recent studies have reported that PI3k/Akt signaling pathways are frequently altered in human cancer. This study investigated the effect of Cassiopeia andromeda venom on the expression of miR-181a-5p, PI3k, and Akt genes in the Jurkat leukemic T-cell line.

Methods: Jurkat T-cells were exposed with IC50 concentrations of Cassiopeia andromeda venom next to peripheral blood lymphocyte cells (PBMC) as a control in RPMI1640 medium, RNA was extracted and cDNA synthesis was performed, then the relative expression level was measured by qPCR method.

Results: The expression level of miR-181a-5p decreased in both Jurkat T-cells and PBMC, while Expression levels of PI3k and Akt differed between examined groups, the expression of PI3k, and Akt genes increased in PBMC but decreased in Jurkat T-cells.

Conclusion: Our results showed that Cassiopeia andromeda toxin decreased the simultaneous expression of PI3k/Akt and miR-181a-5p genes in Jurkat T-cells, so inhibiting PI3k/Akt activity may be a valuable approach to treat cancer and it is possible that it can be used as a drug in cancer treatment.

Keywords: Cassiopeia andromeda, miR-181a-5p, PI3k/Akt, Jurkat cell line

70.

Investigation anticancer role of very low frequency electromagnetic field and doxorubicin treatment on cell line MDA-MB-231 to changes in the expression of genes CD44+/-CD24, CD133,CD326,ALDH **(Research Paper)**

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Introduction: Breast cancer, particularly TNBC, is aggressive with a poor prognosis due to its resistance to conventional therapies. The MDA-MB-231 cell line serves as a model for this aggressive subtype, where despite the efficacy of doxorubicin (DOX), the development of drug resistance remains a significant challenge. According to the clonal evolution theory, cancer originates from a single mutated cell, which accumulates genetic mutations over time, enabling certain clones to become resistant to therapies like DOX. Additionally, the cancer stem cell (CSC) hypothesis suggests that CSCs, a subpopulation within tumors, drive tumor progression, metastasis, and recurrence, contributing to resistance. Emerging research indicates that ELF-EMF could enhance chemotherapy effectiveness by targeting CSCs population. This study evaluates the combined effects of ELF-EMF and DOX on MDA-MB-231 cells, focusing on key CSC markers (CD44, CD133, CD326, ALDH) to reduce CSCs population and improve treatment outcomes.

Methods: MDA-MB-231 cells were exposed to ELF-EMF (1 Hz, 100 mT) for 2 hours daily over 5 days. Four treatment groups were established: Sham, ELF, DOX, and ELF+DOX. Cell viability and apoptosis were assessed using MTT and Annexin V/PI assay and CD44+/-CD24. Gene expression changes in CD44, CD133, CD326, and ALDH were analyzed using real-time PCR.

Results: Cell viability and apoptosis were assessed using MTT and Annexin V/PI assay and CD44+/-CD24. Gene expression changes in CD44, CD133, CD326, and ALDH were analyzed using real-time PCR. DOX Group: Moderate reduction in CD44+/-CD24

expression. ELF+DOX Group: Significant reduction, highlighting the combined effect in targeting CSCs. DOX Group: Moderate reduction in CD44+/-CD24 expression. ELF+DOX Group: Significant reduction, highlighting the combined effect in targeting CSCs.

Conclusion: The combination of ELF-EMF and DOX showed potential in reducing the expression of CSC-related genes, particularly CD326, and increased apoptosis in MDA-MB-231 cells. These findings suggest that ELF-EMF could serve as an adjunct to conventional chemotherapy, improving treatment outcomes for TNBC by targeting CSCs population.

Keywords: MDA-MB-231,Breast cancer, ELF-EMF, Doxorubicin, Cancer Stem cells

71.

Investigation of drug delivery of Aflibercept to retinoblastoma cancer cells by MiRGD peptide and Graphene Quantum Dots nano-carrier (Research Paper)

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Introduction: Retinoblastoma is known as the most common intraocular malignant tumor in childhood and approximately 8000 new cases are diagnosed worldwide each year. Mutations in the retinoblastoma gene (RB1), located on chromosome 13q14.2, are responsible for this condition. Although Retinoblastoma is known as a curable cancer, untreated one can be fatal and even with treatment, advanced tumors can limit globe salvage. Chemotherapy is an effective treatment for retinoblastoma but many affected children suffer from undesirable side effects. Therefore, there is a necessity for designing a new drug delivery system. A novel nano-carrier with MiRGD peptides and graphene quantum dots (GQDs) has been developed due to the structural differences between cancerous and normal cells. The iRGD motif penetrates cancerous tissues, while the other motifs deliver both hydrophobic and hydrophilic drugs. The non-toxic GQDs facilitate biological tracking and enhance drug binding to peptides. Consequently, this nano-carrier seems to be suitable for delivering Aflibercept, an anti-VEGF drug, to prevent the activation of angiogenesis. Therefore, these novel nanoparticles could potentially play a significant role in reducing tumor size and invasion.

Methods: To purify the MiRGD peptide, Ecoli BL21 was cultured in a 2XYT medium containing kanamycin antibiotic and IPTG as inducer of protein expression. After using a lysis buffer, the MiRGD peptide was purified by Ni-NTA column chromatography under a urea-imidazole gradient. Then the impurities were removed by washing buffers. The purity of the peptide was examined by SDS-PAGE. 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 examined.

Results: The MiRGD peptide band was observed on a 15% Tris-glycine SDS-PAGE gel, with a molecular weight of approximately 9.6 kD. The UV/Vis spectrum of the MiRGD peptide, investigated at various wavelengths, demonstrated a peak at 207 nm. Likewise, the UV/Vis spectrum of the synthesized graphene quantum dots (GQDs) showed two peaks at 199 nm and 338 nm. Similarly, Aflibercept's UV/Vis absorption spectroscopy displayed a peak at 216.5 nm, while the fluorescence spectrum of the drug illustrated a peak at 420 nm. The fluorescence spectrum of the synthesized GQDs was analyzed at different excitation wavelengths, with the maximum emission observed at 440 nm. The ζ-potential measurements of GQDs, Aflibercept, and the peptide were found to be −23.3 mV, +4.70 mV, and +6.57 mV, respectively. FTIR spectroscopy of GQDs demonstrated an absorption band in the range of 3000-3500 cm−1, indicating the presence of amino and hydroxyl groups on the surface of the GQDs. The bands at 1700 cm−1 correspond to the vibrational absorption of C=O, and the band at 1400 cm−1 is related to the bending vibrations of C=C. The UV/Vis spectrum of the complexes revealed peaks between 200 and 220 nm. The ζ-potential of the complexes ranged from 10 to 12 mV.

Conclusion: In conclusion, finding a new targeted drug delivery system for the treatment of retinoblastoma is essential. A novel nano-carrier containing MiRGD peptide and graphene quantum dots (GQDs) has been developed for this purpose. The goal of this study is to

investigate the effect of this nano-carrier on retinoblastoma. So far, the MiRGD peptide and GQDs have been prepared and characterized. Aflibercept has also been characterized as an anti-angiogenesis drug which is going to be used in the complex. The assembly and characterization of the complex, which includes MiRGD peptide, 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, Drug Delivery, Aflibercept, Peptide, GQDs

72.

Investigation of the relationship between circ_0000745 (SPECC1) expression and has-miR-145-5p in tissue samples of patients with breast adenocarcinoma (Research Paper)

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Introduction: Breast cancer is one of the most common cancers among women, and early diagnosis plays a key role in improving the prognosis of the disease. In recent years, non-coding RNAs, including circRNAs and miRNAs, have emerged as potential biomarkers for cancer diagnosis and prognosis. circ_0000745 (SPECC1) and hsa-miR-145-5p are two important molecules involved in the regulation of genes related to breast cancer, which may play critical roles in cell proliferation and cancer progression.

Methods: In this study, tumor tissue and normal tissue samples were collected from patients with breast adenocarcinoma. Total RNA was extracted from tissue samples, and cDNA synthesis was subsequently performed. The expression levels of circ_0000745 and hsa-miR-145-5p were then assessed using qRT-PCR. Additionally, the relationship between the expression of these RNAs and the clinical characteristics of the patients was examined.

Results: The findings revealed a significant upregulation of circ_0000745 in cancerous tissues compared to normal tissues. In contrast, hsa-miR-145-5p was significantly downregulated in tumor tissues. These results suggest a potential role for these two molecules in regulating processes related to cell proliferation and migration in breast cancer.

Conclusion: The upregulation of circ_0000745 and downregulation of hsa-miR-145-5p may serve as a novel biomarker pattern for the diagnosis and prognosis of breast cancer. These findings indicate that the circRNA-miRNA axis could be a potential therapeutic target in breast cancer treatment, warranting further investigation.

Keywords: Breast cancer Circular RNA MicroRNA Gene expression Non-coding RNA

73.

Investigation of the Relationship Between Genetic and Environmental Factors Along with Epstein-Barr Virus (EBV) Infection in the Development of Nasopharyngeal Carcinoma from a Cancer Genetics Perspective **(Review)**

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Introduction: Genetic changes can lead to differences in gene function, affecting susceptibility to diseases such as cancer. Nasopharyngeal carcinoma (NPC) is one of the most common malignancies of the head and neck. Significant information has been gathered regarding the role of genetic factors in the pathogenesis of cancer, particularly in relation to the interaction between Epstein-Barr virus (EBV) infection and environmental factors. Complex interactions among various elements, including viral infections, individual genetic predisposition, environmental influences, and dietary factors, contribute to the pathogenesis of this malignancy. NPC is notably prevalent in regions such as: Southern China, North Africa, and Alaska. The pathogenesis of NPC is multifactorial due to interactions between host genetics, viral infections, and environmental factors, and it is closely associated with genetic and epigenetic changes. Despite promising outcomes for early-stage NPC patients, most cases present as locally advanced disease. Currently, access to early diagnosis and treatment for NPC is limited, and the precise molecular pathways leading to NPC development remain unclear. Therefore, research into potential biomarkers for facilitating early identification and improving prognosis for NPC patients is essential. There is limited documented information on targeted molecular therapies for NPC using genetic and epigenetic markers; thus, further studies are needed to fully integrate these biomarkers into NPC management. The aim of this study is to determine the relationship between genetic and environmental factors along with EBV infection in the development of nasopharyngeal carcinoma from a cancer genetics perspective.

Methods: This research is a narrative review study aimed at collecting and presenting information on the relationship between environmental and genetic factors in nasopharyngeal carcinoma (NPC), focusing on articles published up to 2024. The study utilized keyword searches such as "Genetic and Environmental Factors," "EBV,"

"Nasopharyngeal Carcinoma," and "Cancer Genetics" in reputable databases like Science Direct, Scopus, PubMed, and Web of Science.

Results: Previous studies have shown that several factors are associated with the development of nasopharyngeal carcinoma (NPC). These factors include nutritional influences, infection with the oncogenic Epstein-Barr virus (EBV), and genetic predisposition. NPC is linked to genetic changes in specific chromosomal regions and genes, the presence of specific polymorphisms associated with cancer, and familial clustering. Notably, recent studies have confirmed that epigenetic changes, such as: promoter hyper methylation, are also critical factors related to NPC. A multi-step progression model for NPC has been proposed, highlighting the essential roles of genetic and epigenetic factors in its pathogenesis. Case-control studies have indicated a relationship between genetic polymorphisms and the risk of developing NPC. Although most of these studies have not been replicated in other locations, several genes—including human leukocyte antigen (HLA) genes like DRB1, DQA1, DQB1, and DPB1; the DNA repair gene RAD51L1; cell cycle control genes MDM2 and TP53; as well as the cell adhesion/migration gene MMP2—have been consistently associated with NPC occurrence. Additionally, genetic polymorphisms related to cytokine genes are also linked to NPC development; however, further studies are needed to validate their contributions to NPC pathogenesis. Biological signal analysis, understanding these signals, and data management are components of bioinformatics. Recent advancements in artificial intelligence and machine learning algorithms suggest that bioinformatics will play an increasingly significant role in cancer biology. Recent studies have shown that NPC is associated with a low mutation rate, significant epigenetic changes, and disturbances in microRNAs and long non-coding RNAs. Various factors, including host genetics, viral infections, and environmental influences, contribute to NPC tumorigenesis, all playing essential roles in modulating epigenetic changes. Abnormal epigenetic alterations, particularly DNA methylation, have been reported in NPC.

Conclusion: Bioinformatics tools are being developed to address complex issues such as predicting clinical outcomes and identifying factors that influence changes in the tumor-immune environment. With advancements in gene chip technologies and RNA sequencing, these tools play a significant role in screening potential biomarkers for diseases, especially cancers. Additionally, these techniques are applied in rapid diagnosis and targeted molecular therapies for various types of cancer. Bioinformatics is recognized as a key

science in the diagnosis, treatment, prevention, and control of diseases, utilizing diverse information and techniques to enhance clinical processes.

Keywords: Genetic and Environmental Factors, EBV, Nasopharyngeal Carcinoma, Cancer Genetics

74.

Investigation of the Relationship Between Neurocognitive Function Following Chemotherapy and Anti-Angiogenic Agents Combined with Chemotherapy and Radiotherapy for Nasopharyngeal Carcinoma (Review)

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Introduction: Cancer is a complex disease and the second leading cause of death in the United States. According to the American Cancer Society (ACS) report in 2020, more than 1.8 million new cancer cases are expected to be identified in this country, and approximately 606,520 individuals are anticipated to lose their lives due to this disease. In recent decades, new cancer drugs designed as small molecules have demonstrated greater efficacy compared to older drugs. Nasopharyngeal carcinoma (NPC) is a cancer associated with Epstein-Barr virus (EBV) and is prevalent in southern China, Southeast Asia, and North Africa. Biomarkers related to the progression and metastasis of nasopharyngeal carcinoma (NPC) enable researchers to better understand the disease. These biomarkers can be divided into two groups: predictive markers that allow for the assessment of the risk of clinical outcomes such as recurrence, metastasis, and disease progression; and diagnostic markers that identify whether an individual has a specific disease. Thus, biomarkers can enhance early detection and predictive methods. Definitive radiotherapy (RT), with or without chemotherapy, is recognized as the standard treatment for patients with head and neck cancers (HNC). Epidemiological changes, diagnostic advancements, and novel therapeutic approaches have led to increased life expectancy. Given the greater focus on survival, achieving a balance between tumor control and toxicity prevention has become a key challenge. Neurocognitive impairments can be one of the side effects of common cancer treatments, including radiotherapy when doses are delivered to brain tissue and chemotherapy. Neurocognitive function is a performance outcome, and even minor impairments can negatively impact quality of life (QOL) and daily functioning. The aim of this study is to determine the relationship between neurocognitive function following chemotherapy with anti-angiogenic agents combined with chemotherapy and radiotherapy for nasopharyngeal carcinoma.

Methods: This research serves as a narrative review study of secondary studies aimed at gathering and presenting information regarding the relationship between neurocognitive function following chemotherapy and anti-angiogenic agents in conjunction with nasopharyngeal carcinoma. The articles reviewed in this context have been published up to 2024. This study was conducted by searching for keywords such as Neurocognitive Function, Chemotherapy, Anti-Angiogenic Agents, Radiotherapy, and Nasopharyngeal Carcinoma in reputable databases such as Science Direct, Scopus, PubMed, and Web of Science.

Results: In the past three decades, there have been significant advancements in understanding the molecular biology and treatment of nasopharyngeal carcinoma (NPC). Biomarkers are key to preventing the progression, recurrence, and metastasis of NPC, and they are also essential for the development of effective therapies. With the aid of high-throughput "omics" technologies, knowledge regarding the etiology, tumorigenesis, and progression of NPC has progressed rapidly, enabling researchers to identify potential molecular biomarkers. Various types of potential molecular biomarkers for NPC have been identified, including DNA (genomic), mRNA (transcriptomic), protein (proteomic), and metabolite (metabolomic) markers. When radiotherapy is employed in the treatment of head and neck cancers, the brain typically receives incidental doses of radiation that can lead to neurocognitive changes and subsequent effects on quality of life. This issue has not been extensively investigated to date. Most studies have shown that neurocognitive outcomes are inferior compared to control groups at 12 months and beyond following radiotherapy. The neurocognitive domains most affected include memory and language, which appear to be associated with radiation doses received by the hippocampus, temporal lobe, and cerebellum. Magnetic Resonance Imaging (MRI) may be valuable in detecting early microstructural and functional changes that could indicate future neurocognitive alterations. In studies assessing quality of life, the presence of neurocognitive impairments was linked to poorer quality of life outcomes. (Chemo)radiotherapy for head and neck cancer seems to be associated with a risk of long-term neurocognitive impairment. However, only a limited number of studies have been identified, and there exists considerable variability in methodology, which restricts the ability to draw definitive conclusions. There is a need for large-scale, high-quality prospective studies on head and neck cancer that utilize standardized, sensitive, and reliable neurocognitive tests.

Conclusion: The use of anti-angiogenesis agents alongside chemoradiotherapy, compared to chemoradiotherapy alone, can provide greater benefits in terms of short-term efficacy. This combination is particularly effective in improving both the complete response rate and the objective response rate, while the overall adverse effects remain acceptable.

Keywords: Neurocognitive Function, Chemotherapy, Anti-Angiogenic Agents, Radiotherapy, and Nasopharyngeal Carc

75.

Investigation on the effects of silver nanoparticles-attached to intracellular penetrating peptides on gene expression of NLRP3 in human monocyte-like macrophages (Research Paper)

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Introduction: Silver nanoparticles (AgNPs) are among the most widespread materials used in various fields, including therapeutic applications and everyday products such as those in the food industry. Considering their inevitable exposure it is then essential to conduct a comprehensive evaluation of the potential effects of AgNps on immune cells. Inflammation is initiated by the activation of different cells like monocytes and macrophages, which stimulate the inflammatory cytokines. Regulating the overexpression of inflammatory genes, such as NLRP3, could mitigate the potential negative impacts of the innate immune response. Studies show that chemically synthesized AgNPs are highly cytotoxic with low specificity. However, biosynthesis, particularly using plants like barberry, can significantly reduce its toxicity and the presence of unwanted compounds. Since the cell membrane serves as a barrier, nanocarriers should be designed to enhance the stability and permeability of drugs. In this study, conjugation of AgNPs with a cell-penetrating peptide (MiRGD) was performed to facilitate transportation and stimulate apoptosis in monocyte-like macrophages. Due to the positive charge of the peptide, the nanocarrier can specifically permeate into the target cell. Moreover, AgNPs have the

potential to revolutionize cancer treatment by inducing apoptosis in cancer cells. Their functionalization with cell penetrates peptides (MiRGD) could increase the specificity towards cancer cells, with limited damage to healthy non-target tissues. With the development of drug delivery and inducing selective destruction of tumor cells, AgNPs might have significant potential in cancer therapies in the near future, especially in enhancing chemotherapy efficiency and reducing side effects.

Methods: Blood samples were collected from healthy young individuals using tubes containing EDTA as anticoagulant. Blood mononuclear cells (PBMCs) were isolated using Ficoll and concentration gradient using a centrifuge at 2500 rpm for 20-25 minutes. The isolated mononuclear cells were suspended in an enriched RPMI medium. After harvesting monocytes from PBMCs, the monocytes attached to the bottom of the flask were subsequently separated. The monocyte-like macrophages were treated with different doses of green and green-synthesized AgNp conjugated with peptide and peptide alone. Cell viability was then evaluated by flow cytometry, staining with propidium iodide (PI), and annexin V labeled with fluorescein isothiocyanate (FITC). The purification of the Nano peptide and functionalization of the Nano-Ag coating with the Nano peptide were done based on the protocol provided faculty of Biological Science University of Tarbiat Modares . Finally, gene expression analysis was performed using real-time PCR.

Results: Viability of monocyte-like macrophage cells treated with green AgNP conjugated with peptide tested with the minimum concentration (0.2µg/mL) for 24h illustrates a decline in apoptosis rate, suggesting the specificity of penetrating of nanocarrier into the cells. Lastly, Relative expression of the NLRP3 gene compared to control on human monocyte-macrophage was calculated based on the fold change method and results suggest that the samples treated with Ag peptide show a significant downregulation in NLRP3 gene, in comparison to AgNP treated cells.

Conclusion: This study aims to provide insights into the significant down regulatory effects of green AgNP on anti-inflammatory and anti-apoptotic pathways. Moreover, the specificity of the nanocarrier's cellular penetration can be enhanced through the use of cell-penetrating peptides, which facilitate targeted delivery and contribute to a reduction in cytotoxicity in non-target cells. In summary, the findings of this study can provide a promising approach for the downregulation in inflammatory diseases.

Keywords: green synthesis, peptide, inflammatory response, silver nanoparticle

76.

LncRNA NEAT1 remodels chromatin to promote the 5-Fu resistance by maintaining colorectal cancer stemness (Review)

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1.
2.

Introduction: Colorectal cancer (CRC) is the third leading cause of all-cancer-related death1. The treatment of CRC is mainly through surgery and drugs. 5-fluorouracil (5-Fu) is an effective drug for colorectal cancer2. So studying the mechanism of 5-Fu resistance may be a key factor in improving colorectal cancer survival3. At present, more and more studies showed that cancer stem cells have the ability of self-renewal and partial differentiation4–7. They have some mechanisms to escape from damages caused by drugs, such as high drug transporter expression, efficient DNA repair, quiescence, and apoptotic block8. Thus, cancer stem cells are regarded as a main contributor of chemoresistance9–12. LncRNAs are defined as RNA polymerase II transcripts longer than 200 nucleotides in length with limited coding potential13,14. NEAT1 is an essential component of nuclear paraspeckles and can participate in transcriptional regulation15. Studies had shown that lncRNA NEAT1 acted as a scaffold and recruited the chromosome modification enzyme EZH2 to silence target-specific genes, thereby promoting β-catenin nuclear transport and promoting the occurrence of gliomas16. In triple-negative breast cancer, lncRNA NEAT1 confered the oncogenic role through modulating chemoresistance and cancer stemness17. However, the biological role of NEAT1 on CRC cell 5-Fu chemoresistance remains poorly understood. In present study, we want to investigate the role of NEAT1 in CRC chemoresistance and reveal the way NEAT1 affect the resistance to 5-Fu.

Methods: All the human CRC tissues and paratumor normal tissues were collected in the Department of Colorectal Cancer Surgery, the Second Affiliated Hospital of Harbin Medical University. After surgical debulking, patients have undergone XELOX or mFOLFOX6 regimen therapy. Informed consent was obtained from the patients before sample collection in accordance with institutional guidelines. Recurrence was monitored by imaging examination systems (Chest X-ray and CT), gastrointestinal endoscopy with biopsy, and telephone follow-up. In order to obtain two independent cohorts for mutual verification,

cohort A was collected from January 2012 to September 2012 and cohort B was collected from January 2014 to September 2014. The expression of NEAT1 was evaluated in cohort A and cohort B. The prognostic significance of NEAT1 was evaluated in cohort B. Patients were pathologically and clinically diagnosed with colorectal cancer. This study was carried out under the permission of the Clinical Research Ethics Committees of the Second Affiliated Hospital of Harbin Medical University.

Results: To study the role of NEAT1 in CRC, we first detected its expression in CRC tissues and normal tissues in The Cancer Genome Atlas (TCGA) datasets. TCGA shown elevated NEAT1 levels in human CRC tissue relatived to normal tissue (Fig. (Fig.1A).1A). Next, Kaplan–Meier analysis was used to determine whether NEAT1 expression levels in the CRC tissues were associated with clinical patient outcome. Survival analysis of the TCGA cohort revealed that a higher NEAT1 level was associated with poor disease-free survival (DFS) in CRC patients (Fig. (Fig.1B).1B). Next, we measured NEAT1 levels in 66 pairs of normal tissues and tumor tissues of CRC patients without recurrence, and 16 pairs of normal tissues and tumor tissues of CRC patients with recurrence by qRT-PCR. As shown in Fig. Fig.1C,1C, the expression level of NEAT1 in tumor tissues of most patients is significantly higher than that of normal tissues. And we can see that the expression level of NEAT1 in tumor tissues of patients with recurrence is higher than that of patients without recurrence (Fig. (Fig.1D),1D), whose clinical characteristics were shown in Supplemental Table 1. Next, we used another cohort B (55 pairs of normal tissues and tumor tissues of CRC patients without recurrence, and 27 pairs of normal tissues and tumor tissues of CRC patients with recurrence) of our center to validate the results of cohort A, and the results were consistent (Supplemental Table 2 and Fig. Fig.1E).1E). Then we evaluated the prognostic significance of NEAT1 in cohort B. Patients in the NEAT1-high-expression group showed a shorter recurrent free survival (RFS) than those in the NEAT1-low-expression group (P = 0.01, Fig. Fig.1F).1F). This suggests that NEAT1 may play a role in CRC recurrence.

Conclusion: Colorectal cancer is the leading cause of cancer deaths worldwide, and 5-Fu based chemotherapy has been widely used to treat different types of cancer including CRC. Understanding the mechanisms of resistance in CRC is imperative to improve the survival. In recent years, studies have shown that NEAT1 was associated with resistance to chemotherapy in hepatocellular carcinoma24, endometrial cancer25 and others. Moreover, the effects of NEAT1 and cancer stem cells in breast cancer have also been

reported17. In this study, we observed that NEAT1 was highly expressed in colorectal cancer tissues from patients with recurrence and was also associated with poor recurrence-free survival. Thus, NEAT1 may be related to patients' drug resistance and recurrence. To elucidate the underlying mechanism, further research revealed that downregulation of NEAT1 significantly inhibited the growth of CRC cell lines and reduced the sensitivity to 5-Fu. At present, more and more studies have shown that cancer stem cells can evade the damage of chemotherapy drugs through some mechanisms8. We speculated that NEAT1 may mediate drug resistance by regulating the stemness of CRC. Further research showed that the activity of ALDH1 and CD133 was decreased by downregulating the expression of NEAT1 in colorectal cancer cell lines. Next, we found that downregulation of NEAT1 decreased the expression of stemness factors, such as SOX2, NANOG, c-Myc, and OCT4. In summary, knockdown of NEAT1 could reduce the expression of stemness factors to inhibit CSC properties of colorectal cancer cells. NEAT1 is a component of nuclear paraspeckle, so we speculated that knockdown of NEAT1 may affect chromatin remodeling. Studies have shown that NEAT1 can be used as a scaffold to participate in the chromatin remodeling of glioma cells, promote the increase of the trimethylation level of the promoter of downstream genes, and then promote its expression16. In our study, we found that NEAT1 increased H3K27ac by affecting chromatin remodeling and led to an increase in acetylation levels of ALDH1 and c-Myc promoter regions, which increased their expression and thus enhanced the stemness of colorectal cancer cells. In summary, our work demonstrated that NEAT1 was associated with 5-Fu resistance in CRC patients, suggesting that NEAT1 may affect 5-Fu resistance in colon cancer cells by affecting cancer cell stem. In addition to its biological importance, our work may be related to the clinical management of CRC patients. Our data raise an important clinical question: Are conventional chemotherapy regimens, including 5-Fu, suitable for CRC patients with high NEAT1 expression? Alternatively, we suggest that traditional chemotherapy be combined with drugs that target tumor stem cells to treat CRC patients with high levels of NEAT1.

Keywords: Cancer stem cells, Oncogenes, Cancer stem cells, Oncogenes

77.

Machine Learning in Combination with Nanobiosensors for Cancer Diagnosis (Review)

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Introduction: In recent years, the use of advanced technologies such as machine learning (ML) and nanobiosensors in early cancer detection has attracted much attention. The purpose of this research is to investigate how to combine machine learning with nanobiosensors to improve the accuracy and speed of cancer diagnosis. Nanobiosensors with a high ability to detect biomolecules related to cancer can provide highly accurate data that are processed and interpreted using machine learning algorithms. This combination increases diagnostic sensitivity and specificity and has been introduced as a promising method for the rapid and non-invasive diagnosis of cancers. The purpose of this article is to evaluate the performance of this technology and suggest ways to improve it in the future.

Methods: In this study, data related to scientific articles published between 2018 and 2023 were extracted from reliable databases such as PubMed, Scopus, and Google Scholar. Keywords used included "machine learning," "nanobiosensors," "cancer diagnosis," "artificial intelligence in medicine," and "nanostructured biomarkers". The criteria for selecting articles were to be relevant to the topic and provide detailed data on the application of nanobiosensors and machine learning in cancer diagnosis.

Results: The results of the analysis show that the use of machine learning in combination with nanobiosensors has led to a significant improvement in the accuracy and speed of cancer diagnosis, such as colon cancer, lung cancer, breast cancer, melanoma, and hepatic cancer. For example, in one study, the use of nanobiosensors based on gold nanoparticles with neural network algorithms was able to detect breast cancer with 95% accuracy. Also, in another study that examined lung cancer, the use of graphene nanobiosensors along with Random Forest algorithms led to an increase in sensitivity up to 92%. This compound is especially useful in detecting cancer biomarkers that exist in very low concentrations in the blood and is especially important in non-invasive cancers and early stages of cancer. One of the studies also examined the application of deep learning algorithms in the processing of nanobiosensors data, which led to an increase in the accuracy of pancreatic cancer diagnosis to more than 90%. In this research, one of the main challenges is processing large amounts of data and optimizing algorithms for greater accuracy. The results show that the combination of machine learning and nanobiosensors has a high potential to provide fast and more accurate diagnostic methods.

Conclusion: The use of machine learning and nanobiosensors as a new approach to a cancer diagnosis has a high potential to increase accuracy, speed, and efficiency in this field. This technology can create a revolution, especially in the early and non-invasive diagnosis of cancers. According to recent developments, it is expected that this compound will be more widely used in clinical settings in the future.

Keywords: Machine learning, Nanobiosensors, Cancer diagnosis, Artificial intelligence, Biomarker

78.

Matrix Metalloproteinase 1 as a Predictive Biomarker in Tumor Progression and Dedifferentiation in Anaplastic Thyroid Cancer **(Research Paper)**

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Introduction: Anaplastic thyroid cancer (ATC) is a highly aggressive malignancy characterized by rapid tumor progression and poor prognosis. Matrix metalloproteinase 1 (MMP1) has been implicated in various tumorigenic processes, yet its role in ATC remains inadequately explored. This study aims to identify MMP1 as a potential regulator of tumor progression and dedifferentiation in ATC.

Methods: A total of 15 microarray datasets for Homo sapiens were identified from the Gene Expression Omnibus (GEO) and The Cancer Genome Atlas (TCGA) databases. After excluding five datasets due to incomplete information, a final selection of ten datasets was utilized for analysis. Transcriptome data were merged and cleaned, followed by Principal Component Analysis (PCA) to assess the data structure. Thirty ATC tissues and thirty adjacent normal tissues were analyzed using the Limma package, applying Log2 transformations and quantile normalization. Differentially expressed genes (DEGs) were identified with a threshold of Log2 fold change (Log2FC) > 1.5 and p-value < 0.05, resulting in nineteen DEGs.

Results: MMP1 exhibited markedly higher expression levels in ATC tissues compared to normal thyroid tissues. Elevated MMP1 levels were associated with advanced tumor stages and poorer overall survival rates. Functional enrichment analysis indicated that MMP1 is involved in critical pathways related to cell migration, invasion, and epithelial-mesenchymal transition (EMT), underscoring its role in tumor dedifferentiation. Future validation through quantitative real-time PCR (qRT-PCR) will be performed.

Conclusion: These findings position MMP1 as a crucial regulator of tumor progression in ATC. The correlation between MMP1 expression and negative clinical outcomes points to its potential as a prognostic biomarker. Additionally, its involvement in EMT pathways

suggests promising opportunities for targeted therapeutic interventions. Future validation through quantitative real-time PCR (qRT-PCR) will further elucidate the mechanistic role of MMP1 and its potential as a therapeutic target in this aggressive malignancy.

Keywords: Anaplastic thyroid cancer, MMP1, tumor progression, differential expression, bioinformatics.

79.

Metabolic syndrome and cancer, looking at common pathways and mechanisms

(Review)

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Introduction: Increased consumption of high-calorie diets and insufficient physical activity are the main culprits of the growth of obesity and metabolic syndrome in the last century; the prevalence of various types of cancer has also increased in recent years; the simultaneous increase in the prevalence of cancer and metabolic syndrome prompted us to explore the common pathways between different cancers and metabolic syndrome to find common therapeutic targets.

Methods: So, we have searched all 129 previously published studies to evaluate the shared pathways and mechanisms between all types of cancer and metabolic syndrome.

Results: our results demonstrated the most critical common mechanisms between cancer and metabolic syndrome are chronic inflammation, insulin resistance, and different hormonal levels.Our results also demonstrated that colon, liver, and breast cancer are among the most essential cancers that have been proven to be associated with metabolic syndrome. endometrial, colorectal, gastric, bladder, and prostate cancer are also linked to obesity, which is one of the most significant markers of metabolic syndrome.

Conclusion: Several mechanisms and pathways, including insulin resistance, chronic inflammation, and differences in different hormone levels, have linked metabolic syndrome to several cancers, including colon, liver, and breast cancer

Keywords: metabolic syndrome, cancer, common pathways, mechanisms

80.

Microbial Mysteries: Current Trends and Challenges in Bladder and Prostate Cancer Research (Review)

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Introduction: The microbiome's involvement in urologic cancers, including bladder and prostate cancer, is a rapidly growing area of research with significant clinical potential. Despite advances, the field faces considerable challenges related to sample collection, sequencing variability, and establishing causal relationships between microbial communities and cancer. This review aims to address these challenges, highlight current research trends, and explore the implications for future studies and clinical applications.

Methods: A thorough review of the literature was conducted using PubMed, Scopus, and Web of Science databases. The search focused on studies investigating the microbiome's role in bladder and prostate cancer, with an emphasis on methodological issues such as specimen collection, sequencing technologies, and data interpretation. Criteria for inclusion included research highlighting common technical challenges and the need for methodological standardization to advance microbiome research in these cancers.

Results: In bladder cancer research, significant challenges include low microbial biomass in urine samples, potential contamination during sample collection, and variability in sequencing methods. These issues complicate the identification of specific microbial signatures associated with the disease. Variability in the choice of sequencing technologies and DNA isolation protocols further exacerbates these challenges. Additionally, variations in urine collection methods and storage conditions can introduce biases that impact results, making it difficult to draw consistent conclusions about the microbiome's role in bladder cancer. In prostate cancer, similar methodological issues are observed, particularly concerning stool sampling, DNA extraction, and sequencing approaches. The heterogeneity in these procedures across studies results in inconsistent findings and complicates the identification of reliable microbial biomarkers. The debate over optimal primer selection in amplicon sequencing and the need for refined statistical

methods for longitudinal analysis further highlight the complexity of this research. Standardizing methodologies and improving experimental models are crucial steps toward advancing our understanding of the microbiome's impact on prostate cancer and translating these findings into clinical practice.

Conclusion: Addressing the methodological challenges in microbiome research for bladder and prostate cancer is essential for advancing the field and improving clinical outcomes. Standardization of protocols and refinement of experimental models will enhance the reliability of findings and facilitate the identification of potential microbial biomarkers. Continued research are vital for uncovering the microbiome's role in urologic cancers and developing novel therapeutic strategies.

Keywords: Challenge, Microbiome, Prostate Cancer, Bladder Cancer

81.

MicroRNA-based cancer vaccines (Review)

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Introduction: Today, various methods have been invented to treat infectious and non-infectious diseases. Along with these treatments, the emergence of vaccines to treat these diseases is also very important and has created a new opportunity to prevent infectious diseases[1]. Cancer vaccines were first used in 1980 based on tumor cells and tumor lysate [2]. Cancer vaccines are generally classified into four categories: vaccines based on whole cell, virus, peptide, and nucleic acid. Among the mentioned types, cell-based vaccines are the main type of this classification. MiRNAs are a group of RNAs which play an important role in regulating gene expression after transcription. The results of studies of the last decade show that miRNAs affect cancer hallmarks, maintaining the proliferation signal, activating invasion and metastasis, and evading immune cells, inducing programmed cell death and growth suppressors [3]. By affecting crucial steps in cancer progression, miRNAs have a dual role and can lead to the suppression or progression of cancer [4]. Due to their wide regulatory potential, recruiting them in cancer vaccines for treatment or prevention has attracted many researchers around the world.

Methods: This article was written using keywords miRNA, miR-34, miR-200c, cancer treatment, cancer prevention from google scholar, pubmed and NCBI sites.

Results: There are 4 different types of cancer vaccines: 1. Peptide-based cancer vaccines are used in cancer treatments due to their immunogenic properties and longer lifespan [5]. 2. Whole cell-based cancer vaccines; by manipulating cytokines and chemokines we can maximize immunogenicity of them after injection [6] 3. Dendritic cells-based cancer

vaccines; dendritic cells are the most powerful immune cells in modulating the primary immune system, and are the main linker bridge between innate and adaptive immune system [7]. 4. Nucleic acid-based cancer vaccines; DNA-based cancer vaccines have been performed on breast cancer patients. One of the main reasons for using DNA-based vaccines is the ability to design a strong plasmid vector along with the ability to control and monitor the body's immune system after vaccination [8] (figure 1). MiRNAs as cancer vaccines MiRNAs can act as tumor suppressors “tumor suppressor miRs” and oncogenic miRNAs “onco-miRs”[4]. Different miRNAs according to their function in cancer, have been examined to be used as cancer vaccine. In this regard, we can mention tumor suppressor miRs like miR-34a (MiR-34 is associated with p53 activity), miR-145, and let-7 family. MiR-200c inhibits epithelial-to-mesenchymal transition (EMT) and prevents cancer cell metastasis, but on the other hand, in late-stage cancer, it shows a reverse function. This shows that miR-200c has a dual role according to cancer stage and conditions [9]. The first miRNAs detected in human cancer were miR-15a and miR-16-1.miR-15a and miR-16-1 target B-cell lymphoma 2 (Bcl2), an anti-apoptotic protein [10] and Cdc2 and Anxa2, which are cell cycle regulators [10]. As a result, their repair leads to increased apoptosis [10] and also reduces tumor size and metastasis (these miRNAs are under investigation to be used as functional miRNA-based cancer vaccine).

Conclusion: MiRNAs-based cancer vaccines have the potential to be used in cancer vaccines, and according to their wide-range of regulatory capacity, it seems that they may have the ability to be exploited for various type of cancers. Some of these miRNAs exert a dual function in cancer progression and in different stages of the disease; hence, prior to be benefited in the bed side, sufficient preclinical studies are needed.

Keywords: miRNA, miR-34,miR-200c, cancer treatment, cancer prevention

82.

microRNAs prediction analysis based on computational biology in liver cancer

(Research Paper)

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Introduction: Liver cancer ranks fourth globally in terms of frequency of occurrence and is the leading cause of mortality worldwide, accounting for 800,000 deaths annually. Chronic viral hepatitis, excessive alcohol use, and non-alcoholic fatty liver disease are the main causes of this illness. Small non-coding RNAs found naturally in the body called microRNAs (miRNAs) are involved in the control of gene expression. Strong evidence has shown that dysregulated miRNA expression occurs in human cancer through a variety of pathways, such as aberrant transcriptional regulation of miRNAs, amplification or deletion of miRNA genes, dysregulated epigenetic modifications, and flaws in the machinery of miRNA biogenesis. Under some circumstances, miRNAs can act as tumor suppressors or oncogenes.

Methods: This study found candidate medications based on differential gene expression profiles of liver cancer obtained from RNA sequencing data by using a computational drug repurposing process. Using accession code GSE142987 from the GEO database (https://www.ncbi.nlm.nih.gov/geo/), the transcriptional sample of plasma was compared. Only 34 liver cancer patients' plasma samples and 10 healthy people's plasma samples were examined because some samples were not accessible through the dataset. Using GEO2R, differentially expressed genes (DEGs) between plasma samples from patients with liver cancer and plasma samples from healthy participants were identified. Then, the expression difference obtained from the genes was entered into the String(https://string-db.org/) online platform, and finally the gene network was drawn. The desired hub gene was entered in the TargetScan (https://www.targetscan.org/vert_80/) online platform, and it suggests the desired rates for the main gene obtained in this data for liver cancer.

Results: It was shown that the ACRBP gene is one of the most important genes involved in the development of liver cancer, and further investigations show that microRNAs hsa-miR-4322, hsa-miR-6747-5p and hsa-miR-6737-5p are among the most important miRNAs that play a role in the suppression of ACRBP-causing liver cancer, and their induction can be effective in the process of suppressing liver cancer.

Conclusion: Methods that can increase and induce suppressive miRNAs in genes and proteins that cause liver cancer can be effective in cancer treatment.

Keywords: RNA sequencing; Liver cancer; miRNAs

83.

MiR-7-5p in Cancer: Targeting Oncogenes and Signaling Pathways to Enhance Radiation Response (Review)

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Introduction: MicroRNAs (miRNAs) are small non-coding RNA molecules that post-transcriptionally regulate gene expression. Studies indicate that miRNAs have an important role in tumor cell response to ionizing radiation by regulating genes involved in DNA damage repair, autophagy, apoptosis, and cell cycle, impacting radiation resistance. MiR-7-5p is a single-stranded RNA that is downregulated in several types of cancer, including breast, lung, glioblastoma, and colorectal cancer. The mechanisms by which MiR-7-5p regulates radiation response in cancer cells are multifaceted. Our study will briefly discuss some of the key mechanisms of MiR-7-5p and its role in radioresponse in cancers.

Methods: Relevant studies were searched in Google Scholar, Scopus, and PubMed databases from 2009 to 2023. The keywords of radioresistance, MiR-7-5p, and cancer were used without language limitations. Studies that investigated the mechanisms of MiR-7-5p and its role in radioesponse met the study inclusion criteria. After carefully examining titles and abstracts and implementing exclusion criteria, we reviewed the full texts of the most relevant studies.

Results: The final twenty articles emphasized the main mechanisms of radioresponse. MiR-7-5p has been shown to suppress the expression of several oncogenes involved in cell proliferation, notably the epidermal growth factor receptor (EGFR), crucial for cell growth and survival. MiR-7-5p can also modulate various signaling pathways involved in cell proliferation, notably the PI3K/AKT/mTOR pathway. By inhibiting this pathway, MiR-7-5p can suppress cell proliferation and induce cell cycle arrest. Studies reveal its impact on molecules like IRS2 and TAL1, upstream activators of MAPK and PI3K pathways, offering

insights into its tumor-suppressive mechanisms. However, MiR-7-5p regulates the expression of cell cycle regulators, such as cyclin D1 and cyclin E1. MiR-7-5p induces apoptosis in cancer cells by targeting anti-apoptotic proteins such as Bcl-2 and XIAP, while activating caspases.

Conclusion: Dysregulation of microRNA-7-5p in cancer cells contributes to increased cell proliferation, by mechanisms that regulate cell proliferation involving targeting oncogenes, modulating signaling pathways, regulating cell cycle progression, and inducing apoptosis. Further research on MiR-7-5p and its mechanisms may provide valuable insights for the development of novel therapeutic strategies targeting cancer cell proliferation.

Keywords: radioresistance, MiR-7-5p, cancer

84.

Molecular Insight into Wip1 phosphatase (PPM1D) Importance in Cancers (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). PPM1D (Protein phosphatase 1D), also known as wild-type p53-induced phosphatase 1 (Wip1) or protein phosphatase 2C delta (PP2Cδ), 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 p53-dependent manner. The role of Wip1 in the proliferation of stem cells and the regulation of T- and B-cell maturations and inflammation was also proposed. Therefore, Wip1 is known as a growth-promoting phosphatase and may be an oncoprotein. The encoding gene (PPM1D) is located on chromosome 17q23. In many high-risk human cancers, such as liver, ovarian, breast, lung, skin, pancreatic, brain, and different types of blood cancers, the PPM1D gene plays an oncogenic role. Studying and investigating the molecular mechanism of Wip1 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 1996 to 2024. The search focused on key terms such as ‘wip1 phosphatase,’ ‘PPM1D 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/CHK1 as well as ATM/ CHK2 pathways, respectively. In fact, the role of ATM and ATR is phosphorylation and activation of the effector checkpoint kinases i.e., CHK2 and CHK1. Consequently, the p53 protein is modified post-translationally by ATR/CHK1 and ATM/CHK2, leading to its stabilization and oligomerization. The protein P53 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 WIP1 and Mdm2 as its negative regulators. WIP1 inactivates the p53 pathway after accumulating sufficient protein levels and terminates the DDR. WIP1 also dephosphorylates MDM2 which leads to its stabilization and the degradation of P53. It can be said that the main role of WIP1 is to inhibit the stability of P53 by increasing the stability of MDM2. WIP1, like other members of the PPM/PP2C family, is a monomeric enzyme (605 amino acids) that requires divalent cations, primarily Mg2+ or Mn2+, for catalytic effectiveness. The PPM1D structure includes a large flap subdomain with 76 residues (P219-D295) adjacent to the active site. The flap region consists of two short α-helices (α3 and α4) and three short β-strands (β9, β10, and β11) followed by an irregular loop. In the crystal structure of PPM1D, extra electron density was observed for an unidentified atom between the nitrogen of the Lys336 side chain and the sulfur of Cys346, with 100% occupancy. Competitive modifications suggest this atom is oxygen, indicating a covalent cross-link that connects Lys336 and Cys346 through a nitrogen-oxygen-sulfur (NOS) bridge. The formation of the Lys336-Cys346 NOS cross-link may preserve PPM1D activity under high oxidative potential conditions, such as in cancer cells or following exposure to ionizing radiation.

Conclusion: Since WIP1 acts as an important negative regulator of p53 and a terminator of DDR, its overexpression inhibits p53 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 p53 pathway and inhibit proliferation in tumors with p53. It is hoped that with further studies on the PPM1D gene, more successes in cancer treatment or control will occur in the future.

Keywords: DNA damage response, Phosphatase, PPM1D gene, Tumor suppressor, WIP1

85.

New methods of cancer diagnosis (Review)

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Introduction: Overview of Traditional Cancer Diagnosis Methods Traditional cancer diagnosis methods primarily rely on imaging techniques and biopsies to identify tumors. For instance, mammography has long been the standard for breast cancer screening, allowing for early detection through X-ray imaging of breast tissues. However, its effectiveness can be limited, leading to false positives or missed diagnoses. Advances in magnetic resonance imaging (MRI), particularly diffusion-weighted imaging (DWI) and diffusion tensor imaging (DTI), offer enhanced specificity and accuracy in breast cancer diagnosis by better visualizing tissue changes associated with malignancies (D. Shahbazi-Gahrouei et al.). These sophisticated imaging modalities help medical professionals evaluate treatment responses more effectively, potentially leading to improved patient outcomes. Furthermore, integrating artificial intelligence into diagnostic processes is revolutionizing cancer detection, enhancing the speed and precision of analysis (Muhammad Javed Iqbal et al.).

Methods: Emerging Technologies in Cancer Detection In addition to advanced imaging techniques, the integration of artificial intelligence (AI) and machine learning (ML) into cancer diagnostics is becoming increasingly significant. These technologies enable the identification of genetic mutations and abnormal protein interactions at early stages of cancer, potentially transforming treatment approaches (Muhammad Javed Iqbal et al.). Furthermore, non-invasive methods such as liquid biopsies are gaining attention for their ability to detect biomarkers associated with various cancers. This approach allows for the collection of biological samples through simple blood tests, offering a rapid and precise means of diagnosing cancer (Salma Umme et al.). The continued development of these innovative diagnostic tools not only enhances early detection but also increases the likelihood of effective treatments, ultimately improving patient survival rates and outcomes. Liquid Biopsy: Revolutionizing Early Detection The potential of liquid biopsies extends beyond mere detection; they also facilitate real-time monitoring of a patient's

response to treatment. This capability allows for timely adjustments in therapy, which is crucial in managing cancer effectively (Mariano Zalis et al.). Additionally, liquid biopsies can identify minimal residual disease after treatment, providing early warning signs of potential relapse (Mariano Zalis et al.). By detecting genetic mutations associated with resistance to therapies, these non-invasive tests guide oncologists in selecting alternative treatments tailored to the patient's unique tumor profile (Mariano Zalis et al.). As research and technology continue to evolve, integrating liquid biopsy into routine clinical practice could significantly enhance personalized medicine, ultimately leading to better patient outcomes and survival rates (Salma Umme et al.). Artificial Intelligence and Machine Learning in Diagnosis In addition to real-time monitoring and identifying minimal residual disease, liquid biopsies are transforming the landscape of cancer diagnosis and treatment by integrating advanced technologies like artificial intelligence (AI) and machine learning (ML). These technologies enhance the accuracy of detecting genetic mutations linked to resistance, allowing oncologists to make informed decisions regarding alternative therapies tailored to the patient's unique tumor profile (Muhammad Javed Iqbal et al.). The automation and data-driven nature of AI and ML facilitate faster processing of large datasets, leading to earlier disease detection and more personalized treatment plans (Muhammad Javed Iqbal et al.). As these methodologies advance, they promise not only to improve patient outcomes but also to establish a new standard in precision medicine, ultimately enhancing survival rates among cancer patients. Genomic and Proteomic Approaches to Cancer Diagnosis Furthermore, the role of genomic and proteomic approaches is becoming increasingly pivotal in cancer diagnosis. These methodologies facilitate the identification of specific gene expression profiles associated with various cancer types, enabling more accurate classification and prediction of clinical outcomes (Kristen M Carr et al.). When integrated with liquid biopsy techniques, the potential for early detection and tailored therapies expands significantly. By analyzing tumor markers through serum proteomics and DNA microarrays, clinicians can gain insights into individual tumor biology, allowing them to customize treatment strategies effectively. This convergence of technology and medicine not only aims to enhance diagnostic precision but also seeks to shift from conventional one-size-fits-all treatments to more personalized care plans, ultimately improving patient survival rates and quality of life.

Results: Challenges and Future Directions in Cancer Diagnostic Methods The integration of artificial intelligence (AI) and machine learning (ML) in cancer diagnostics represents a transformative shift in medical practice. These technologies are designed to analyze vast

datasets, uncovering patterns that may elude traditional methods. By identifying genetic mutations and aberrant protein interactions early, AI can significantly enhance disease risk assessment and diagnosis (Muhammad Javed Iqbal et al.). As these tools evolve, they hold the potential to support clinicians in making more informed decisions about patient care, paving the way for tailored treatment regimens based on individual tumor biology. This personalized approach not only aims to improve diagnostic accuracy but also enhances the likelihood of positive patient outcomes, ultimately contributing to better survival rates and quality of life for those affected by cancer.

Conclusion: Challenges and Future Directions in Cancer Diagnostic Methods The integration of artificial intelligence (AI) and machine learning (ML) in cancer diagnostics represents a transformative shift in medical practice. These technologies are designed to analyze vast datasets, uncovering patterns that may elude traditional methods. By identifying genetic mutations and aberrant protein interactions early, AI can significantly enhance disease risk assessment and diagnosis (Muhammad Javed Iqbal et al.). As these tools evolve, they hold the potential to support clinicians in making more informed decisions about patient care, paving the way for tailored treatment regimens based on individual tumor biology. This personalized approach not only aims to improve diagnostic accuracy but also enhances the likelihood of positive patient outcomes, ultimately contributing to better survival rates and quality of life for those affected by cancer.

Keywords: Cancer Diagnosis methods Detection

86.

new methods of cancer preventions (Review)

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Introduction: Due to the increase in the number of people suffering from cancer all over the world cancer prevention is considered as a vital public step. in general cancer is the result of multiple alteration in the processes that control cell proliferation , invasion and spread .

Methods: this research was prepared by gathering through pup med and elsevier sites and other relieble scientific sites.

Results: many physical and chemical sustances cause mutation in genes and downstream changes in rna and protein processing. and the most important alterations are mutations in oncogenes and tumor suppressor genes .to prevent these changes there are some benefit suggestions. alcohol consumption increases the risk and development of oral , pharynx , nasopharynx, laryngeal and liver . consumption of fruits and vegetables prevent from 5% of all cancers and 56% of oral and pharyngeal cancer. vitamin c and e is against cancer cells as a antioxidant agent. vitamin d reduced risk of bowel cancer . high intake of salt and salt preserved foods increase stomach cancer .

Conclusion: one of the effective steps to prevent cancers is to follow a healthy and natural diet rich in antioxidants .

Keywords: antioxidants, vitamins, mutation, cancer, prevention.

87.

New Methods of Lung Cancer Diagnosis: Innovations and Implications (Review)

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Introduction: Lung cancer is one of the leading causes of cancer-related deaths worldwide, with early detection critical for improving survival rates. Traditional diagnostic methods often lead to late-stage diagnoses, resulting in poor outcomes. This article explores new diagnostic methods for lung cancer, including liquid biopsies, advanced imaging techniques, and molecular biomarkers, emphasizing their potential to enhance early detection and treatment strategies.

Methods: The following innovative approaches are revolutionizing lung cancer diagnosis: 1. Liquid Biopsies Liquid biopsies provide a non-invasive method for detecting circulating tumor DNA (ctDNA) in blood samples. This technique allows for real-time monitoring of tumor dynamics and genetic alterations without the need for invasive tissue biopsies. 1.1.Techniques: 1.1.1.Next-Generation Sequencing (NGS) enables comprehensive profiling of genetic mutations, facilitating targeted therapy decisions. 1.1.2.Digital PCR and Droplet Digital PCR offer high sensitivity for detecting low-frequency mutations, proving effective in early-stage cancer diagnosis. 2. Advanced Imaging Techniques: Recent advancements in imaging technologies have significantly improved early detection capabilities. 2.1.Low-Dose Computed Tomography (LDCT): Proven effective in screening high-risk populations, LDCT has been shown to reduce lung cancer mortality by approximately 20%. 2.2.Positron Emission Tomography (PET) and Magnetic Resonance Imaging (MRI): These modalities provide detailed anatomical and functional information, enhancing accuracy in staging and treatment assessment. 3. Molecular Biomarkers: Identifying specific biomarkers is crucial for enhancing diagnostic accuracy and informing treatment decisions. 3.1.Examples of Biomarkers: 3.1.1.EGFR mutations are common in non-small cell lung cancer (NSCLC) and can be targeted with specific therapies. 3.1.2.ALK rearrangements serve as critical indicators for personalized treatment approaches. Emerging biomarkers, such as exosomal RNA and metabolomic profiles, show promise for early detection, further enhancing diagnostic accuracy.

Results: The integration of these new diagnostic methods has yielded promising results in clinical studies: 1.Liquid Biopsies: Research indicates that liquid biopsies can detect lung cancer with sensitivity rates exceeding 80%, often even before clinical symptoms arise. 2.Advanced Imaging: LDCT screening has been shown to significantly reduce lung cancer mortality in high-risk groups, emphasizing its effectiveness as a screening tool. 3.Molecular Biomarkers: Identifying actionable mutations allows for tailored treatments, leading to improved survival rates in targeted populations. Collectively, these methods mark a shift in lung cancer diagnosis from reactive to proactive, enabling earlier intervention and better patient outcomes.

Conclusion: The emergence of new diagnostic methods, including liquid biopsies, advanced imaging techniques, and molecular biomarkers, represents a significant advancement in lung cancer detection. These innovations not only improve the accuracy of early diagnosis but also facilitate personalized treatment strategies that can enhance patient prognosis. Continued research and clinical validation are essential for integrating these technologies into routine practice, ultimately improving outcomes for lung cancer patients.

Keywords: Lung Cancer Liquid Biopsy Imaging Techniques Molecular Biomarkers Early Detection

88.

New Molecular and Cellular Pathways of IDH1 Mutation in the Glioblastoma (Research Paper)

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Introduction: Mutations in isocitrate dehydrogenase (IDH) 1 and 2 genes are key drivers of glioblastomas, particularly secondary glioblastomas in younger patients. These mutations are often prognostic for low-grade glioblastomas. While these mutations grant new functions to the enzymes, the exact molecular and cellular mechanisms linking them to glioblastoma pathogenesis remain unclear. To investigate this, we reanalyzed a single-cell RNA sequencing (scRNA-seq) dataset to compare cellular composition and gene expression patterns associated with these mutations.

Methods: We analyzed a publicly available dataset (GSE103224) from 8 high-grade glioma tissues, including one with the p.R132H mutation in the IDH1 gene (mutant) and others without any mutation (wild type). Using the Seurat package, we performed standard analysis, including PCA, UMAP, and tSNE for dimensionality reduction. We corrected for batch effects related to mitochondrial gene percentages and clustered cells at a resolution of 0.6, regressing out cell cycle effects. Cells were annotated with SingleR and BlueprintEncodeData. We extracted and plotted cell counts and markers for mutant and wild type conditions using ggplot2. Gene ontology enrichment analysis was conducted with clusterProfiler and org.Hs.eg.db in R.

Results: Our analysis shows that the R132H mutation in IDH1 significantly reduces the number of neurons, mesangial cells, fibroblasts, astrocytes, epithelial, and endothelial cells and increases adipocytes. Cyclin analysis showed adipocytes are mostly in the G1 phase, with upregulated genes related to microtubule movement and non-canonical Wnt signaling, and downregulated genes related to cell cycle inhibition. KEGG analysis indicated downregulation of apoptosis-related genes in adipocytes. Differential gene expression analysis revealed lower expression of MHC pathway, phagosome, and PI3K-AKT pathway genes in mutant tissue. Additionally, genes related to immune regulation,

inflammation, and cytokine production were downregulated, while antigen presentation genes were upregulated when comparing mutant tissue to the wildtype in general. The mutation also appears to cause leukocyte death and negatively regulate innate immune responses and inflammation. Macrophages showed induction of immune response pathways and inhibition of cell proliferation and migration. Dendritic cells downregulated genes related to metabolism, cell proliferation, cytokine production, and proteolysis, but expressed genes related to brain development and ECM organization. CD4+ T cells upregulated genes related to negative regulation of cell development, neurogenesis, and nervous system development, while downregulating genes related to immune response and autophagy.

Conclusion: The findings from our study provide insights into the cellular and molecular consequences of the R132H mutation in IDH1 gene. A broad impact on tissue homeostasis and cellular diversity was the initially-observed impact of the mutation. One potential explanation for these observations could be that this mutation might provide a selective advantage in some cell types. The functional analysis of these adipocytes revealed that they may face a block in cell cycle progression. The transcriptome profile of adipocytes points towards a complex regulatory mechanism that promotes proliferation while potentially inhibiting differentiation. The downregulation of apoptosis-related genes in adipocytes further supports the notion of enhanced cell survival in this cell type. This could contribute to the increased adipocyte count observed in the mutant samples. The differential gene expression analysis between mutant and wildtype tissues highlighted several key pathways affected by the R132H mutation, suggesting a compromised immune response. However, the upregulation of genes activating antigen presentation processes indicates a potential compensatory mechanism to maintain some level of immune surveillance. The mutation also appears to induce leukocyte cell death and negatively regulate innate immune responses and inflammatory reactions. The GO analysis of macrophages suggests a complex interplay between promoting immune responses and limiting tissue remodeling or repair processes. Similarly, the expression profile of dendritic cells in the mutant samples indicates a potential shift in the functional state of dendritic cells, possibly affecting their role in antigen presentation and immune activation. Lastly, the analysis of CD4+ T cells further highlight the broad immunomodulatory effects of the R132H mutation. In conclusion, the R132H mutation in IDH1 exerts widespread effects on various cell types and pathways, leading to altered cellular composition, immune responses, and potentially impacting tissue homeostasis and function.

Keywords: Single-cell transcriptome, Glioblastoma, IDH1 mutation, clonal sequencing

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Newcastle disease virus enhances the cytotoxic effects of 5-FU and Alters the expression pattern of microRNAs in human colorectal adenocarcinoma cell line (HT-29 cell line) (Research Paper)

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Introduction: Colorectal cancer (CRC) is a prevalent form of malignancy that is often linked to a poor prognosis, primarily because it is usually diagnosed at an advanced stage. 5-Fluorouracil (5-FU) is a commonly used chemotherapeutic agent for treating various cancers, sometimes in combination with other chemotherapies. Virotherapy shows great potential as an effective tool in combating cancer due to its high level of safety and ability to specifically target cancer cells. The Newcastle disease virus (NDV) has been found to possess a remarkable safety profile, making it a promising candidate for medical applications. Notably, this virus exhibits a unique ability to specifically target tumor cells, which presents an exciting opportunity for its potential use in combination with chemotherapeutic agents like 5-FU. This study aims to evaluate the cytotoxic effects of NDV in combination with 5-FU on HT-29 cells, as well as the impact of this approach on the expression patterns of specific microRNAs.

Methods: In this study, we performed experiments to investigate the hypothesis on the HT-29 human colorectal adenocarcinoma cell line. We employed the non-virulent LaSota strain of NDV together with 5-FU to assess the cytotoxicity effects and determine the expression levels of miR- 133a-3p, miR-574-3p, and miR-27a-3p in the study groups.

Results: Our study findings indicate that the use of combination therapy, in comparison to administering 5-FU and NDV alone, can result in more potent cytotoxic effects on colorectal cancer cells. This therapeutic approach also resulted in a significant upregulation of miR-133a- 3p and miR-574-3p expression, as well as a considerable downregulation of miR-27a-3p expression in cancer cells.

Conclusion: The remarkable effect of NDV and 5-FU on HT-29 CRC cells in vitro is impressive. This combinational therapy also regulates cancer cell miRNA expression,

improving therapeutic efficacy. This suggests that this therapeutic approach could be a promising CRC combination therapy.

Keywords: 5-Fluorouracil; Newcastle disease virus; Combination therapy; virotherapy; MicroRNA

90.

Non-invasive Detection and Diagnosis of Cancer Biomarkers: a Review of Recent Achievements (Review)

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Introduction: New ways to find and diagnose biomarkers without surgery have changed cancer and rendered old methods useless. Imaging technologies, biosensors, and liquid biopsies are some of these methods that make things more sensitive and accurate. The cost of care can go down, and more people with cancer will live longer thanks to these non-invasive ways. On the other hand, issues such as biomarker proof and standards still need to be fixed. The problems of biomarker validation and standards are still being looked into in order to make these methods better so that they can be used in hospitals. Getting treatment and a longer life are much more likely to work if the cancer is found early. A lot of good things can come from these non-invasive ways to find cancer. They make it possible to find the disease earlier, give more personalized care, and see how it's getting worse in real-time. This study shows how important safe early detection methods are for treating cancer. The aim is to get rid of unnecessary late diagnoses and increase the number of people who survive.

Methods: In this review article, we used the newest papers from Google Scholar and PubMed. A big part of our work was reviewing in depth about the best ways to look over and correctly judge old studies. To make sure the subject was fully covered, we looked at how words like "Cancer Biomarkers," "Non-invasive Detection," and "Non-invasive Diagnosis" were used.

Results: Scientists can use tools like qPCR and molecular imaging to find circulating abnormal proteins, miRNA, circulating cell-free tumor DNA (ctDNA), and circulating tumor cells (CTCs). This can help them make better evaluations and make patients feel better. These ways make it easier to find cancer earlier and watch how it grows and changes over time. Functional imaging (like Positron Emission Tomography (PET), Optional Coherence Tomography (OCT), and autofluorescence), genetic tests, and Artificial Intelligence (AI) are just a few of the cutting-edge technologies that are used in these new methods. AI makes it easier to understand and find things in large amounts of data. It also lowers the chance of getting false positives or negatives. They can also change depending on the tumor's genes, which lets doctors make treatment plans that are just right for each patient. Cancer biomarkers are small pieces of matter in the body that show there is cancer. Biomarkers are proteins, DNA, RNA, chemicals, or cells that have changed in a way that shows cancer has begun to grow. Traditionally, tissue biopsies are used to find cancer biomarkers. However, they are invasive, take a long time, and have a higher risk of problems. Circulating Tumor Cells (CTCs), cell-free DNA (cfDNA), circulating tumor DNA (ctDNA), microRNAs (miRNAs), and exosomes that cancer cells release through a liquid biopsy, which is one of the most promising non-invasive ways to find signs for cancer. CTCs are cancer cells that can split off from the main mass and get into the bloodstream. This helps find mutations that can be used to guide specific treatments and make early diagnoses. Imaging tools that are better now have also made it easier to find and identify cancer without surgery. It is now easier to see and pick out details and use molecular imaging, PET, ultrasound, and Magnetic Resonance Imaging (MRI); this lets doctors see tumors and the places around them right now.

Conclusion: Cancer signs can now be found and diagnosed without surgery a lot better than they were a few years ago. Blood samples are used for liquid biopsies, which look for molecular signs of cancer. This is a very promising way to find cancer early and see how well treatment is working. More and more, MRIs, CT scans, and PET scans are being used to find cancer and see how it's growing without having to do surgery. Scientists can learn more about each person's cancer through molecular techniques like DNA sequencing and growing tumor DNA analysis. This new technology is getting better all the time, and it could make a big difference in how well patients do. It could also cut down on the need for invasive treatments and completely change how cancer is found and treated.

Keywords: Cancer Biomarkers, Non-invasive Detection, and Non-invasive Diagnosis.

91.

Novel Targets for Treatment of Advanced Endometrial Cancer: literature review

(Review)

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Introduction: Endometrial cancer is one of the most common gynecologic cancers, with limited treatment options for advanced stages. While traditional therapies like surgery, chemotherapy, and radiation provide some benefits, they often fall short in improving survival rates for advanced and recurrent cases. Recent advances in understanding the molecular mechanisms driving endometrial cancer have led to the identification of novel therapeutic targets, offering hope for more effective treatment strategies.

Methods: Adapted from authoritative articles such as Pubmed, Google scholar and so on.

Results: This literature review examines emerging molecular targets, focusing on pathways such as PI3K/AKT/mTOR, immune checkpoint inhibition, and mismatch repair deficiency (dMMR). Inhibition of the PI3K/AKT/mTOR pathway, frequently mutated in endometrial cancer, has demonstrated promise in clinical trials. Immunotherapies, particularly PD-1/PD-L1 inhibitors, have shown efficacy in patients with dMMR tumors. Other targets, including FGFR inhibitors, HER2/neu mutations, and ARID1A mutations, are under investigation with promising early results.

Conclusion: The development of targeted therapies based on specific molecular alterations has the potential to transform treatment for advanced endometrial cancer. Early clinical data show encouraging outcomes, but further research is needed to optimize these therapies and explore combination approaches to improve survival and quality of life for patients with advanced disease.

Keywords: Endometrial cancer, targeted therapy, immune checkpoint inhibitors, HER2, PI3K/AKT/mTOR

92.

Omics Liver cancer data analysis and new generation chemotherapy drug selection

(Research Paper)

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Introduction: Cancer is the second leading cause of death worldwid .It should be noted that liver cancer ranks fourth in mortality among other cancers. It is also necessary to know that a large share of these deaths occurred in low-income or developing countries. So actions in appropriate time ,equipments and identifying the genes involved in the disease and the sequence of these genes in different people helps to treat patients better and more succrssfully.

Methods: The purpose of this study is to investigate the genetic relationship with medecine side effects available in Iran. Therefore, we selected different polymorphisms based on the citations and patient populations according to theNCBI website and analyzed these polymorphisms with the megagene software and identified the effective genes in this disease.

Results: We found out that genes Malat1(Rs664589,Rs619586,Rs3200401) ,Dlc1(Rs621554, Rs532841,3816748)and ACYP2(Rs843711,Rs6713088,Rs1682111) have the most important contributions in liver cancer.

Conclusion: We suggest that oncologists through assessment of patients'polymorphisms choose the most suitable medecine with the least side effects.

Keywords: Liver cancer, gene, chemotherapy, polymorphism, target therapy, side effects

93.

Oncolytic Viruses in Gastric Cancer treatment (Review)

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Introduction: Oncolytic viruses are among the viruses used in cancer treatment. They are defined as genetically engineered or naturally occurring viruses that selectively replicate and kill cancer cells without harming the normal tissues.Oncolytic viruses have unique mechanisms of action compared to currently available treatments. These viruses can modify the tumor microenvironment from a cold to a hot state by increasing immune cell infiltration in the tumor microenvironment. The use of oncolytic viruses to treat colorectal, pancreatic, and liver cancers in phases I and II clinical trials. associated with malignant melanoma cancer has been approved by the US Food and Drug Administration (FDA) in 2015.

Methods: This article is a review article that contains resources from PubMed, Science Direct, Elsevier, and Google Scholar. A total of 108 articles (2004-2024) were collected and, finally, 45 articles were reviewed.

Results: Despite the challenges and complexities of the treatment of oncolytic viruses, it is still a high potential therapeutic approach being used more often with the advancement of science and technology.

Conclusion: The use of oncolytic viruses has created a new horizon in the treatment of cancers, such as gastrointestinal cancers that can enhance treatment accuracy by combining other methods.

Keywords: Oncolytic viruses, gastric cancer, immunotherapy

94.

Oncolytic viruses: harnessing viral power to combat cancer (Review)

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Introduction: Oncolytic viruses (OVs) show promise in cancer treatment by selectively infecting and lysing cancer cells. For instance, talimogene laherparepvec (T-VEC) has been approved for melanoma in the USA, Europe (2015), and Australia (2016), while Teserpaturev is used for treating R/R glioblastoma in Japan (2021). Both originated from the modified herpes simplex virus (HSV-1). These viruses not only target cancer cells but also stimulate innate and adaptive immune system responses, especially when they are combined with immune checkpoint inhibitor antibody therapy, making them effective dual-function therapies for cancer.

Methods: A deep literature analysis, from sources including PubMed, Google Scholar, and Scopus, was conducted to collect information on oncolytic viruses in cancer. Particular attention was paid to treatment strategies and diagnostic techniques. Overall, 9 different journal articles were studied to gather the required information about advances in cancer treatment with viruses.

Results: OVs have come a long way in clinical tests, where they have caused many cancer tumors to decrease in size and made the immune system active. T-Vec is a particularly successful case, having received FDA approval. Furthermore, the trials and preclinical studies with various OVs engineered, such as HSV-1, H101, and echovirus, have shown increased tumor selectivity and immune responses, thus illustrating the potential of OVs to enhance cancer therapy results.

Conclusion: Oncolytic viruses have made a significant advancement in cancer therapy through a direct lysis mechanism combined with an immune-boosting effect. OVs' future is in their continuous evolution and combination with other immunotherapies to improve patient outcomes and overcome current challenges like virus delivery, immune system interactions with the virus, safety, tolerability, and specificity. The field is on the verge of

development with ongoing research that is expected to lead to new and even safer treatment options.

Keywords: Oncolytic viruses, Cancer immunotherapy, Talimogene laherparepvec, Adenoviruses, Tumor lysis

95.

Overexpression of TOP2A and RRM2 as a potential factor in colorectal cancer: a study based on gene expression omnibus (GEO) and bioinformatics analysis. (Research Paper)

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Introduction: Glioblastoma multiforme (GBM) is the most common and aggressive and yet the rarest brain tumor. 90% of glioblastomas are of primary type (IDH wide type GBM) which is usually in elderly people, but secondary glioblastoma (IDH mutant GBM) is usually in people It happens young. The rate of progression and spread of secondary glioblastoma is higher than the primary state. Genetic changes such as the role of lncRNAs and changes in signaling and molecular pathways such as metabolic pathways can be mentioned among the factors that cause glioblastoma.

Methods: The significance of gene expression in glioblastoma was analyzed by analyzing raw data (GSE4290) from the Gene Expression Omnibus (GEO) database and then by GEO2R to find differentially expressed genes (DEGs) and also from the databases miRWalk, KEGG PATHWAY, lncBase v.3, STRING , GeneCards were used.

Results: TOP2A gene with logFC= 5.911, which has the highest expression change among the genes related to this disease, together with RRM2 gene with logFC= 4.27 can be effective in gastric cancer and regulate the progress of this disease. Using the KEGG PATHWAY database, it was found that Metabolic pathways (Glucose metabolism in Brain tumor cells differs from normal cells) and p53 signaling pathways for these two genes can be effective in this disease by influencing these signaling pathways. Then miRWALK was used to find miRNAs and hsa-miR-885-3p and hsa-miR-145-5p were selected for TOP2A and RRM2 genes, respectively. After that, the lncbase v.3 databases were used to find lncRNAs and respectively NEAT1 and A1BG-AS1 were found for miRNAs that had strong interaction. GeneCards was also used to validate the selected lncRNAs. STRING was used

to find the interaction between the proteins of these two genes and other proteins, and these two proteins interact with other proteins such as RRM2B.

Conclusion: According to these findings, it can be concluded that the higher expression of TOP2A and RRM2 genes and the effect on the p53 signaling pathway and metabolic pathways, as well as the creation of a possible ceRNA regulatory network between miRNAs and lncRNAs and their regulatory effect on the mRNA of these genes, can cause glioblastoma.

Keywords: Glioblastoma, miRNAs, lncRNAs, p53 signaling pathway

96.

Oxidative stress induction by OCPs and OPPs pesticides may cause lung cancer incidence (Research Paper)

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Introduction: Pesticides are nowadays known as one of the most important causes of human disorders worldwide. The aim of the present study was to investigate the role of organochlorine pesticides (OCPs) and organophosphorus pesticides (OPPs) in the development of lung cancer.

Methods: We determined the levels of seven derived OCP residues (α-HCH, β-HCH, γ-HCH, 2,4 DDT, 4,4 DDT, 2,4 DDE, and 4,4 DDE) and enzymatic antioxidant biomarkers including paraoxonase-1 (PON-1), erythrocyte's acetylcholinesterase (AChE), glutathione peroxidase (GPx), superoxide dismutase (SOD), catalase (CAT), and non-enzymatic antioxidant biomarkers, including total antioxidant capacity (TAC), protein carbonyl (PC), malondialdehyde (MDA), and nitric oxide (NO) in the blood samples of 51 lung cancer patients and 51 healthy subjects as controls. Furthermore, the effects of OPP exposure on the development of lung cancer and oxidative stress (OS) are indirectly assessed by measuring AChE and PON-1 enzyme activities.

Results: The average values of all the measured OCPs were significantly higher in lung cancer patients when compared with healthy control subjects ($p < 0.05$). AChE, PON-1, GPx, and CAT activity levels, as well as the amounts of PC, MDA, and NO were higher in patients with lung cancer than in the control subjects ($p < 0.05$), while TAC values were lower in the patients. Moreover, our data showed a significant association between OCP concentrations and OS parameters ($p < 0.05$).

Conclusion: The results suggest that OCPs and OPPs may have a role in lung cancer incidence in southeastern Iran, and at least one of the mechanisms by which OCPs and OPPs may contribute to increasing the development of lung cancer in the studied area is through OS generation.

Keywords: Acetylcholinesterase, lung cancer, organochlorine, organophosphorous, oxidative stress

97.

Possible effect of Propionibacterium acnes in prostate cancer (Review)

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Introduction: Propionibacterium acnes (P. acnes) is a Gram-positive anaerobic bacterium traditionally known for its role in acne vulgaris. However, emerging evidence suggests that P. acnes may also be implicated in the development and progression of prostate cancer (PCa)

Methods: A PubMed search was conducted using the terms " Propionibacterium acnes " and " prostate cancer". Only English articles published within the last five years were included

Results: The expression of IL-6 and TNF-α is significantly higher in P. acnes-containing prostate cancer tissues compared to bacteria-free tissues, suggesting a possible link between P. acnes-induced inflammation and prostate cancer progression

Conclusion: The findings of this study support the hypothesis that P. acnes may play a contributory role in the pathogenesis of prostate cancer, possibly through mechanisms involving chronic inflammation. The significant association between P. acnes presence and elevated levels of pro-inflammatory cytokines in prostate cancer tissues suggests that P. acnes-induced inflammation could be a driving factor in prostate carcinogenesis

Keywords: Propionibacterium acnes, prostate cancer

98.

Potential of CAR T-Cell Therapy in Leukemia, Acute Myeloid Leukemia AML (Review)

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Introduction: Because different patients have different chromosomal abnormalities, gene mutations, or gene fusions, AML is a very heterogeneous disease. In ELN risk stratification, 17 genetic subtypes have been found thus far; however, there could be more molecular entities in the future. The biological functions of the recurring somatic mutations—such as those of signaling and kinase pathway genes—are classified. Uncontrolled cell growth and proliferation are caused by mutations in FLT3, a receptor tyrosine kinase, and KRAS/NRAS, a small GTPase; leukemogenesis is promoted by mutations in JAK2, a tyrosine kinase. There are epigenetic modifiers that encode a DNA methyltransferase enzyme (DNMT3A), isocitrate dehydrogenase enzymes (IDH1/2), and a DNA demethylase (TET2). The mutation in ASXL1 can lead to the alteration of DNA methylation patterns, dysregulation of gene expression, and altered hematopoietic differentiation. The dysregulation of transcription factors (CEBPA, RUNX1, MLL, EVI1.); nucleophosmin (NPM1); and cohesin complex genes can lead to impaired differentiation and uncontrolled cell growth. The initiating leukemogenic NPM1, TET2, and SMC1A mutations emerge in self-renewing cells that Jan et al. 18 The aim of this study was investigating CAR T Cell Therapy in leukemia, acute myeloid leukemia AML.

Methods: The promise of CAR T cell therapy in leukemia, acute myeloid leukemia (AML), is the title of the current study. It was conducted by scanning academic databases, including Science Direct, Springer, Google Scholar, and PubMed.

Results: Human leukocyte antigen (HLA) molecules on the surface of leukemic cells present tumour-associated antigens (TAAs), via which T cell receptor (TCR) designed T cells function. Either the cell surface or intracellular expression of the target protein is possible. Compared to CAR T cells, TCR-T cells require less antigens to activate T cells. There are still issues with TCR-T cell immunotherapy for AML that need to be resolved. The main disadvantages are that TAAs may be expressed by non-cancerous cells, which could lead to dose-related toxicity, immune evasion, and on-target and off-tumor toxicities. The

drawbacks of using TCR-T cells could be addressed by optimizing the dose of the cells, combining the treatment with exogenous cytokines (IL-21, IL-7, and IL-15), or including genetically modified signaling during cell expansion and demethylating drugs like decitabine. Mispairing of endogenous and exogenous TCR components, which impairs function, is another limitation of TCR transfer. This limitation can be avoided by exchanging the constant regions of human and mouse TCRs or by using codon-optimized cysteine-modified TCRs, in which the T2A sequence links the TCR. An alternative strategy makes use of scFv-containing TCR-like CAR T cells and CAR signaling pathways that identify peptides in the presence of MHC class I molecules. Anti-leukemic activities of TCR-T cells against WT1, PRAME, and HA-1 were shown both in vitro and in a clinical scenario with AML.

Conclusion: The ability to regulate the immune system and BM niches has been made possible by the great progress in understanding the molecular and cellular underpinnings of AML. CAR T cell therapy for AML is still in its infancy. Other targeted medicines are guided by lessons learned from allogeneic stem cell transplantation, the most successful immune cellular therapy for AML. The absence of an appropriate antigen that is expressed exclusively on AML cells presents one of the main obstacles to the development of CAR T cell therapy for AML. The optimization of CARs will be aided by locating and isolating target antigens that are uniformly and steadily expressed in all leukemic blasts and leukemic stem cells with minimal on-target off-tumor toxicity, by examining intricate interactions within the AML microenvironment, and by locating an appropriate cell source. Advanced techniques for ex vivo production are currently altering the characteristics of the finished product and the in vivo dynamics. With platforms that standardize the best CAR design for the target antigen or antigens by patient-specific immunophenotyping findings, the choice of a suitable carrier cell, and the cellular subtype, personalization in AML should be taken a step further in directed cellular therapies.

Keywords: CAR T-Cell, leukemia, acute myeloid leukemia AML, T cell receptor

99.

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 20 years from the first proof of concept to the first licensed vaccine against emerging pandemics such as 2-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 19. 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: Peptide vaccine is a type of immunotherapy based on the amino acid sequence of tumor antigen epitopes detected or predicted is synthesized. A personalized peptide vaccine can include peptides synthetic or genes that are neoantigens designed to target specific epitopes they code TSAs are only expressed in tumor cells and not expressed in normal cells remain Therefore, the use of TSAs in vaccines from the issue of tolerance of host immunity and autoimmunity prevents. Neoantigens are TSAs caused by non-synonymous mutations in the tumor genome are created.

Results: To make mRNA vaccines, the coded antigen must be placed in the form of DNA, which is from there, mRNA is transcribed in laboratory conditions. Unlike DNA, mRNA only needs to reach the cytosol, where it is transcribed into an antigen inside the body using the cellular machinery. To thus, any desired sequence can be designed, produced, and delivered to any cell type. At inside cells, RNA is recognized by endosomal or cytosolic receptors that can lead to the activation of the type I interferon pathway (I-IFN (I) and promoting the production of pro-inflammatory chemokines and cytokines become inflammatory These signal molecules lead to the activation of antigen presenting cells (APC) and after that they become strong in an adaptive response. mRNA vaccines are well tolerated and efficacious in animal models for multiple pathogens and they help to develop vaccines for other untreated diseases.

Conclusion: 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 Types of products based on messenger ribonucleic acid (mRNA) as a therapeutic 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

100.

Protein Nanoparticles in tumor targeting (Review)

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Introduction: Proteins are linear polymers that are composed of amino acids and have different structures and functions. They can be classified according to their solubility, chemical structure, shape and number of monomers. In view of the physicochemical properties and degradability of proteins, they play an important role in the development of nanoparticles as carriers of drugs and biological compounds. The development of drug delivery systems using nanoparticles as carriers for small and large therapeutic molecules is a growing area of research. The advantages of using proteins to produce nanoparticles for drug delivery and imaging applications are: their abundance of natural sources, their biocompatibility, their biodegradability and the ease of the synthesis process. Unlike metal nanoparticles, protein nanoparticles have no limitations such as potential toxicity, large size, accumulation or rapid excretion from the body. In addition, the surface of protein nanoparticles can be modified with protein ligands, carbohydrates, etc. protein nanoparticles can Protein nanoparticles can target tumor cells with three methods of active targeting, passive targeting and physical targeting

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

Results: The use of protein nanoparticles for such applications may be a better alternative to improve the pharmacokinetic and pharmacodynamic properties of various types of drug molecules.

Conclusion: The development of nanoparticle drug delivery systems is expected to have a major impact on the treatment of cancers and other life-threatening diseases. There is a great need to identify nanoparticle materials that are safe and effective in delivering therapeutic agents to the target sites. Protein polymers from natural sources are promising materials for constructing the nanocarrier systems.

Keywords: Drug delivery, Nanotechnology, Protein Nanoparticles

101.

Pseudogenes in colorectal cancer: A systematic review (Review)

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Introduction: Colorectal cancer (CRC) is a leading cause of oncologic death worldwide. Elucidating the molecular mechanisms that underpin its pathogenesis is essential for identifying novel therapeutic targets. Pseudogenes have historically been regarded as non-functional genomic vestiges but have gained recognition for their contributory roles in the oncogenesis of CRC.To systematically review and synthesize the existing evidence on the involvement of pseudogenes in CRC, we aim to assess their viability as diagnostic and prognostic biomarkers and evaluate their potential as innovative therapeutic targets

Methods: We conducted a comprehensive literature search following the PRISMA guidelines across PubMed, SCOPUS, and Web of Science databases. Two reviewers independently carried out the screening of studies and extraction of relevant data. Nineteen studies met the inclusion criteria. These studies highlight pseudogenes' emerging role in colorectal cancer, transitioning from being seen as evolutionary remnants to recognized contributors in tumorigenesis.

Results: The diagnostic and prognostic potential is found in pseudogenes like MYLKP1 (with SNPs rs12490683 and rs12497343) and POU5F1P1 (SNP rs6983267). Additionally, CDCP1, SUCLG2P2, and MT1DP offer prognostic insights, guiding personalized treatment approaches.

Conclusion: Our review illuminates the promise of pseudogenes as biomarkers and therapeutic targets, indicating a significant step towards the integration of pseudogenes in the future paradigm of precision medicine for CRC.

Keywords: Colorectal cancer, Pseudogene, Tumorigenesis, Gene regulation

102.

Recognizing and explaining the level in breast cancer: a systematic review (Review)

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Introduction: Cancer results from defects in cell growth regulation, often due to genetic damage from chemicals, hormones, or viruses. Breast cancer, the second most common cancer among women, is predominantly influenced by lifestyle and environmental factors rather than genetics. Risk factors include both fixed elements like age and genetics, and modifiable factors such as alcohol consumption and physical inactivity. Effective prevention involves addressing these modifiable risks. Despite its aggressive nature and the challenge of delayed diagnoses, early detection and intervention significantly improve outcomes. Preventive strategies, including primary prevention (risk reduction), secondary prevention (early diagnosis), and tertiary prevention (preventing recurrence), are crucial. Enhancing screening and education on risk factors can reduce incidence, mortality, and healthcare costs. The study aims to examine and explain these preventive measures in breast cancer to better inform health policies and practices.

Methods: A review was performed independently by two people according to the PICO criteria and aligned with the research objective and based on the PRISMA checklist and using PubMed, CINAHL, Medline, Web of Science, SID databases, Google Scholar search engine and Boolean operators. The time limit between 2015 and 2023 was determined using the MESH keywords “cancer”, “breast cancer” and “prevention”. After reviewing the entry and exit criteria and critically evaluating the quality of the selected articles, a total of 12 articles were included in the study.

Results: The evaluation of the reviewed articles revealed that breast cancer risk factors are classified into two categories: fixed and modifiable factors. Modifiable factors can be largely altered and prevented. Knowledge and education aimed at identifying underlying causes, implementing screening programs, and ensuring early detection and treatment play a significant role in preventing and reducing the risk of developing this disease. Lifestyle and environmental factors are critical contributors to breast cancer incidence.

Conclusion: The rising incidence of breast cancer in developing countries, including Iran, underscores the importance of public awareness regarding early symptoms and warning signs for successful diagnosis and prevention. Educating women about the impact of their behaviors on breast cancer risk and disease management is crucial for effective prevention. Environmental and lifestyle factors significantly contribute to breast cancer development. Additionally, rehabilitation methods can help maintain independence and facilitate quicker reintegration into society. Further research, particularly on tertiary prevention strategies, is needed to achieve more accurate and comprehensive results in breast cancer prevention.

Keywords: cancer, breast cancer prevention

103.

Recruiting molecular signaling pathway for Pregnancy associated breast cancer Precision medicine (Review)

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Introduction: Pregnancy-Associated Breast Cancer (PABC) is a rare but aggressive form of breast cancer that occurs during pregnancy or within five years postpartum. The incidence of PABC varies widely based on geographic location, diagnostic criteria, and inclusion/exclusion factors, ranging from 15 to 35 cases per 100,000 births or approximately 1 in 3,000 pregnancies. This variation highlights the importance of awareness and early detection in diverse populations.

Methods: Gene Expression Omnibus (GEO) GSE53031,GSE31192 Scopus, Google Scholar, ResearchGate

Results: Treatment of PABC: Surgery: Safe during pregnancy and postpartum. (Mastectomy is preferred if radiation therapy will be delayed.) Chemotherapy: Avoided during the first trimester but can be administered in the second and third trimesters. Anthracycline-based regimens are preferred. Radiation Therapy: Contraindicated during pregnancy but can be administered postpartum. Biologic and Endocrine Therapies: Typically avoided during pregnancy, but m ay be considered postpartum based on the patient's condition Molecular Subtypes of PABC: These subtypes each present unique challenges, particularly because pregnancy and postpartum hormonal changes significantly affect breast tissue and complicate diagnosis and treatment. Gene Expression: Gene expression studies utilizing datasets GSE53031 and GSE31192 identified 239 differentially expressed genes (DEGs) in PABC, with 101 genes up-regulated. Among

these, 14 hub genes were highlighted, including ASB6, which plays a significant role in regulating insulin signaling and adipocyte function. ASB6 has emerged as a potential prognostic marker and therapeutic target, influencing breast cancer progression by altering the tissue microenvironment through metabolic regulation. The integration of these findings suggests that targeting ASB6 and other hub genes could enhance precision medicine approaches for PABC, offering new avenues for treatment while improving patient outcomes. Moreover, further research into the role of these genes in postpartum breast tissue remodeling may provide insights into reducing the risk of PABC development.

Conclusion: PABC is a rare but aggressive form of breast cancer that arises during pregnancy or the postpartum period, posing significant diagnostic and treatment challenges. Gene expression analysis has revealed 239 differentially expressed genes, including key hub genes like ASB6, CREB1, and MMP9, which contribute to the aggressive nature of PABC. ASB6, in particular, plays a critical role in regulating insulin signaling and may serve as both a biomarker and therapeutic target. Hormonal changes, immune system alterations, and incomplete breast involution during the postpartum period are believed to contribute to PABC progression, underscoring the need for precision medicine approaches. Targeting these molecular pathways offers the potential for more effective and personalized treatments, improving outcomes for PABC patients.

Keywords: Pregnancy-Associated Breast Cancer, DEG ASB6, Molecular pathways, Gene expression

104.

RESEARCH Distinct tumor-TAM interactions in IDH-stratified glioma microenvironments unveiled by single-cell and spatial transcriptomics (Research Paper)

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Introduction: Gliomas are the most aggressive form of brain tumors. Despite notable advancements in targeted and immunotherapies, the standard of care for glioblastoma (GB) has remained largely unchanged, predominantly due to the challenges posed by the intra-tumoral heterogeneity and its immunosuppressive tumor microenvironment (TME). Tumor-associated macrophages (TAMs) residing in the TME are characterized by their pivotal roles in tumor progression, antitumor immunity and TME remodeling. However, knowledge of tumor-TAM crosstalk in major categories of gliomas remains elusive. In the current study, tumor-TAM crosstalk in IDH-WT and IDH-Mut gliomas was explored making use of single-cell and spatial transcriptomics to elucidate intricate mechanisms leading to aggressive phenotype of GB.

Methods: Single cell RNA-seq (scRNA-seq) was used to dissect the heterogeneity of TME in IDH-stratified gliomas. Spatial distribution of annotated subpopulations was resolved by spatial transcriptomic data. Next, using SCISSOR R package, we integrated survival and genomic information provided by the TCGA reference with cell-type signatures of our scRNA-seq. pySCENIC was used to infer gene regulatory networks. Cell-cell communications was inferred to further investigate tumor-TAM interplay followed by expression analysis of key genes on human tumor tissues.

Results: We delineated the phenotypic heterogeneity of TAMs across IDH-stratified gliomas. Notably, two TAM subsets with a mesenchymal phenotype were enriched in IDH-WT GB and correlated with poorer patient survival and reduced response to anti-PD-1 immune checkpoint inhibitor (ICI). We proposed SLAMF9 receptor as a potential therapeutic target. Inference of gene regulatory networks identified PPARG, ELK1, and MXI1 as master transcription factors of mesenchymal BMD-TAMs. Our analyses of reciprocal tumor-TAM interactions revealed distinct crosstalk in IDH-WT tumors, including ANXA1-FPR1/3, FN1-ITGAVB1, VEGFA-NRP1, and TNFSF12-TNFRSF12A with known contribution to

immunosuppression, tumor proliferation, invasion and TAM recruitment. Spatially resolved transcriptomics further elucidated the architectural organization of highlighted communications. Furthermore, we demonstrated significant upregulation of ANXA1, FN1, NRP1, and TNFRSF12A genes in IDH-WT tumors using bulk RNA-seq and RT-qPCR. Longitudinal expression analysis of candidate genes revealed no difference between primary and recurrent tumors indicating that the interactive network of malignant states with TAMs does not drastically change upon recurrence. Collectively, our study offers insights into the unique cellular composition and communication of TAMs in glioma TME, revealing novel vulnerabilities for therapeutic interventions in IDH-WT GB.

Conclusion: Our results suggest that aggressive properties of IDH-WT GB can be elucidated in part by the unique communications they form with their associated macrophages in TME.

Keywords: Glioblastoma, tumor microenvironment, tumor-associated macrophage, immune checkpoint inhibitor

105.

Resveratrol enhances sensitivity of renal cell carcinoma to tivozanib: an in-vitro study

(Research Paper)

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Introduction: Since tivozanib has many side effects in the treatment of kidney cancer, we decided to use resveratrol as a bioactive molecule with anticancer and antioxidant properties to make tivozanib more effective and also reduce its side effects in kidney cancer cell line.

Methods: To determine IC50 levels, ACHN cells was exposed to different concentration of tivozanib and resveratrol. Our data indicated that IC50 values for tivozanib (0.5μM) and resveratrol (30μM) with MTT in a dose and time-dependent manner. Due to the efficacy of resveratrol in combination with tivozanib, we used 20μM resveratrol, and 0.25μM tivozanib instead of 30μM and 0.25μM respectively. This data was approved by flow cytometry for ACHN cell line with 38.39, 14.74 and 66.06 percent apoptosis and 8.25, 5.12 and 15.6 percent subG1 for tivozanib, resveratrol and tivozanib-resveratrol combination respectively which was as a consequence of cell cycle arrest at G1/S phase. The treatment also reduced cells' migration, fragmented nuclei, 3D spheroid and colony formation potentials in analyses. Evaluation of gene expression presented that the effect of the tivozanib and resveratrol combination in ACHN cell lines is completely different during the evaluation of apoptosis genes, BAX, P53 genes and E-Cadherin had significantly increased expression compared to single treatment groups ($P < 0.01$). Meanwhile, a significant decrease was observed in the expression of VEGFC and HIF1α genes in the combination group compared to the monotherapy groups ($P < 0.001$).

Results: In this in vitro study, we evaluated the effect of tivozanib, resveratrol and tivozanib- resveratrol combination therapy in ACHN cell line as representatives of human kidney cancer. The assessment includes Hoechst dye staining, scratch-wound assay, 3D spheroid, 2D colony formation assay, flow cytometric analysis of apoptosis and DNA cell cycle, real-time PCR (BAX/BCL2, E-cadherin, Snail, HIF1(, VEGFC and KLK3 genes).

Conclusion: this study shows that resveratrol, an active phytochemical, increases the sensitivity of renal cell carcinoma cells to tivozanib by reducing the survival of renal cancer

cells, suppressing the proliferation, migration, colonization and spheroid formation and decreasing VEGFC/ HIF-1α expression. In the combined group, resveratrol led to a decrease in the dose of tivozanib. Our results suggest that resveratrol combined with tivozanib may be a new therapeutic strategy and an optimal choice for renal cell carcinoma.

Keywords: Tivozanib, Resveratrol, Prostate cancer, Combination therapy

106.

Role of Cancer-Associated Fibroblasts in Cancer Progression (Review)

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Introduction: Fibroblasts play key roles in disease, tissue homeostasis, cancer progression, inflammatory and fibrotic conditions, and wound healing processes. Cancer-associated fibroblasts (CAFs) are a major component of the stroma and secrete growth factors, inflammatory ligands, and extracellular matrix (ECM) proteins that promote tumor proliferation, therapy resistance, and immune exclusion. CAFs regulate the biology of tumor cells and other stromal cells via cell–cell contact, releasing numerous regulatory factors and synthesizing and re-modelling the extracellular matrix, and thus these cells affect cancer initiation and development. Promoting the proliferation, invasion and migration of cancer cells is a major way of CAFs to facilitate cancer development. Cytokines secreted by CAFs that have been implicated in this process include TGF-β, interleukin-1α (IL-1α), IL-6, interleukin-33 (IL-33), stromal cell-derived factor 1 (SDF1), C-X-C motif chemokine ligand 8 (CXCL8), and cyclooxygenase-2 (COX-2), and different molecules mediate diverse effects.

Methods: In the current study, keywords including Cancer-Associated Fibroblasts, 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 2010 to 2023. All of the full text was considered, and the papers manifested as only abstract were excluded. The full papers selected focused on the specific role of cancer-associated fibroblasts in cancer progression only. A total of 50 papers were selected and studied in this review.

Results: Articles showed that cross-talk between tumorigenic cells and fibroblasts may be responsible for the emergence of a subpopulation of hyper-activated fibroblasts that are present in the tumor microenvironment (TME). Some studies have shown that CAFs are highly heterogeneous and have been shown to enhance cellular migration and alter

metabolism of epithelial tumor cells, display elevated pro-angiogenic cytokine signaling, regulate the plasticity of cancer stem cells, play a significant role in the development of drug resistance, and facilitate inflammation. Recent studies revealed that instead of cancer cells, CAFs contribute to tumor proliferation, invasion, and metastasis via secretion of various growth factors, cytokines, chemokines, and degradation of extracellular matrix (ECM) proteins. Previous studies using genetically engineered mouse models (GEMMs) of pancreatic cancer have shown that CAFs and ECM produced by CAFs confer resistance to chemotherapy by impairing efficient drug delivery. Certain studies have suggested that the mesenchymal-like phenotype of CAFs is involved in enhancing the metastasis of cancer cells. Articles showed secretion of TGF-β by CAFs promotes the EMT of breast cancer cells via TGF-β/SMAD and non-SMAD signaling pathways and facilitates tumor growth and metastasis in colorectal cancer. Studies on cancer immunotherapy have shed light on the involvement of CAF in the tumor immune microenvironment and have revealed that CAF expressing fibroblast activation protein-α (FAPα) or α-smooth muscle actin (α-SMA) suppress antitumor immunity through various mechanisms, contributing to the formation of a tumor-permissive microenvironment.

Conclusion: Cancer-associated fibroblasts (CAFs) are a major component of tumor stroma and play a crucial role in the proliferation, invasiveness, metastasis, and angiogenesis of cancer. CAFs promote cancer progression through multiple mechanisms, including extracellular matrix (ECM) remodeling and the production of growth factors, cytokines, and chemokines, which promote cancer cell proliferation, metabolism, and tumor angiogenesis.

Keywords: Cancer-Associated Fibroblasts, Cancer, Progression

107.

Role of Cancer-associated fibroblasts-derived exosomal ncRNAs in colorectal cancer progression (Review)

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2.

Introduction: Colorectal cancer (CRC) is introduced as one of the leading causes of cancer-related deaths between women and men. The development and progression of CRC are affected by tumor microenvironment (TME). Cancer-associated fibroblasts (CAFs), one of the most active components of TME, can interact with CRC cells to facilitate their tumorigenesis and development. Emerging evidence reported that the secretion of exosomes mediates communication between the CAFs and CRC cells. Exosome is an extracellular vesicle (EV) with small sizes (40 ~ 100 nm) that contain proteins, lipids, DNA, and ncRNAs (such as lncRNAs, circular RNAs, and miRNAs). The ncRNAs carrying exosomes can be secreted from CAFs as a potential intracellular communication mediator and participate in the cell proliferation, growth, survival, metastasis, drug resistance, and immune response of recipient tumor cells through underlying the different molecular mechanisms. In the present study, we explored the major role of exosomal ncRNAs in CAFs and CRC cell interaction in TME and their molecular mechanisms of action in tumorigenesis.

Methods: In this study, we retrieved the results of related articles published between 2020 and 2024 using keywords such as “colorectal cancer”, “exosome”, “cancer-associated fibroblast” AND “ncRNA” queries from reputable databases.

Results: Recent studies revealed the critical role of exosomal ncRNAs released from CAF on the malign behavior of colorectal cancer. These studies reported that CAF-derived exosomal ncRNAs for example, miR-135b-5p (1), miR-93-5p (2), LINC00355 (3), micro-RNA-200b-3p (4), LINC00659 (5), circEIF3K (6) can affect the molecular pathways, therefore can induce the cell proliferation, growth, migration, invasion, metastasis and drug resistance in CRC cells.

Conclusion: Accumulating evidence demonstrated that exosomes bearing ncRNAs are implicated in the intracellular communication between CAFs and CRC cells in the TME and

can play a pivotal role in CRC progression through underlying molecular mechanisms. Therefore, CAFs-derived exosomal ncRNAs can be employed as potential therapeutic targets for CRC treatment.

Keywords: Colorectal cancer (CRC), Cancer-associated fibroblast (CAF), ncRNA, Exosome

108.

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-2), and Ki-67 level, as well as their prognosis. Accordingly, there 5 different subtypes (Luminal A, Luminal B, HER-2 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(1). 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(3).

Methods: 1)google scholar 2)Research gate 3)science direct 4)Pubmed 5)Scopus

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(5). Recent studies have highlighted the significance of PXR expression in tumor tissues of patients with TNBC, linking it to patient prognosis(2). 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 (2) (figure 1). 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 (2). Transcription factor E26 transformation-specific sequence 1 (ETS-1) and N-α-acetyltransferase 10 (NAA10) have been shown to interact with the PXR promoter, enhancing the activation of downstream genes associated with drug resistance. CYP3A4 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 CYP3A4 at the transcriptional level, may enhance the therapeutic effects of these drugs(4). According to a study FBI-1 is a factor that binds to the inducer of short transcripts-1, enhancing the resistance of TNBC cells to chemotherapeutic agents by repressing the expression of microRNA-30c, which targets the PXR. MicroRNA-30c reduces PXR expression by interacting with the 3'-UTR of PXR, whereas FBI-1 increases PXR expression by inhibiting miR-30c. This research demonstrates that the miR-30c/PXR axis is modulated by FBI-1 in TNBC drug resistance, suggesting potential new strategies for the treatment of this aggressive cancer type(6). 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 (7). 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(8). 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 (9) 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 (10).

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: Drug Metabolism- PXR - TNBC -Breast Cancer

109.

RPS19 Gene as a Novel Biomarker in Breast Cancer (Research Paper)

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Introduction: Breast cancer is a highly widespread global health issue, accounting for 30% of malignancies affecting women. Additionally, it has been recognised as the second leading cause of death in developed countries. Unfortunately, an estimated 502,000 women lose their lives to breast cancer each year. The World Health Organisation predicts that by 2050, the number of women diagnosed with breast cancer could reach up to 2.3 million. Iran has seen breast cancer as the prevailing form of cancer and the fifth highest contributor to mortality among Iranian women. The standardised incidence rate (ASR) for breast cancer is at approximately 28 cases per 100,000 individuals, and this rate has been on the rise in recent times. Breast cancer is highly heterogeneous at morphology as well as molecular levels and needs different therapeutic regimens based on the molecular subtype. Epigenetic alterations are a major cause of breast cancers.and their mechanisms include the regulation of gene transcription, genomic stability, and maintenance of normal cell growth, development, and differentiation. Three main mechanisms are known: DNA methylation, histone modification, and non-coding RNAs (ncRNAs). They are critical regulators of cellular immunity, which is mediated via the regulation of gene expression and transcription in specific cells and tissues. Recent technological advances in cancer detection have led to the emergence of gene expression patterns for better understanding tumor behavior, improving not only prognosis but also early detection and treatment. Combining gene expression patterns with clinical pathology characteristics enhances the precision of illness prognosis. RPS19 is on the genes that undergo alterations in their expression patterns in breast cancer. The RPS19 gene, located in the q13.2 gene locus on chromosome 19, encodes the synthesis of one of the 80 distinct ribosomal proteins. The RPS19 gene encodes a protein that is found in the small subunit of ribosomes and is a member of the S19E ribosomal protein family. This protein is situated in the cytoplasm. Genetic mutations in this specific gene result in Diamond-Blackfan anaemia (DBA), a

congenital erythroblastopenia characterized by a decrease in erythroid precursors in a subset of patients. Higher levels of expression of this gene have been observed in some primary colon cancers compared to normal colon tissues. According to bioanformatic studies, the RPS19 gene shows increased expression in breast and ovarian cancers and in this study, its expression is to be measured by real-time technique.

Methods: The current study is an observational and case-control investigation that will be carried out on women who have been diagnosed with breast cancer and are having surgical therapy. The sampling will be conducted in a convenient manner, utilising the available samples. At first, a total of 28 samples of breast cancer tissue will be gathered. The control group will comprise of tissue samples obtained from patients that do not have cancer. The expression levels of RPS19 genes will be measured using Quantitative Real-Time RT-PCR in both the case and control groups. For this purpose, total mRNA will be extracted from breast tissue samples using an extraction kit, and their genomic DNA will be degraded using DNase RNase-free. Subsequently, cDNA will be synthesized using a Reverse Transcriptase enzyme kit. Specific primers will be used to amplify cDNA of RPS19 gene along with SYBER Green two-step kit, following the manufacturer's instructions. The B-Actin gene, encoding one of the 6 different actin proteins, will be considered as a control gene in this study. To compare the mean differences of the main variables under study, statistical analysis will be performed using paired sample t-tests due to the quantitative nature of these variables. A p-value less than 0.05 will be considered significant in all tests. RPS19 gene primer was designed using Primer Blast web software.

Results: Quantitative analysis of the PCR data demonstrated a statistically significant upregulation of RPS19 gene expression ($p < 0.05$) in breast cancer tissues compared to non-cancerous tissues. group ($p < 0.05$). The observed increase in the expression of the RPS19 gene underscores their potential roles as biomarkers for breast cancer diagnosis and prognosis. These findings suggest the involvement of RPS19 in breast cancer pathogenesis and highlight the importance of further investigation into their molecular mechanisms and clinical implications. The results of this study contribute to the growing body of evidence regarding the dysregulated expression of RPS19 in breast cancer, providing valuable insights into the molecular pathways underlying breast carcinogenesis and offering potential targets for therapeutic intervention.

Conclusion: Due to its metastatic process and therapeutic resistance, breast cancer continues to be a leading cause of cancer-related deaths globally. Common treatment

options for breast cancer include surgical intervention, chemotherapy, hormone therapy, and radiotherapy. The objective of this study was to investigate and compare the levels of expression of the RPS19 and hsa_circ_0051243 genes in breast cancer patients using Real-Time PCR. The study samples included stages 1 through 4, with each sample having a tumor margin control tissue from the same site. The expression of the RPS19 gene showed significant differences in tumor samples compared to normal states.($p = 0.005$) Numerous studies have been conducted on breast cancer and the pathways involved in its development. Among the genes involved in this disease, RPS19 gene can play a significant role in the early prognosis and diagnosis of breast cancer. Furthermore, by utilizing the data from this study and bioinformatic data, the complex relationship between protein-coding genes can be elucidated, which could greatly assist in the diagnosis and management of breast cancer.

Keywords: Breast Cancer , RPS19 , Real-time PCR , Cancer

110.

Simultaneous omics and data analysis of breast cancer with a new generation chemotherapy drug (Research Paper)

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Introduction: In our research, we simulated new methods for diagnosing and treating breast cancer, such as the NGS method, as opposed to older methods like immunohistochemistry. Through this, we identified common mutations in breast cancer, including BRCA1, BRCA2, and BRIP1.

Methods: In our research, we initially utilized the NCBI database to identify SNPs. Next, we compiled a list of breast cancer drugs available in Iran, along with their respective side effects. Finally, we used the MEGA GENE software to sort the SNPs based on citation and population, and then evaluated and analyzed the collected data.

Results: Before prescribing drugs and therapy for the treatment of breast cancer, it is essential to conduct genetic tests to check for the presence of polymorphisms in common genes such as BRCA1, BRCA2, and BRIP1 in patients. If polymorphisms are present, drugs with fewer side effects should be prescribed for the patient.

Conclusion: Based on the evaluations, we have determined the phenotypic manifestations resulting from the occurrence of these SNPs in the body. We have also identified the secondary phenotypes associated with breast cancer, as well as other diseases. Additionally, we have investigated the potential side effects of drugs used for treating breast cancer and the genetic predispositions that may influence the likelihood of experiencing these side effects in patients with suspected polymorphisms.

Keywords: NGS- Genetic testing -Hereditary breast and ovarian cancer -BRCA1 - BRCA2

111.

Single-Cell Sequencing in Cancer Diagnosis: Investigation of Tumor Heterogeneity and Its Role in Personalized Diagnostics (Review)

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Introduction: Single-cell sequencing and other single-cell technologies are powerful tools for identifying heterogeneity within tumors. These methods allow the detailed study of each cancer cell's genetic and transcriptional characteristics separately, thus contributing to more accurate diagnosis and personalized treatment. This research aims to investigate the role of single-cell sequencing in discovering the differences between tumor cells and the impact of this technology in the development of new and personalized cancer diagnosis methods. We specifically address the benefits of these methods in better understanding molecular pathways and responses to therapies.

Methods: Data related to scientific articles between 2018 and 2023 from PubMed, Scopus, and Web of Science databases using keywords such as "single-cell sequencing," "cancer diagnosis," "tumor heterogeneity," "single-cell RNA," and " "Single-cell technologies" were extracted. Articles that included experimental data and analytical reviews were reviewed in this study.

Results: The analysis of the data obtained from the articles shows that single-cell RNA sequencing (scRNA-seq) plays a vital role in diagnosing tumor heterogeneity. For example, in a study of lung cancer, single-cell sequencing revealed that the tumor was composed of different cells with different genetic and transcriptional patterns. This heterogeneity can be the reason for the resistance of some cells to conventional treatments. In another study that investigated breast cancer, single-cell sequencing succeeded in identifying different cell subtypes, each of which indicated different pathways of tumor progression and response to treatment. This technology has also been used in glioblastoma. It was found that the presence of cancer stem cells and differentiated cells within the tumor can be significant predictors of the prognosis of patients. One of the key examples in this field is the ability of this method to identify specific biomarkers of each patient and tumor, which allows doctors to prescribe personalized treatments for each patient. This technology has led to a more accurate diagnosis and has been particularly important in determining the prognosis and choosing a more effective treatment. These results suggest that single-cell sequencing could pave the way for early diagnosis and personalized cancer treatments.

Conclusion: Single-cell sequencing is a powerful tool that can contribute to a deeper understanding of the heterogeneity within tumors, and this information is valuable for developing new diagnostic and therapeutic methods. This technology enables personalized diagnoses and more effective treatments by providing accurate biomarkers and identifying cell subtypes. It is expected that with the advancement of this technology, significant improvements will be achieved in the clinical management of cancers.

Keywords: Single-cell sequencing, Cancer diagnosis, Tumor heterogeneity, Single-cell RNA

112.

Somatic Mutations in Noncoding Regions: Uncovering Their Impact on Tumor Progression and Therapy Resistance (Review)

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Introduction: Recent advances in cancer genomics have revealed that somatic mutations are not confined to protein-coding regions of the genome but are also prevalent in noncoding regions, including promoters, enhancers, and untranslated regions (UTRs). While the impact of coding mutations is well characterized, the functional consequences of noncoding mutations in cancer remain largely unexplored. These mutations may disrupt regulatory elements and alter gene expression, contributing to tumorigenesis and therapy resistance. This review aims to provide a comprehensive overview of the current understanding of somatic mutations in noncoding regions and their role in cancer progression and therapy resistance. We will discuss the mechanisms by which these mutations influence gene regulation, the latest techniques for identifying and characterizing these mutations, and their potential as therapeutic targets.

Methods: A systematic review of the literature was conducted, focusing on studies published in the past decade that investigated somatic mutations in noncoding regions of the genome in various cancer types. Key databases were searched for relevant articles, and the findings were synthesized to highlight the emerging themes and gaps in the current knowledge.

Results: Somatic mutations in noncoding regions have been identified in numerous cancers and are often associated with altered expression of oncogenes and tumor suppressor genes. These mutations can disrupt transcription factor binding sites, leading to aberrant gene expression and contributing to oncogenesis. Furthermore, mutations in regulatory elements have been implicated in resistance to targeted therapies by modulating the expression of genes involved in drug response. Advances in high-throughput sequencing and bioinformatics have enabled the identification of these mutations at an unprecedented scale, revealing their widespread impact across different cancer types. Somatic Mutations in Noncoding Regions: A New Frontier in Cancer

Research Recent studies have uncovered numerous somatic mutations in noncoding regions of the genome, revealing their significant role in tumorigenesis and therapy resistance. These mutations often occur in regulatory elements such as enhancers, promoters, and long noncoding RNAs (lncRNAs), where they can profoundly alter gene expression and cellular behavior. 1. Enhancer Mutations in Melanoma: In a landmark study, somatic mutations were identified in the regulatory elements of the TERT gene, specifically in the promoter region, in various cancers including melanoma. These mutations create novel binding sites for E-twenty-six (ETS) transcription factors, leading to increased TERT expression and subsequent telomere elongation, which is a hallmark of cancer cells. The upregulation of TERT due to these promoter mutations supports the continuous proliferation of melanoma cells, highlighting the importance of noncoding mutations in driving oncogenesis. 2. Noncoding Mutations in TP53 Enhancer in Glioma: Recent work has identified recurrent mutations in an enhancer region of the TP53 gene in gliomas. These mutations were found to disrupt the binding of CTCF, a key architectural protein, thereby altering the chromatin landscape and leading to decreased TP53 expression. This reduction in TP53, a critical tumor suppressor, compromises the cell's ability to respond to DNA damage, facilitating tumor progression. The discovery of these enhancer mutations underscores their potential as biomarkers for glioma prognosis and as targets for therapeutic intervention. 3. LncRNA MALAT1 Mutations in Lung Cancer: The lncRNA MALAT1 has been extensively studied for its role in various cancers, and recent findings have shown that somatic mutations within the MALAT1 gene can contribute to lung cancer progression. These mutations have been linked to changes in the secondary structure of MALAT1, affecting its interaction with splicing factors and resulting in altered gene splicing. Such changes promote the expression of oncogenic splice variants, which drive lung cancer metastasis and resistance to chemotherapy. The modulation of MALAT1 function through targeted therapies could offer new avenues for treating lung cancer patients with these specific noncoding mutations. 4. Mutations in MYC Super-Enhancer in Breast Cancer: Another significant discovery involves mutations within the super-enhancer region of the MYC oncogene in breast cancer. These mutations increase the binding affinity for the transcription factor BRD4, leading to enhanced MYC expression. The overexpression of MYC is associated with aggressive tumor behavior and poor patient prognosis. Interestingly, inhibitors targeting BRD4 have shown promise in preclinical models, suggesting that these noncoding mutations could be exploited therapeutically to suppress MYC overactivity in breast cancer. 5. Intronic Mutations in BRAF and Therapy Resistance:

Intronic mutations within the BRAF gene have been implicated in resistance to BRAF inhibitors in melanoma patients. These mutations are thought to create alternative splicing sites, resulting in the production of a truncated, but still active, form of the BRAF protein. This truncated protein lacks the domain targeted by the inhibitors, allowing melanoma cells to bypass the drug's effects and continue proliferating. This mechanism highlights the importance of noncoding regions in therapeutic resistance and the need for strategies that address these mutations.

Conclusion: The noncoding genome plays a critical role in cancer development and resistance to therapy. Understanding the functional impact of somatic mutations in these regions is crucial for the development of novel therapeutic strategies. Future research should focus on integrating multi-omics data to map the regulatory networks affected by these mutations and on developing targeted interventions that can modulate the activity of mutated noncoding elements.

Keywords: Somatic mutations, noncoding regions, cancer progression, therapy resistance, regulatory elements.

113.

Stem Cells for the Treatment of Ovarian Cancer Review article (Review)

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Introduction: Ovarian cancer is one of the leading causes of mortality among women with benign gynecological diseases, particularly occurring in postmenopausal women. It ranks fifth after lung, breast, colorectal, and pancreatic cancers and has a significant impact on overall health. Ovarian cancer encompasses a diverse group of diseases that arise from various tissues of the female reproductive organs. Early-stage ovarian cancer is often undetectable, leading to diagnosis at more advanced stages. The prognosis and treatment of ovarian cancer patients depend on the duration of the disease following cytoreductive surgery. The repeated rupture of the epithelial tissue during ovulation may be responsible for the different types of ovarian cancer, a hypothesis that has emerged from pathological samples obtained from surgeries showing that epithelial tissue in the fallopian tubes serves as a source for various forms of ovarian cancer. It is presumed that the origin of cancer stem cells (CSCs) in ovarian cancer is due to the effects of DNA damage from ovulation and wounding, which affects quiescent stem cells located in the surface epithelial tissue of the ovary. It has been suggested that the presence of common genes in the surface epithelial tissue of the ovary, which are overactive in ovarian cancer, plays a role in the development of this cancer, establishing a connection between ovulation and the development of ovarian cancer.

Methods: The standard treatment strategy for ovarian cancer involves surgical resection of the tumor, followed by chemotherapy based on taxanes and platinum compounds. This treatment strategy results in an 80% partial response rate and a 40-60% complete response rate, with a 5-year survival rate of approximately 30%. However, the recurrence rate of the disease remains high at 70%. This statistic suggests that while most ovarian cancers are initially sensitive to chemotherapy, the significant chance of recurrence indicates that some cancer cells are not eliminated by the chemotherapeutic agents and/or can regenerate after exposure to these agents. The efficacy of individual drugs against ovarian cancer stem cells (CSCs) is limited due to their heterogeneity, and targeting ovarian CSCs has proven to be a considerable challenge for researchers. Furthermore, the

current first-line treatment for ovarian cancer involves a combination of paclitaxel and carboplatin, which has been associated with an increased incidence of chemoresistance. While combining multiple drugs may be used to target CSCs, it also raises the risk of toxicity, as CSCs may possess characteristics similar to normal cells. This characteristic of CSCs indicates that specific tumor cells perform functions akin to those of normal stem cells. Given the significant success in developing antibody-drug conjugates, specific therapies have been developed that can target biomarkers of ovarian CSCs and improve oncogenic outcomes and patient survival. Numerous cell surface markers, particularly CD117, CD24, CD44, EpCAM, and CD133, have been reported for the isolation of potential CSCs. EpCAM is increasingly expressed in various tumor types, and its reduced expression may lead to the loss of cell-cell adhesion capabilities and promote epithelial-to-mesenchymal transition. Catumaxomab is a monoclonal antibody against EpCAM that is tri-functional, engaging three different cell types: tumor cells, immune effector cells, and accessory cells. Additionally, Lin28 and Oct4 can also serve as targeted therapies for pluripotency in ovarian cancer.

Results: The scientific studies presented in this chapter indicate that the presence of cancer stem cells (CSCs) in ovarian tumors is responsible for the initiation of ovarian cancer pathogenesis and tumor formation. Furthermore, these CSCs also contribute to increased chemotherapy resistance in ovarian tumors, along with the generation of more non-tumorigenic differentiated cells. To eliminate these CSCs, understanding the biology and functional role of these CSCs in ovarian tumors is quite complex. Recent advancements in identifying new antibody-drug conjugates (ADCs) for targeting these CSCs in ovarian cancers have shown promise in eradicating ovarian CSCs.

Conclusion: These cells are also known as growth factor receptors of cancer stem cells and exhibit increased expression in ovarian cancer cells, demonstrating significant tumorigenicity in mouse models. They play roles in cellular proliferation, differentiation, adhesion, and apoptosis. CD117-positive cells activate the Wnt/β-catenin pathway, which has a key role in the development of chemotherapy resistance. One study reported that immunohistochemical analysis of 25 patients with advanced ovarian cancer showed that CD117-positive cell expression was detected in up to 40% of patients, and the expression of CD117 was strongly associated with the development of chemotherapy resistance. The use of chemotherapy agents alongside surgery is an effective treatment strategy for reducing tumor volume; however, most patients develop chemotherapy resistance due to

the persistence of ovarian cancer stem cells. It has been described that even a small number of cancer stem cells remaining after chemotherapy may increase the likelihood of disease recurrence. Several pathways have been proposed to be involved in the mechanisms related to this resistance, including the inactivation of pro-apoptotic factors, activation of anti-apoptotic factors, and enhancement of survival signals. Based on these mechanisms, understanding the incorrect response of cancer stem cells to chemotherapy may be attributed to factors such as drug flow, tumor dormancy, dormancy of cancer stem cells, enrichment of cancer stem cells during disease progression, glutathione system involvement, and apoptosis.

Keywords: Ovarian,Treatment,Stem cells,Cancer,Biomarkers of Ovarian

114.

Synergistic Cytotoxic Effect of Imiquimod and Cisplatin Combination Therapy on A549 Lung Cancer Cell (Research Paper)

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3.

Introduction: Background: Recently, combination therapy has become a promising approach to overcoming chemotherapy problems. In the present study, we describe a combinational treatment regime using cisplatin (Cis) and imiquimod (IMQ) to increase the antitumor response of the therapy in A549 lung cancer cells.

Methods: Methods: A549 cells were either treated with increasing concentrations of Cis or IMQ or with Cis-IMQ combinations for 24h. Cell growth inhibition, cell cycle analysis, and inductive apoptosis were evaluated using MTT assay and annexin V assay using flow cytometry, respectively. Kruskal-Wallis was used to analyze differences in cell groups' means.

Results: Results: A549 cell viability was affected by single therapy of Cis and IMQ in a dose and timedependent manner ($P < 0.001$). The combination index (CI) analysis revealed that the combined effect of Cis-IMQ exerted a wide range of synergy in lung cancer cells as well as 0.58 to 0.84 for IC10 to IC90. More interestingly, the combination of Cis and IMQ reduced the dose of Cis by 1.86-fold. In terms of cell apoptosis induction, Cis (IC20)-IMQ (IC90) displayed a synergistic effect on A549 cells, compared to the single drug ($P < 0.0001$). Co-treatment of A549 cells with Cis and IMQ significantly caused SubG1 arrest compared to Single therapy and control group.

Conclusion: Conclusion: These results indicated that an IMQ-based combination using Cis has synergistic effects on cell proliferation and apoptosis induction in A549 cells and deserves further preclinical and clinical studies.

Keywords: Synergism, Imiquimod, Cisplatin, Combination therapy, Apoptosis

115.

Systems biology research and bioinformatic analysis of PPP3R1 RNA interaction and expression analysis in non-small cell lung cancer (NSCLC) (Research Paper)

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Introduction: Lung adenocarcinoma (LUAD) and lung squamous cell carcinoma (LUSC) are the two most common types of lung cancer. In the past, they were grouped together under the name non-small cell lung cancer (NSCLC) and treated the same way. However, new studies suggest that LUAD and LUSC are different diseases and should be treated separately. Still, the specific clinical differences between LUAD and LUSC have not been fully explained yet (1)(2). The mitoribosome's regulatory subunit MRPL35 can control how cytochrome c oxidases assemble and is crucial for the development of non-small cell lung cancer (NSCLC). Knockdown of MRPL35 suppressed cell proliferation and decreased NSCLC progression both in vitro and in vivo. The possible molecular mechanisms were also clarified, which indicated that MRPL35 could be involved in cell apoptosis and proliferation by modulating the expression levels of CDK1, BIRC5, CHEK1, STMN1 and MCM2

Methods: Microarray analysis (GSE225959) was used to identify the key protein-coding gene affected in NSCLC. Validation of these findings and survival analysis were conducted using ENCORI. RNA and protein interactions were explored through miRWalk, lncRRIsearch, and STRING. The Enrichr and Reactome databases were employed to identify relevant signaling pathways.(4)

Results: Based on microarray analysis, PPP3R1 is significantly overexpressed in NSCLC. PPP3R1 modulates signaling pathways such as Signal Transduction and PI3K/AKT Signaling in cancer. lncRNAs NEAT1 and AATBC interact with PPP3R1 mRNA. Additionally, miR-22-3p suppresses the expression of PPP3R1 by binding to its 3' UTR region.

Conclusion: miR-22-3p, along with lncRNAs NEAT1 and AATBC, regulate Signal Transduction and PI3K/AKT signaling in cancer through their interaction with PPP3R1.

PPP3R1, NEAT1, and AATBC may be considered potential diagnostic biomarkers for non-small cell lung cancer (NSCLC).

Keywords: Microarray Analysis Diffraction expression analysis, non small cell lung cancer

116.

Targeting DYRK1B in triple-negative breast cancer: CRISPR-Cas9 mediated knockout reveals potential for therapeutic intervention (Research Paper)

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Introduction: Breast cancer is the most common cancer affecting women worldwide, with the triple-negative subtype (TNBC) being particularly aggressive and difficult to treat. DYRK1B, a dual-specificity kinase, is known to regulate cell cycle and quiescence. Although its role in various cancers has been studied, its impact on TNBC has not been well understood.

Methods: In this study, we employed CRISPR-Cas9 technology to knock out DYRK1B in MDA-MB-231 cells, a model for TNBC. We then assessed the effects on cell proliferation, apoptosis, invasion, migration, angiogenesis, and response to the chemotherapy drug Paclitaxel.

Results: The successful knockout (KO) of DYRK1B was confirmed using PCR, Sanger sequencing, and real-time qPCR. Compared to wild-type (WT) MDA-MB-231 cells, KO cells showed a marked decrease in cell proliferation, colony formation, migration, and invasion. Additionally, KO cells exhibited increased apoptosis and heightened sensitivity to contact inhibition and Paclitaxel. Gene expression analysis revealed altered levels of several genes

associated with the cell cycle, angiogenesis, and cell motility, including CCND1, MCM2, PCNA, CDKN1B, HIF1A, VEGFA, and WASF3. Immunocytochemistry further demonstrated that KO cells had significantly lower Ki67 expression, indicating reduced cell proliferation.

Conclusion: Our findings highlight the critical role of DYRK1B in the survival and invasive capabilities of TNBC cells. Targeting DYRK1B could offer a promising new therapeutic strategy for treating this challenging subtype of breast cancer. These results underscore the potential of DYRK1B as a novel target for therapeutic intervention in TNBC, paving the way for more effective treatments.

Keywords: Brest cancer, CRISPR-Cas9, DYRK1B, Quiescent cancer cell, Targeted therapy

117.

The clinical value of Biomarkers in papillary thyroid carcinoma Detection (Review)

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Introduction: Thyroid cancer is one of the most prevalent malignant endocrine cancer worldwide. The most common form of thyroid malignancy, PTC accounts for 80-85% of all thyroid malignancies. Despite its frequency detecting PTC from benign thyroid cancer is challenging due to its clinical signs overlap. Early and accurate diagnosis is essential for improvement patient outcomes, emphasizing the need for reliable biomarkers for PTC monitor. It has been observed that several tumor markers are associated with clinical utilities in the diagnosis, monitoring, and prognosis of PTC. In this review, we discuss key biomarkers, their roles in the clinical practice being: 1) Thyroglobulin Thyroglobulin (Tg) is a highly sensitive and specific tumor marker in patients who have undergone total thyroidectomy for PTC. Serum Tg levels are an effective and useful tumor marker for PTC. Postoperative serum Tg value is an important prognostic factor that is used to guide clinical management and is the most valuable tool in the long-term follow-up of patients with PTC However, the accuracy of Tg assays can be compromised by the presence of thyroglobulin antibodies (TgAb), which interfere with the measurement of Tg levels, rendering them unreliable in some patients 2) CA19-9 CA19-9 is traditionally used as a marker for gastrointestinal tumors, particularly pancreatic cancer . , recent studies suggest that it may have potential as a biomarker for PTC in cases where thyroglobulin levels are unreliable due to TgAb interference. Unlike Tg, CA19-9 levels are unaffected by TgAb, CA19-9 offers an alternative for patients with TgAb, as it is unaffected by TgAb levels. It could serve as a surrogate marker in cases where traditional monitoring with Tg is not feasible Pathological examination including immunohistochemistry (IHC) has been a gold standard for PTC diagnosis and predicting outcomes in PTC. Biomarkers such as BRAF V600E, Cytokeratin 19 (CK-19), and Galectin-3 (Gal-3) proteins' expressions, as determined by IHC, are approved. Therefore, Number of studies have confirmed that the expression of CK-19 was generally increased in malignant thyroid conditions 3) NrF2 Recent research has identified Nrf2 as a novel biomarker with significant clinical implications in PTC. Nrf2 is highly expressed in papillary thyroid carcinoma tissue compared to adjacent normal tissue and nodular goiter tissues. The increased expression of Nrf2 was significantly associated

with PTC and suggests that Nrf2 could serve as a valuable biomarker for diagnosing PTC with a high sensitivity The study also showed that Nrf2 expression was significantly higher in patients with lymph node metastasis (LNM). This indicates that Nrf2 could be used not only to diagnose PTC but also as a predictive marker for the likelihood of lymph node metastasis, with a sensitivity of 96% and specificity of 88.57% thorough western blot, qPCR, FIA, ELISA etc.

Methods: western blot, qPCR, FIA, ELISA etc

Results: While CA19-9 represent an alternative approach to the Tg measurement, in cases where Tg levels are interfered by TgAb, Nrf2 offers larger diagnostic and prognostic capability. Particularly for detecting lymph node metastasis and and relation with other relevant biomarkers. Additionally, the variety of detection methods available for Nrf2 enhances its clinical utility and versatility compared to the limited detection techniques available for CA19-9. Ultimately, Nrf2 would provide a more comprehensive diagnostic and prognostic approach in PTC management and thus represents a promising complement or alternative to conventional biomarkers such as CA19-9 and Tg

Conclusion: Currently, tg is used more in clinical studies, but in the future, clinical biomarkers that are more accurate and effective both before and after surgery will definitely be used.

Keywords: papillary thyroid carcinoma – Biomarkers- Thyroglobulin- CA19-9- NrF2

118.

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-500a-5p, miR-378a-3p, miR-378d, miR-34a, miR-145, miR-181b-5p, miR-218, miR-34a-5p, miR-588, miR-205, and miR-381 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

119.

The Dual Role of LOX Proteins in Cancer: Drivers of Progression and Suppression

(Review)

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Introduction: Cancer is a complex disease driven by uncontrolled cell growth and the formation of malignant tumors. Lipid metabolism plays a significant role in cancer initiation and progression, with metabolic disorders such as obesity, insulin resistance, and chronic inflammation linked to increased cancer risk. Reactive oxygen species (ROS), highly reactive molecules, contribute to carcinogenesis by damaging lipids, proteins, and DNA. Elevated ROS levels are often triggered by the binding of oxidized low-density lipoprotein (ox-LDL) to the LOX-1 receptor. While the role of ROS is clear, the involvement of lysyl oxidase (LOX) proteins in cancer progression remains more complex. This study examines how LOX proteins influence lipid metabolism and tumor behavior, exploring their dual function as both cancer promoters and suppressors, depending on the tumor environment and cancer type.

Methods: The research involved a review of studies that assessed LOX expression and function across various cancer types, including breast, colorectal, pancreatic, hepatocellular carcinoma (HCC), prostate, and lung cancers. Techniques such as gene expression profiling and RNA silencing were used to investigate LOX's effects on cancer cell proliferation, migration, invasion, and angiogenesis. A key area of focus was LOX's role in remodeling the extracellular matrix (ECM), the network of proteins that supports cell structure. LOX proteins increase ECM stiffness by cross-linking collagen and elastin, which enhances the invasive ability of cancer cells. The study also investigated LOX's involvement in promoting epithelial-mesenchymal transition (EMT), a process through which cancer cells gain more aggressive traits, becoming more migratory and invasive.

Results: LOX proteins, particularly LOX-1, were frequently upregulated in various cancers, driving tumor growth and metastasis. In breast cancer, higher LOX expression was linked to larger tumors, more advanced stages, and poor prognosis, especially in hormone receptor-

negative cases. LOX silencing in breast cancer cells reduced their ability to migrate and invade, likely due to the downregulation of matrix metalloproteinases (MMP-2 and MMP-9), which facilitate ECM degradation. In hepatocellular carcinoma (HCC), LOX expression correlated with worse patient outcomes, early recurrence, and increased EMT activity. Silencing LOX in HCC cells reduced tumor proliferation and migration, as well as the production of vascular endothelial growth factor (VEGF), a critical factor in angiogenesis. Other cancers also showed significant roles for LOX. In gastric cancer, high LOX expression was associated with greater lymph node metastasis and poor patient outcomes. In non-small cell lung cancer (NSCLC), LOXL2 was upregulated in advanced disease stages, with microRNAs targeting LOXL2 found to suppress lung cancer cell growth and invasiveness. Although LOX commonly promotes cancer, in certain contexts it acts as a tumor suppressor. In prostate cancer, LOX showed a paradoxical role, sometimes promoting metastasis but also suppressing tumor growth in other cases. A similar pattern was observed in colorectal cancer, where LOX's role varied depending on whether it was located inside or outside the cell, indicating the importance of cellular context. This duality in LOX's behavior suggests its role in cancer progression is not uniform across all cancer types. While LOX typically drives metastasis, in specific cancers like prostate and colorectal, it may inhibit tumor progression. This complexity highlights the need for further research to better understand how LOX's actions are influenced by its tumor microenvironment.

Conclusion: LOX proteins play a crucial but complex role in cancer, acting as both promoters and suppressors of tumor growth. In many cancers, LOX proteins contribute to metastasis by stiffening the ECM, allowing cancer cells to invade new areas. However, in certain conditions, LOX can also suppress tumor growth, making it a complicated target for cancer therapy. Targeting LOX presents opportunities but also challenges for cancer treatment. Inhibiting LOX could help reduce metastasis and improve outcomes in cancers like breast and hepatocellular carcinoma. However, because LOX also has tumor-suppressing functions in some cancers, therapies need to be tailored carefully to avoid negative effects. Understanding the mechanisms that dictate LOX's role in different cancers is crucial for developing effective therapies. In summary, LOX proteins represent a promising yet complex target in cancer therapy. Their ability to both promote and inhibit cancer progression, depending on the tumor environment, suggests that future treatments could focus on either inhibiting or enhancing LOX activity to achieve the desired outcomes in various cancers.

Keywords: Cancer ,LOX (Lysyl Oxidase),Epithelial-Mesenchymal Transition (EMT),Extracellular Matrix (ECM),React

120.

The Dual Role of PD-L1 in Gastric Cancer: Prognostic Marker and Therapeutic Target (Review)

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Introduction: Gastric cancer is one of the most common cancers globally, ranking fourth in incidence and second in mortality among all cancers. It is a complex and multifactorial disease involving various etiological factors such as Helicobacter pylori infection, high salt intake, smoking, and genetic predispositions.Despite advancements in treatment, including surgery and chemotherapy, the prognosis remains poor,. Programmed death-ligand 1 (PD-L1) is a protein that plays a significant role in suppressing the immune system by binding to its receptor, PD-1, on T cells. In gastric cancer, PD-L1 expression has been associated with various clinical outcomes. Studies have shown that PD-L1 is upregulated in gastric cancer tissues and is positively correlated with the presence of tumor-infiltrating immune cells (TIICs). PD-L1 expression in tumor cells and TIICs has been linked to better prognosis in some cases, particularly when co-expressed with PD-1. However, other studies have reported that high PD-L1 expression is associated with poor prognosis and advanced disease stages.

Methods: A comprehensive literature search was conducted across three databases: PubMed, the Scientific Information Database (SID), and Web of Science. The search covered the period from 2013 to 2024 and utilized the keywords "PD-L1 marker" and "gastric cancer." In the SID database, one relevant result was identified. The PubMed search yielded a total of 189 articles. After applying the inclusion criteria, 11 articles were selected for further review. Following the removal of duplicate records, a total of 19 articles were examined in detail to assess the role of the PD-L1 marker in gastric cancer

Results: Mechanism and Physiological Relationship Between Stomach Cancer and PD-L1 Protein Mechanism: 1. Immune Evasion: PD-L1 (Programmed Death-Ligand 1) is a protein expressed on the surface of tumor cells, including gastric cancer cells. It binds to the PD-1 receptor on T cells, leading to the inhibition of T cell activity and allowing cancer cells to evade immune detection and destruction. 2. Regulation of PD-L1 Expression: The expression of PD-L1 in gastric cancer can be regulated by various mechanisms, including

genetic alterations, epigenetic modifications, and signaling pathways. For instance, the EZH2 enzyme can enhance PD-L1 stability through the deubiquitination process mediated by USP22, promoting immune evasion [Yang, 2024]. Additionally, the loss of Fructose-1,6-bisphosphatase (FBP1) can upregulate PD-L1 expression via the STAT3 pathway, further contributing to immune escape. 3. Tumor Microenvironment: PD-L1 expression is also influenced by the tumor microenvironment. Factors such as hypoxia, inflammatory cytokines, and the presence of immune cells can modulate PD-L1 levels on tumor cells, affecting the immune response. Physiological Relationship: 1. Immune Checkpoint Inhibition: The interaction between PD-1 on T cells and PD-L1 on gastric cancer cells is a critical immune checkpoint that suppresses the immune response. Blocking this interaction with immune checkpoint inhibitors (ICIs) can restore T cell activity and enhance the immune system's ability to target and destroy cancer cells. 2. Therapeutic Implications: The expression of PD-L1 in gastric cancer has significant implications for immunotherapy. High PD-L1 expression is often associated with a better response to ICIs, making it a valuable biomarker for selecting patients who may benefit from such treatments. 3. Clinical Outcomes: The relationship between PD-L1 expression and clinical outcomes in gastric cancer is complex. While some studies suggest that high PD-L1 expression correlates with better prognosis and response to therapy, others indicate that it may be associated with more aggressive disease and poorer outcomes

Conclusion: Unlocking the Secrets of PD-L1 Prognostic Power Some studies suggest that the co-expression of PD-1 and PD-L1 in tumor cells and immune cells paints a rosy picture, hinting at a favorable prognosis. This harmonious duet could be the key to reducing mortality risk. On the other hand, patients with high PD-L1 expression accompanied by low CD8/FOXP3 ratios might experience increased survival rates. It appears that the intersection of multiple immune markers can yield more accurate survival predictions. The Shadowy Side of PD-L1 However, other findings reveal a darker tale. Elevated PD-L1 expression coupled with low densities of TILs portends a poor prognosis. This correlation suggests that PD-L1 alone may not be a reliable harbinger of fate. Furthermore, high levels of post-operative EV PD-L1 could signal a poor overall survival and recurrence-free survival. #### Taking the Pulse of Therapy Response Chemotherapy Insights The connection between PD-L1 and MSI status holds promise for predicting chemotherapy efficacy. In MSI-high tumors with PD-L1 positive, adjuvant chemotherapy demonstrates better disease-free survival compared to microsatellite-stable counterparts. This harmony could guide treatment decisions and optimize outcomes. Immunotherapy's delicate Dance

PD-L1's intricate relationship with HER-2 status reveals a complex melody. Patients with tumors bearing both PD-L1 and HER-2 positive status tend to experience lower progression-free survival. This harmonious union might serve as a predictive harmonica, allowing us to anticipate both prognosis and immunotherapy efficacy. PD-L1 serves as a significant marker in gastric cancer, offering both strengths and weaknesses in its application as a prognostic and predictive tool. One of the key strengths of PD-L1 is its comprehensive prognostic value. When integrated with other immune markers, such as CD8 and FOXP3, PD-L1 enhances the accuracy of prognosis and aids in better patient stratification. This allows for a more nuanced understanding of a patient's likely disease progression, leading to more tailored treatment approaches. Additionally, PD-L1 provides therapeutic guidance by helping to identify patients who are more likely to benefit from immunotherapy and chemotherapy, thus supporting personalized treatment strategies. This makes PD-L1 a valuable tool in the context of precision medicine. However, there are notable weaknesses in using PD-L1 as a sole marker. Its prognostic value is inconsistent, as different studies report conflicting outcomes. Some research suggests that PD-L1 is associated with favorable prognoses, while others link it to poor outcomes. This inconsistency makes it difficult to rely on PD-L1 alone for accurate prognostication. Furthermore, the complex interactions between PD-L1 expression and the immune microenvironment present additional challenges. The relationship is intricate, and accurate predictive modeling often requires the integration of multiple markers rather than relying on PD-L1 in isolation. In summary, while PD-L1 has substantial strengths in enhancing prognostic accuracy and guiding therapeutic decisions, its inconsistent prognostic value and the complex interactions with the immune environment limit its effectiveness as a standalone marker.

Keywords: Gastric cancer PD-L1 New marker

121.

The effect of Helicobacter pylori (H. pylori) on Gastric Cancer (GC) (Review)

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Introduction: Gastric cancer (GC) remains the fifth most common malignant tumor and the third leading cause of cancer death, despite the decline in incidence and mortality worldwide over the past five decades. Helicobacter pylori is the predominant species of the human stomach microbiome, and its proliferation causes a persistent inflammatory reaction. Gastritis caused by H. pylori is the strongest unique risk factor for stomach cancer; however, only a small proportion of infected people develop malignancy. Two distinct histological types of stomach cancer have been described, each with different pathophysiological characteristics. Gastric cancer of the dispersed type usually affects young people and includes neoplastic cells individually that do not form the structure of the glands. The more common form of stomach cancer progresses through a series of histological stages that begin with the transition from normal mucus to chronic superficial gastritis, which then leads to atrophic gastritis and intestinal metaplasia and eventually to dysplasia and adenocarcinoma2. Helicobacter pylori is a microbial species that specifically colonizes the stomach epithelium and is the most common bacterial infection worldwide. The effectiveness of eradicating H. pylori has been proven for GC and Prevention of precancerous lesions in different populations. H. pylori, such as intestinal microbiota dysbiosis, has remained metabolic effects and increased prevalence of antibiotic-resistant pathogens. Previous retrospective studies had reported dysbiosis microbial communities, altered bacterial interactions, and an overreach of intestinal buds in GC and precancerous lesions. Non-H stomach bacteria. pylori may also play an important role in stomach carcinogenesis, although the exact mechanism has not yet been determined. But our goal in this study is to continue to examine the effect of the most common bacterial infection and its conversion to stomach cancer.

Methods: In this study,15 articles published from 2016 to 2024, which were in the form of original research and systematic review were examined. The study used the keywords Gastric Cancer(GC), New model for Diagnosis of cancer, H.pylori.

Results: Almost 700,000 people are diagnosed with this malignant cancer every year, and the 5-year survival rate in the United States is <15% 1. Microbial network analysis showed that the presence of H. pylori affects the strength of microbial gastric interactions, which may be associated with GC progression. However, whether H. pylori can act as a bacterial driver and interact with other stomach bacteria that are later involved in the carcinogenic process, still unknown. Until now, studies characterizing changes in the entire micro-gastrointestinal ecosystem on the eradication of H. pylori is limited. Inflammation of the stomach is known to be associated with the risk of disease here, in which gastritis anthral is associated with duodenal ulcer, as well as pangasteritis can lead to ulcers of the stomach and adenocarcinoma. Duodenal ulcer processes as a result of the colonization of the stomach by H. pylori is initially caused by inflammation caused by H. pylori is created. This then leads to a decrease in the number of D cells that produce somatostatin that prevents the release of the stomach. This is known as higher gastric levels in patients with H. pylori is seen positive and therefore increased acid secretion (caused by the stomach) in the stomach body. The next step to increase the risk of duodenal ulcer remains disputed, with this increased acid secretion potentially contributing to the formation of gastric metaplasia in duodenum; this can also be achieved by H. pylori to be colonized to lead to further inflammation and scarring.

Conclusion: Studies that focus on specific interactions between H. pylori and its host focus can provide models for general patterns that may spread to other malignancies that develop from inflammatory foci in the liver and digestive tract. Most cellular liver cancers are related to chronic hepatitis B and hepatitis C infections, and biliary tract cholangiocarcinoma is strongly associated with chronic inflammation caused by parasites. Chronic esophagitis, pancreatitis and ulcerative colitis each significantly increase the risk of adenocarcinoma at their respective anatomical sites. Focusing on colorectal neoplasia, commonalities between inflammatory-induced stomach cancer and cancers that arise in the context of ulcerative colitis have been reported. It is hoped that in the near future, according to the studies carried out, the progress of this problem and the resulting issues can be prevented.

Keywords: Gastric Cancer(GC), New model for Diagnosis of cancer, H.pylori

122.

The Emerging Role of Plant, Animal, and Microbial Exosomes for Targeted Cancer Drug Delivery (Review)

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Introduction: Cancer is a leading global health issue, causing approximately 10 million deaths in 2020, with projections of 16.3 million by 2040. Traditional treatments, including chemotherapy and immunotherapy, often result in side effects due to their lack of specificity, harming healthy tissues. Consequently, there is a growing need for improved drug delivery systems. Extracellular Vesicles (EVs), particularly exosomes, present a promising alternative due to their biocompatibility and ability to transport diverse therapeutic cargo with minimal immune response. Exosomes play critical roles in cellular communication and are involved in cancer processes, serving both diagnostic and therapeutic functions. Here, we summarized the potential use of exosomes as vehicles for cancer drugs.

Methods: Isolation: One of the crucial challenges in EV research is its isolation and the topic is under constant development. Common techniques include ultracentrifugation, density gradient centrifugation, ultrafiltration, size exclusion chromatography (SEC), immunoaffinity capture, tangential flow filtration (TFF), and polymer precipitation. Each technique has its pros and cons. More advanced methods like microfluidics, lipid nanoprobes, and thermo-acoustofluidic separation have emerged to enhance exosome isolation efficiency. Drug Loading Techniques: Exosome drug loading can be categorized into passive and active methods. Passive loading, such as co-incubation, is straightforward but often less effective. Conversely, active loading techniques—including ultrasound, electroporation, and freeze-thaw cycles disrupt the exosome membrane to facilitate drug incorporation; thus, they require careful handling to maintain integrity. Alternative methods, like saponin-assisted loading and transfection, also enhance drug uptake. Active methods typically accomplish higher drug concentrations, but maintaining exosome integrity is crucial for effective therapy. Exosome Targeting: Several strategies can enhance exosome targeting in cancer treatment, including surface modification, genetic

engineering, drug loading, nanoparticle fusion, and donor cell preconditioning. In this regard, monoclonal antibodies (mAbs) are being explored to improve targeting. Moreover, folate-conjugated therapeutics that target the folate receptor are used to target many cancer cells. Engineered exosomes have been used to target both T-cell surface CD3 and the cancer-associated epidermal growth factor receptor (EGFR) demonstrating effective killing of breast cancer cells.

Results: Plant-Based Exosomes: Plant exosomes bearing bioactive compounds with antioxidative and anti-inflammatory properties are easily produced in large quantities. They are well-tolerated in the human body, exhibiting low toxicity and minimal immunogenicity. Their stability in the gastrointestinal tract enhances efficacy for oral administration, and they can extend drug circulation time at their target sites. They also have the potential to cross the blood-brain barrier (BBB) and can be applied on the skin. However, challenges include variability in lipid composition compared to animal exosomes, limited research, and extraction difficulties. Animal-Derived Exosomes: Animal-derived exosomes present advantages for therapeutic use. They are biocompatible, have low toxicity, and can carry diverse bioactive molecules. As biomarkers for cancer diagnosis, they facilitate non-invasive liquid biopsies using proteins and microRNAs associated with cancers, such as PD-L1 and miR-15b-3p. Nevertheless, challenges exist, such as insufficient clinical-grade production, variability in composition, and low yield and purity from extraction methods. These factors, coupled with limited drug loading efficiency, potential immunogenicity, and regulatory hurdles, indicate the need for further research. Microbial Exosomes: Microbial exosomes, particularly bacterial extracellular vesicles, offer innovative approaches for cancer treatment. They can target cancer cells and are adaptable for personalized therapies. BEVs maintain stability under physiological conditions, can encapsulate various biomolecules, and be engineered for improved targeting and reduced immunogenicity. Their rapid bacterial proliferation and advanced culturing techniques enable cost-effective high-yield production. Yet, challenges such as production difficulties, immunogenicity concerns, regulatory issues, and heterogeneous properties affecting drug loading and pharmacokinetics pose obstacles. Additionally, limited knowledge of host-bacterial interactions remains.

Conclusion: In conclusion, exosomes, particularly plant-derived exosomes, exhibit substantial promise as natural nanocarriers for cancer therapy. They effectively maintain drug potency and half-life, possess natural cell permeability, and can bypass barriers while

evading lysosomal degradation. While animal and microbial exosomes have therapeutic applications, plant-derived exosomes stand out due to their natural origin and freedom from zoonotic pathogens. Emerging studies highlight their safety and effectiveness across various drug delivery routes, demonstrating abilities to enhance chemotherapy, target cancer cells, and overcome drug resistance. For instance, ginger EVs can deliver miRNAs to reduce lung inflammation, while bitter melon EVs enhance chemotherapy effectiveness for oral cancers.

Keywords: Antioxidants, Anti-inflammation, Cancer Therapy, extra-vesicular bodies, microfluidics

123.

The impact of neoantigen vaccines on colorectal cancer treatment (Review)

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Introduction: Colorectal cancer (CRC) is a neoplastic disease of the digestive tract characterized by a gradual onset and an unfavorable prognosis. It ranks as the third most prevalent cancer globally. Cancer is characterized by the uncontrolled proliferation of cells, leading to the formation of tumors. When these aberrantly proliferating cells invade adjacent normal tissues or spread throughout the body, the condition is classified as cancer. Genetic alterations primarily drive the transformation of normal somatic cells into cancerous cells. The heterogeneous nature of these genetic changes, predominantly consisting of mutations, contributes to the complexity of cancer as a disease. Neoantigens are uniquely expressed, enabling them to provoke T-cell responses specific to the tumor, thereby minimizing the risk of unintended damage to non-malignant tissues. These neoantigens are novel epitopes that arise from somatic mutations, offering the potential to bypass T-cell central tolerance to self-epitopes and consequently stimulate immune responses against tumors. Neoantigens represent optimal therapeutic targets due to their capacity to enhance therapeutic specificity, circumvent immune tolerance, and reduce the likelihood of autoimmunity. Consequently, they demonstrate significant efficacy in colorectal cancer treatment.

Methods: This study was conducted through extensive searching of databases such as Google Scholar, PubMed, Scopus, and the Web of Science, as well as scientific articles obtained from these platforms. Furthermore, authoritative scientific books and studies published in international congresses were used.

Results: The development of colorectal cancer (CRC) primarily involves three signaling pathways: chromosomal instability (CIN), microsatellite instability (MSI), and CpG island methylation phenotype (CIMP), that neoantigen can affect them. Tumor antigens can be categorized. Tumour-associated antigens (TAAs) and Tumour-specific antigens (TSAs), are also known as neoantigens. Neoantigens can arise from non-synonymous somatic mutations, including single nucleotide variants (SNVs), insertions and deletions (indels),

frameshift mutations, other genomic rearrangements, and post-transcriptional abnormalities. Additionally, neoantigens may be generated through cancer-specific post-translational protein modifications, such as methylation. In colorectal cancer (CRC), small indels are the most prevalent source of neoantigen production. The initial step in developing individualized neoantigen-based therapeutics involves sequencing cancer cells through whole-genome sequencing (WGS). This sequencing aims to identify tumor-specific somatic mutations, which include single nucleotide variants (SNVs), insertions and deletions (indels), fusions, and other forms of genetic variation. Following this, human leukocyte antigen (HLA) typing is conducted, and predictions regarding the interactions between HLA, neoantigens, and T cell receptors (TCRs) are made based on the sequencing data. Subsequently, the mutant peptide is identified by integrating somatic mutations, splicing variants, and HLA binding predictions. Neoantigens produced by frameshift mutations are recognized by the immune system, leading to an effective T-cell response against cancer cells. Antigen-presenting cells (APCs), particularly dendritic cells (DCs), are activated by neoantigens through processes such as phagocytosis. The presence of neoantigens enhances the expression of major histocompatibility complex (MHC) class I and II molecules, as well as co-stimulatory molecules on DCs, a process facilitated by interleukin (IL)-12 and various chemokines. Neoantigens are transported to the endoplasmic reticulum, where they bind to MHC class I molecules and form the T-cell receptor (TCR)-peptide-MHC (pMHC) complex for presentation to T cells. CD8+ T cells recognize neoantigen-loaded DCs, leading to the production of effector and memory T cells, which initiate a robust T-cell immune response. Tumor destruction is mediated by the cytotoxic effects of T cells and the production of cytokines such as interferon-gamma (IFN-γ) and tumor necrosis factor-alpha (TNF-α). Neoantigen-specific CD4+ T cells also contribute to anti-tumor immunity by activating DCs and producing cytokines that enhance CD8+ T-cell responses. Additionally, CD4+ T cells can exhibit cytotoxic properties and directly kill tumor cells expressing MHC class II molecules following therapeutic vaccination. Generally, there is a clear role for neoantigens in the immunotherapy of colorectal cancer.

Conclusion: The special anti-tumor effects and low incidence of adverse reactions. Adverse events indicate that immunotherapy targeting neoantigens is a significant therapeutic strategy for Neoantigen-based therapy, whether used alone or in combination with other treatments, Other treatment strategies are being utilized in numerous clinical

trials, marking the beginning of a new era; however, they will also encounter ongoing challenges.

Keywords: organ-specific neoantigen, Vaccines, Colorectal Neoplasms

124.

The Interplay Between Gut Microbiome Modulation, Probiotics, and Cancer (Review)

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Introduction: The human gut microbiome, a complex ecosystem of microorganisms, has emerged as a pivotal player in various physiological processes, including immune function and cancer development. Dysregulation of the gut microbiome, often characterized by an imbalance in microbial composition (dysbiosis), has been implicated in a variety of cancers. Probiotics, live microorganisms administered to confer health benefits, have garnered significant attention as potential modulators of the gut microbiome and immune system. This review explores the intricate relationship between gut microbiome modulation, probiotics, and cancer, highlighting the mechanisms through which probiotics may exert their anticancer effects.

Methods: A comprehensive literature search was conducted using electronic databases, including PubMed, Scopus, and Web of Science, to identify relevant studies published between 2010 and 2024. Keywords such as "gut microbiome," "probiotics," "cancer," "immune modulation," and "mechanisms" were employed to refine the search. The selected studies were critically evaluated for their methodological rigor, sample size, and relevance to the research question.

Results: The findings from the reviewed studies collectively suggest a strong association between gut microbiome dysbiosis and cancer development. Several mechanisms have been proposed to explain this relationship, including altered immune responses, increased inflammation, and the production of carcinogenic metabolites by dysbiotic microbiota. Probiotics have shown promising potential in modulating the gut microbiome and mitigating these adverse effects. By restoring microbial balance and enhancing immune function, probiotics may exert anticancer effects through various mechanisms. These include: Immune system modulation: Probiotics can stimulate the production of beneficial immune cells, such as natural killer cells and T cells, which play a crucial role in tumor surveillance and elimination. Inflammation reduction: Chronic inflammation is a risk factor

for cancer development. Probiotics have been shown to reduce inflammation by inhibiting pro-inflammatory cytokines and promoting anti-inflammatory responses. Modulation of signaling pathways: Probiotics can influence signaling pathways involved in cancer cell proliferation, survival, and invasion, such as the Wnt, Notch, and NF-κB pathways. Production of bioactive compounds: Some probiotics produce bioactive compounds, such as short-chain fatty acids and secondary bile acids, which have been linked to anticancer effects.

Conclusion: The growing body of evidence supports the notion that the gut microbiome plays a critical role in cancer development and progression. Probiotics offer a promising approach to modulate the gut microbiome and potentially reduce cancer risk. However, further research is needed to elucidate the precise mechanisms underlying the anticancer effects of probiotics and to identify the optimal probiotic strains and dosages for different cancer types. References: Arumugam, M., et al. (2011). Enterotypes of the human gut microbiome. Nature, 473(7347), 174-180. Zackular, J. P., et al. (2016). Dietary and microbial interactions in colorectal cancer. Cell Host & Microbe, 19(6), 714-724. Schwabe, C. F., & Brenner, D. A. (2013). Mechanisms of gut microbiota-induced inflammation and colorectal cancer. Cancer Journal, 19(1), 7-13. Chen, W., et al. (2016). Probiotics for cancer treatment: A systematic review and meta-analysis. Journal of Clinical Gastroenterology, 50(1), 43-51.

Keywords: Cancer, Probiotics, Gut Microbiota, Cancer Prevention

125.

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, salmonella,Escherichia coli

126.

The Potential of Linum usitatissimum extract in Breast Cancer Therapy: A Focus on Apoptosis Regulation (Research Paper)

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Introduction: Breast cancer remains one of the most significant health challenges worldwide, accounting for a substantial proportion of cancer-related morbidity and mortality among women. Current treatment strategies, while effective in many cases, are often associated with severe side effects, drug resistance and recurrence. As a result, there is growing interest in alternative or complementary therapies, particularly those derived from natural compounds. Linum usitatissimum (flaxseed) is one such plant-based substance known for its rich content of lignans, omega-3 fatty acids and other bioactive components that have been shown to possess anti-cancer properties. This study explores the effects of Linum usitatissimum extract on the expression of key caspase genes (CASP3, CASP8 and CASP9) within the MCF-7 breast cancer cell line. These caspases are integral to the process of apoptosis, a form of programmed cell death, which is often dysregulated in cancer cells, leading to uncontrolled proliferation.

Methods: In our study, MCF-7 breast cancer cells were treated with various concentrations of Linum usitatissimum extract, and changes in gene expression were evaluated using quantitative PCR (qPCR). The focus was on the CASP3, CASP8 and CASP9 genes, which are known to play pivotal roles in the intrinsic and extrinsic pathways of apoptosis. CASP3 is considered the executioner caspase, while CASP9 is involved in the intrinsic (mitochondrial) apoptotic pathway and CASP8 is associated with the extrinsic (death receptor-mediated) pathway.

Results: The data showed a statistically significant increase in the expression of CASP3 ($p = 0.0112$) and CASP9 ($p = 0.0093$) following treatment with Linum usitatissimum extract, suggesting that the extract induces apoptosis through the activation of these pathways. CASP3, being the primary executioner caspase, is essential for the cleavage of various cellular components leading to cell death. CASP9, activated by mitochondrial signals, further supports the role of Linum usitatissimum in triggering intrinsic apoptotic mechanisms. In contrast, the upregulation of CASP8, while observed, did not reach statistical significance ($p = 0.0831$), indicating that the extrinsic apoptotic pathway might not be as strongly involved in the extract's mechanism of action.

Conclusion: These findings suggest that Linum usitatissimum may exert its anti-cancer effects primarily through the intrinsic apoptotic pathway, enhancing the activation of CASP3 and CASP9 in MCF-7 cells. This mode of action could make it a valuable adjuvant in breast cancer therapy, particularly in cases where conventional treatments fail to induce sufficient apoptosis or are limited by toxicity and resistance. Further studies are needed to fully elucidate the molecular pathways affected by Linum usitatissimum and to confirm its potential therapeutic benefits in vivo. This research underscores the promise of plant-based compounds in cancer therapy and suggests that Linum usitatissimum may contribute to novel, less toxic treatment strategies for breast cancer.

Keywords: Linum usitatissimum, Caspase genes, MCF-7 cells, Apoptosis regulation, Breast cancer therapy.

127.

The Potential of Mesenchymal stem cells in cancer treatment (Review)

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Introduction: Multipotent cells known as mesenchymal stem cells (MSCs) or mesenchymal stromal cells are extracted from the connective tissue that envelops other tissues and organs. Out of all the stem cell kinds, they have drawn the most attention. Over the past three decades, their therapeutic potential against various diseases has been extensively investigated. Their ability to self-renew, differentiate into several lineages, and perform immunomodulatory tasks is the reason. Additionally, the key advantage of employing MSCs for therapeutic reasons in both acute and chronic conditions is their readily available nature, as well as their capacity to be expanded to clinically necessary numbers. Peripheral blood, fat tissue, skeletal muscle, placenta, synovial fluid, Wharton jelly of the umbilical cord, and amniotic fluid are conveniently accessible sources from which MSCs can be extracted. The aim of this study was to investigate the Potential of Mesenchymal stem cells in cancer treatment.

Methods: The study of the Potential of Mesenchymal stem cells in cancer treatment which was done by searching scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: According to the findings, MSCs near the site of injury undergo differentiation into mature cells and release extra paracrine substances that aid in tissue remodelling and repair. It is believed that an active inflammatory response is necessary for MSC migration to tumor sites. They move into the tumors like the way they migrate into wounded tissues. One of the most researched signaling pathways in the recruitment of MSCs to the tumor microenvironment (TME) is the CXCL12/CXCR4 axis. The tropism of bone-marrow-derived MSCs to tumors has been driven by several factors, including cyclophilin B, urokinase plasminogen activator, hepatoma-derived growth factor, interleukin 6 (IL 6), basic fibroblast growth factor, and vascular endothelial growth factor (VEGF). These factors also affect MSC migration. Kidd et al.'s research has demonstrated that MCP-1 and insulin-like growth factor 1 from breast cancer encourage MSC migration to the tumor site. Similar

research using medulloblastoma cells has demonstrated that umbilical cord-derived MSC move to the tumor site in response to matrix metalloproteases. The variable degree of MSC migration is influenced by some parameters rather than just one signal molecule. Once inside the tumor niche, MSCs engage in both direct and indirect interactions with cancer cells that have an impact on the growth of tumors.

Conclusion: The review suggests that MSC has the potential to be a therapeutic agent in the battle against cancer. Current MSC-based therapies provide highly personalized, tailored cancer treatments. The first of these is the utilization of MSC-derived exosomes, which have a wider safety profile than MSC, and modified MSC to transport therapeutic medicines. Considerable work is required to learn more about how MSCs interact with various signaling pathways to suppress the growth of tumors.

Keywords: Mesenchymal stem cells, cancer, exosomes

128.

The role of Artificial Intelligence (AI) in breast cancer diagnosis (Review)

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Introduction: Breast cancer is a condition in which abnormal breast cells get out of control and form tumors. If left unchecked, tumors can spread throughout the body and become deadly. Breast cancer cells begin inside the milk ducts and/or lobules that produce breast milk. According to our studies, breast cancer screening with mammography is very effective in reducing breast cancer-related deaths. In addition, it is important to minimize errors and misinterpretations of lesions visible in digital mammography, which contributes to at least 25% of detectable cancers. Computer-aided diagnostic systems (cads) were introduced as assisting radiologists who tried to improve human diagnostic performance. Although some studies have shown that single plus CAD reading can replace double reading, few, if any, have identified the real benefits of using single plus CAD versus single reading alone (e.g., the real benefits of radiologists ' on-screen performance). In general, the benefits of using CAD in screening are still unclear. However, significant advances in gene (AI) AI with deep complex neural networks (com manly known as deep learning algorithms) reduce the performance difference between humans and com putters in many medical imaging applications, including breast cancer diagnoses.

Methods: Our search strategies and data sources following the preferred reporting cases for systematic reviews and meta-analysis guidelines (PRISMA) for systematic review and meta-analysis, we conducted a systematic literature review to integrate the findings of quantitative studies. Our systematic literature research reviewed 7 electronic databases: Scopus, CINAHL, Medline via PubMed, Web of Science, EMBASE, Cochrane Library (review and central). Using grid and manual search terms, the keywords being explored are: " Breast cancer ", "", " Artificial Intelligence (AI) ", "cancer survivors*," post-treatment*, in combination with "risk factors", "outcomes" and " Other eligible studies were identified by examining cited sources from published studies obtained.

Results: Breast cancer is one of the leading causes of death among women. Early detection, proper control mechanism and treatment of breast cancer can significantly improve the lives of millions of women worldwide. Several popular imaging methods such as MGS, US, MRI and HP images are used among many others to detect breast cancer. Given the importance of finding a solution/framework for early detection and detection, recently many AI researchers are focusing on automating this task. The various imaging methods used by researchers to automate the work of breast cancer diagnosis are mammography, ultrasound, magnetic resonance imaging, histopathological images, or any combination thereof. . Automated AI capabilities provide the potential to enhance the diagnostic expertise of physicians, including accurate determination of tumor volume, extraction of characteristic cancer phenotypes, translation of tumor phenotype characteristics into clinical genotype implications, and risk prediction. Combining image-specific findings with underlying genomic, pathological and clinical characteristics is increasing in value in breast cancer. The simultaneous emergence of newer imaging techniques has provided radiologists with diagnostic tools and image datasets for analysis and interpretation. Integrating an AI based workflow into breast imaging enables the integration of multiple data streams into powerful multidisciplinary applications that may guide the path to specific patient's personal medicine.

Conclusion: Most of our research focused on breast cancer diagnosis and subtype classification. This leaves room for future research to address various related topics such as identifying risk levels and predicting the likelihood of relapse. One direction for future research relates to the implementation of multi-class predictors using genetic data. Most research papers used genetic sequencing data only by binary classification, with the primary focus being breast cancer diagnosis and the likelihood of survival. As a result, radiologists improved their diagnosis in the diagnosis of breast cancer in mammography using an AI computer system for support without the need for additional reading time. However as promising as these findings may be Studies in a screening scenario need to be done to verify them.

Keywords: Breast cancer, Artificial Intelligence (AI), post-treatment

129.

The role of circadian gene timeless in gastrointestinal cancers (Review)

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Introduction: Timeless is an evolutionarily preserved protein involved in the circadian rhythm of melanogaster flies while its role in mammalian circadian clock systems has not been fully elucidated. Timeless is deemed essential to protect genomic replication and stability. Destruction of timeless in the rat suprachiasmatic nucleus disrupted the rhythm of suprachiasmatic neural activity, reducing PER1, PER2, and PER3 and increasing cryptochrome CRY1 and CRY2.

Methods: In addition, the full-length timeless protein showed a 24-hour fluctuation, while a truncated isoform was substantially expressed, indicating the active role of mammals timeless in the circadian clock system. Timeless is also involved in DNA replication, telomere length, genome integrity maintenance, and ATM/ATR signaling pathway regulation. Recent studies have shown that timeless interacts with poly (ADP ribose) polymerase 1 and regulates homologous recombination pathways and non-homologous end-binding pathways, both of which are required to repair double-stranded DNA fractures.

Results: Recently, it has been reported that timeless is regulated in different types of human tumors and is involved in the development and progression of cancer. Studies showed that timeless, a factor involved in DNA repair, is overexpressed in cancerous tissues and is essential for the proliferation of tumor cells. Timeless knockdown inhibits

tumor growth, induces apoptosis and aging, and disrupts the DNA repair pathway in cancer cells.

Conclusion: Therefore, timeless can be a promising diagnostic marker and an effective strategy for cancer treatment. However, more clinical research is needed to achieve many achievements in this field.

Keywords: Circadian genes DNA repair Targeted cancer therapy Gastrointestinal cancers

130.

The Role of CRISPR In Cancer Treatment in Chronic Myeloid Leukemia (Review)

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Introduction: 15% of all new instances of leukemia are caused by the myeloproliferative disease chronic myeloid leukemia (CML), which has an incidence of 1-2 cases per 100,000 years. It does not often occur in children and is more common in adults, with a mean age of incidence of roughly 55 years. Both sexes may be affected, however, men are affected at a somewhat higher rate than women—2.2 men for every 100,000 affected compared to 1.4 women. The majority of CML patients experience fatigue, anaemia, splenomegaly, stomach pain, and recurrent infections as their primary clinical symptoms. On the other hand, a lot of asymptomatic people receive a diagnosis following an unrelated medical evaluation. The quantity of scholarly publications detailing CRISPR/Cas9 research in the context of leukemia research has skyrocketed over the past five years. Many of them are related to in vitro research aimed at elucidating the function of various genes in the development of leukemia. These investigations pinpoint important genes that CRISPR/Cas9 technology will later be used to modify in leukemic cells. This study sought to determine how CRISPR functions in the therapy of cancer in CML

Methods: The present was done by searching scientific databases such as Science Direct, Springer, Google Scholar, and PubMed.

Results: The results have shown the CRIPSR/Cas9 system's potential. A single oncogene drives the malignancy of CML, which is an HSC. CML is a prime target for gene therapy because of the unique characteristics of HSCs, which maintain the long-term production of all hematopoietic lineages. Given the unique properties of self-renewing and multipotent HSCs, it is likely that all daughter cells will acquire any gene editing or CRISPR ablation, hence regaining hematopoiesis. Additionally, the characteristics of the hematopoietic compartment, which permit HSC collection and reinfusion, facilitate the creation of ex vivo treatments and, in turn, the assessment and choice of the modified HSCs, enhancing the procedure's safety and effectiveness. The understanding that the BCR/ABL1 fusion is the fundamental cause of CML pathogenesis is the basis of imatinib therapy. This is why one

could reasonably assume that the BCR/ABL1 gene disruption caused by CRISPR/Cas9 would provide a permanent treatment. The capacity to disrupt the BCR/ABL1 oncogene has been the subject of several recent research, demonstrating the potential of the CRISPR-Cas9 system as a therapeutic tool that is about to enter clinical trials. The potential of CRISPR/Cas9 to eliminate the BCR/ABL1 gene fusion has been investigated in several recent in vitro and in vivo investigations. In 2017, Garcia-Tuñón et al. showed for the first time that the BCR/ABL1 oncogene's tumorigenic activity can be reversed by the CRISPR/Cas9 system. In an animal model of CML xenograft, they demonstrated how modified CRISPR cells lost their capacity to divide and survive, and that when the edited cell was chosen, no tumors appeared. Their findings established the fundamental idea that the CRISPR system's abrogation of BCR/ABL1 causes a decrease in tumorigenicity.

Conclusion: The biggest drawback of in vivo CRISPR therapy, similar to other gene therapy techniques, is the challenge of determining the most effective and secure delivery mechanism. However, new Cas proteins should be used, and humans' innate adaptive immunity to Cas9 proteins could be taken into account. It is also necessary to find a solution for the CRISPR off-target problem. Although the CRISPR-Cas9 system can cause unwanted cleavages outside of on-target sites, it also produces double-strand breaks (DSBs) at target loci in genomic DNA. Gene disruption may occur as a result of mutations brought on by cleavage at off-target locations. A remedy will soon be available thanks to efforts to find new Cas variants with high fidelity and a protospacer neighbouring motif that is less limiting than the NGG sequence. However, in haematological cancers that are clinically treated, like BCR/ABL1 disruption in CML, ensuring the absence of unmodified cells is crucial. In conclusion, a plethora of studies and clinical trials have strongly shown the tremendous therapeutic promise of the CRISPR/Cas tools. This technique has certain technical restrictions, but the number of workarounds for those restrictions has grown at a similar rate. We are certain that CRISPR/Cas gene therapy will become a routine clinical practice soon

Keywords: CRISPR, cancer, Chronic myeloid leukemia

131.

The Role of Cyclooxygenase-2 Expression in the Pathogenesis and Progression of Bladder Cancer (Review)

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Introduction: Bladder cancer is a significant global health burden, ranking as the ninth most common cancer worldwide. In 2020, there were approximately 573,000 new cases of bladder cancer and 213,000 deaths globally. The high incidence and mortality rates of bladder cancer underscore the need for effective therapeutic strategies to combat this disease.The enzyme cyclooxygenase-2 (COX-2) has been implicated in various cancers, including bladder cancer. Indeed, numerous studies have shown that COX-2 is not merely a bystander in the process of carcinogenesis, but rather actively participates in the development and progression of cancer. Furthermore, COX-2 has been linked to several key mechanisms that contribute to cancer malignancy, including the suppression of apoptosis, evasion of host immune surveillance, and promotion of angiogenesis.In light of these findings, targeting COX-2 may offer a promising approach to cancer therapy. Specifically, COX-2 inhibitors have been shown to exhibit anti-tumor activity by inhibiting the growth and spread of cancer cells, as well as by improving the response to chemotherapy and radiation. Given the importance of COX-2 in bladder cancer, an in-depth understanding of the mechanisms underlying its antitumor activity is crucial for the optimal application of COX-2 inhibitors in clinical practice

Methods: A comprehensive literature search was conducted using three major databases: PubMed, Web of Science, and SID, covering publications from 1996 to 2024. The search focused on the key terms "bladder cancer" and "COX-2 expression."In the SID database, only one relevant study was identified. The PubMed search initially retrieved 200 articles. After applying the inclusion criteria, 13 articles were selected for detailed analysis. The search in Web of Science was also performed, and after the removal of duplicate studies, a total of 17 articles were reviewed in-depth.

Results: Cyclooxygenase-2 (COX-2) is a critical enzyme responsible for converting arachidonic acid into prostaglandins, molecules that play a significant role in inflammation

and cell growth. Typically, COX-2 is induced by various stimuli, including growth factors, cytokines, and bacterial lipopolysaccharides. Mechanism of COX-2 in Cancer Induction and Overexpression COX-2 is overexpressed in many cancers, including colorectal, breast, and gastric cancers. This overexpression often arises from inflammation and oncogenic pathways. It is crucial to understand this mechanism to develop effective treatments. Prostaglandin Production COX-2 catalyzes the production of prostaglandin E2 (PGE2), which plays a critical role in promoting tumor growth. PGE2 enhances angiogenesis, inhibits apoptosis, and stimulates cell proliferation. This process creates a positive feedback loop, where PGE2 induces COX-2 expression, sustaining high levels of both in the tumor microenvironment. Pathways and Effects Angiogenesis COX-2 promotes the formation of new blood vessels, which supplies tumors with the necessary nutrients and oxygen for growth and metastasis. Invasion and Metastasis COX-2 enhances the invasive capabilities of cancer cells by modulating the extracellular matrix and promoting epithelial-mesenchymal transition (EMT). This process enables cancer cells to migrate and invade surrounding tissues. Immune Suppression COX-2 can suppress the immune response against tumors, allowing them to evade detection and destruction. Understanding the role of COX-2 in immune suppression is crucial for developing immunotherapy strategies. In summary, COX-2 plays a central role in cancer progression through its involvement in inflammation, angiogenesis, and immune modulation. Its overexpression and the subsequent increase in prostaglandin production create a tumor-promoting environment that fuels cancer growth and metastasis.

Conclusion: The cumulative evidence from multiple studies suggests that Cyclooxygenase-2 (COX-2) plays a multifaceted role in the development and progression of bladder cancer.Gee (2006) and Dhawan (2008) found that COX-2 inhibitors can impede bladder cancer cell growth, although the underlying mechanisms may not involve COX-2 activity. Shariat (2003) demonstrated a link between COX-2 expression and advanced disease stages, but its prognostic value is limited. Additionally, Badawi (2002) highlighted the influence of smoking on COX-2 expression, which may contribute to bladder cancer development. Recent studies have explored the feasibility of using targeted therapies, such as fluorocoxib A (Bourn, 2019), to monitor COX-2 expression changes and potentially enhance treatment outcomes. Zuo (2014) also provided evidence that ART can induce apoptosis through COX-2 downregulation, offering a promising novel therapeutic approach. Overall, these studies indicate that while COX-2 plays a significant role in bladder cancer, its inhibition may have both COX-2-dependent and -independent effects,

and its expression is influenced by various factors, including smoking and targeted therapies.

Keywords: Cox-2

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The role of ferroptosis in carcinogenesis (Review)

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Introduction: Although iron is a trace element, it plays a crucial role in cellular metabolic processes. Ferroptosis, a newly discovered form of cell death, is dependent on iron and lipid metabolism, driven by phospholipid peroxidation, and is distinct from apoptosis, necrosis, and autophagy. Ferroptosis is associated with the dysfunction of cellular antioxidant systems. The imbalance of iron metabolism homeostasis leads to an increase in intracellular free iron, which is a hallmark of ferroptosis. Studies have shown a connection between ferroptosis and tumor-associated signaling pathways, indicating that ferroptosis and epithelial-mesenchymal transition (EMT) in cancer promote each other, and ferroptosis can determine the survival and growth of cancer cells. Interestingly, treatment-resistant cancer cells, especially those in a mesenchymal state prone to metastasis, are highly vulnerable to ferroptosis.

Methods: This review article compiles and discusses research on the role of ferroptosis in carcinogenesis. Information was sourced from databases such as PubMed, NCBI, MDPI, The Cell's, and Google Scholar.

Results: Excess iron can directly induce ferroptosis. The antioxidant system GPX4, a central regulator of ferroptosis, can inhibit ferroptosis by reducing lipid peroxidation. Glutathione (GSH), the cofactor for GPX4, and cysteine, a key component of GSH, are critical in this process. The reduction of GSH can be considered one of the mechanisms leading to ferroptosis. Direct or indirect inhibition of GPX4 can trigger ferroptosis. Malignant mutations in YAP2-NF signaling may predict the responsiveness of cancer cells to future ferroptosis-inducing treatments, despite the fact that these pan-caspase inhibitors effectively suppress cell death caused by other apoptotic triggers. Ferroptosis also plays a role in pathological cell death associated with degenerative diseases. In plants, ferroptosis may act as a tumor suppressor under heat stress, which could be leveraged for cancer treatment. The p53 protein can sensitize cells to ferroptosis by suppressing the expression

of SLC7A11, which inhibits cystine uptake. Melanoma cells exposed to the lymphatic environment are protected from ferroptosis, enhancing their ability to survive during subsequent metastasis through the bloodstream. Promoting ferroptosis offers significant benefits for cancer prognosis. Ferroptosis was first observed using erastin to selectively kill genetically engineered cells with RAS mutations. The mechanical consequences of uncontrolled lipid peroxidation leading to ferroptotic cell death remain unclear. Fundamentally, ferroptosis can be conventionally induced by deactivating GPX4 or increasing the labile iron pool. Two mechanisms have been described for GPX4 inactivation. Additionally, recent findings suggest an unconventional ferroptosis induction pathway in the case of iron overload. The role of mitochondria in ferroptosis is established but remains ambiguous. Depending on the stimulus, ferroptosis may also involve autophagic processes. Recently, it has been proposed that oxytosis and ferroptosis should be considered as a single cell death pathway or at least have significant overlap. Induction of ferroptosis can reverse drug resistance or even overcome resistance to immunotherapy. Identifying specific vulnerabilities in cancer cells that make them prone to ferroptosis allows for more personalized treatment approaches, potentially improving outcomes. However, there is growing evidence that current ferroptosis activators can cause cell death in normal cells, leading to adverse effects during cancer treatment. Induction of ferroptosis may result in the death of stem cells and damage to bone marrow, potentially impacting hematopoiesis and leading to bone marrow suppression. Inhibition of GPX4 may have toxic effects on the liver and kidneys. Secondary tumors may emerge as a potential side effect of drug-induced ferroptosis.

Conclusion: The findings of this review suggest that ferroptosis, as a novel form of iron-dependent and lipid metabolism-related cell death, has significant potential in cancer therapy, particularly in treatment-resistant cancer cells. While ferroptosis is associated with cancer cell death and can reverse drug resistance, there is evidence indicating that inducing ferroptosis may lead to adverse effects during cancer treatment. These effects may include damage to stem cells, bone marrow, and possibly the development of secondary tumors. Therefore, a deeper understanding of the mechanisms of ferroptosis and its effects on normal cells is essential for developing more effective and safer treatments.

Keywords: Cell death, Ferroptosis, Iron-dependent, Carcinogenesis, Peroxidation

133.

The Role of Long Non-coding RNAs In Breast Cancer Progression and Potential Therapeutic Applications (Review)

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Introduction: Breast cancer continues to pose significant health challenges as the most common cancer in the world[1]. Among the many molecular entities implicated in its progression, long non-coding RNAs (lncRNAs) have emerged as important regulators of gene expression and cellular functions[2]. This essay reviews the roles of lncRNAs in breast cancer progression and treatment.

Methods: lncRNAs play a crucial role breast cancer progression by regulating key significant pathways involves in cell proliferation, migration, invasion and metastasis. As an instance, long non-coding RNA known as LOC127814295 (lnc-RGS5) is notably overexpressed in breast cancer. Higher levels of lnc-RGS5 are linked to poorer overall survival in patients with triple negative breast cancer. In addition, upregulation of lnc-RGS5 promotes breast cancer cell proliferation in vitro, while its knockdown inhibits tumor cell proliferation both in vitro and in vivo[3].

Results: Another example includes lncRNA NR2F1-AS1. High levels of lnc NR2F1-AS1 were found in BC cells undergoing EMT and were linked to poor prognosis in BC patients. Knocking down lnc NR2F1-AS1 significantly reduced BC cell migration, invasiveness, and metastasis[4]. Mechanistically, lnc NR2F1-AS1 binds to binds to miR-25-3p, preventing the degradation of ZEB2, a positive EMT transcription factor[5].

Conclusion: In conclusion, whereas long non-coding RNAs (lncRNAs) are essential for the development of breast cancer, their functions go beyond just contributing to the pathophysiology of the illness. These compounds show potential as biomarkers and therapeutic targets, opening up new therapeutic options for the detection and management of breast cancer. By utilizing the special qualities of lncRNAs, we can improve patient outcomes by advancing our tactics against this common cancer.

Keywords: Breast cancer, Long non-coding RNAs, lncRNAs

134.

The Role of Microbiome in Genetic Risk and Cancer Prevention: From Probiotics to Skin-Enhancing Biotechnologies (Review)

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Introduction: The human microbiome, an intricate ecosystem of microorganisms, has gained considerable attention for its influence on various aspects of health, including cancer development. There is growing evidence that microbial communities may interact with genetic factors to either exacerbate or mitigate cancer risk. At the same time, microbiome-targeted interventions, such as probiotics and topical treatments, are being explored as innovative strategies for cancer prevention. In recent years, these approaches have even crossed over into biotechnology, where products like skincare and cosmetics are being developed with a focus on promoting health, including reducing cancer risk. This review delves into the connection between the microbiome and genetic cancer risk, highlighting both internal (probiotics) and external (topical) interventions and their translation into practical biotech solutions.

Methods: To gather relevant information, we performed a detailed search using PubMed and Google Scholar, focusing on peer-reviewed articles published between 2010 and 2023. Search terms included "microbiome," "genetic risk," "cancer prevention," "probiotics," and "biotechnologies." Research articles, clinical trials, and systematic reviews were included, with a focus on studies that explored the role of the microbiome in modulating genetic cancer risk. We also included studies on how probiotics and topical microbiome-based products are being developed and used for preventive measures, particularly in the biotech and skincare sectors.

Results: The literature reveals growing evidence that the microbiome can influence genetic susceptibility to cancer by modulating immune responses, inflammation, and metabolic pathways. Studies show that alterations in gut and skin microbiota are associated with both increased and decreased cancer risk, depending on the microbial composition and its interaction with the host's genetic makeup. For instance, the gut microbiota has been linked to colorectal cancer through its impact on gene expression related to inflammation and DNA repair mechanisms. Additionally, skin microbiota plays a significant role in

protecting against skin cancers by enhancing the skin's barrier function and immune surveillance. Probiotics, particularly those containing strains of Lactobacillus and Bifidobacterium, have been shown to reduce cancer risk through several mechanisms, including the modulation of inflammatory pathways, reduction of DNA damage, and enhancement of immune function. Clinical trials have demonstrated the potential of probiotics in preventing colorectal, gastric, and breast cancers. Topical applications targeting skin microbiota are also gaining traction in cancer prevention. Biotechnological innovations are integrating beneficial microbes into skincare and cosmetic products designed to enhance the skin's natural defenses, improve immune function, and reduce inflammation, all of which are critical factors in cancer prevention. Several biotech companies are now incorporating microbiome research into product development, using live probiotics, postbiotics, and prebiotic ingredients in skincare formulations. These products are designed to support the skin's natural microbiome, thereby promoting skin health and potentially lowering cancer risk by enhancing the skin's immune responses to environmental carcinogens, UV radiation, and oxidative stress.

Conclusion: The modulation of the human microbiome offers a promising avenue for reducing genetic risk factors for cancer and developing preventive strategies. Both dietary interventions, such as probiotics, and topical applications in the form of skincare biotechnologies, represent novel approaches to cancer prevention. While current evidence supports the efficacy of these interventions, further research is needed to fully elucidate the mechanisms by which the microbiome interacts with genetic factors and to optimize microbiome-based products for cancer prevention. Biotechnological innovations that harness the power of the microbiome are poised to play an increasingly significant role in personalized cancer prevention strategies.

Keywords: Microbiome, genetic risk, cancer prevention, probiotics, skincare biotechnologies

135.

The Role of Non-Coding RNAs in Chemotherapy Drug Toxicity (Review)

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Introduction: Non-coding RNAs (ncRNAs) are a group of RNA molecules that do not encode proteins but play crucial roles as regulators in various biological processes, including gene expression regulation, transcription control, and mRNA stabilization. Recent studies have highlighted the significant role that ncRNAs can play in modulating cellular responses to chemotherapy drugs. Chemotherapy, a primary cancer treatment method, utilizes chemical agents to inhibit the growth and division of cancer cells. However, these drugs often come with substantial side effects due to their toxicity in healthy cells. Chemotherapy-induced toxicity can manifest in various forms, such as DNA damage, oxidative stress, apoptosis, and inflammatory responses. NcRNAs are broadly categorized into two groups: small ncRNAs and long ncRNAs (lncRNAs). Small ncRNAs, including microRNAs (miRNAs) and small interfering RNAs (siRNAs), primarily regulate gene expression at the post-transcriptional level. In contrast, lncRNAs, which are longer than 200 nucleotides, have diverse functions, including transcriptional regulation, RNA processing, and protein interactions. This review article aims to compile and discuss the role of ncRNAs in chemotherapy-induced drug toxicity.

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 ncRNAs in drug-induced toxicity.

Results: MiRNAs, a type of small ncRNA, have been identified as key regulators of gene expression and can influence cellular responses to chemotherapy drugs. For instance, miR-34a is recognized as a tumor suppressor that enhances the sensitivity of cancer cells to chemotherapy by regulating genes related to the cell cycle and apoptosis. Conversely, certain miRNAs, such as miR-21 and miR-155, can promote resistance to chemotherapy by

suppressing tumor suppressor genes, thereby exacerbating drug toxicity in healthy tissues. LncRNAs, another category of ncRNAs, have also been implicated in cellular responses to chemotherapy. LncRNAs like HOTAIR and MALAT1 can interact with specific proteins or other ncRNAs, affecting cellular processes such as epigenetics, translation, and inflammatory responses. For example, HOTAIR has been shown to increase chemotherapy resistance by inhibiting tumor suppressor pathways, indirectly enhancing drug toxicity in healthy tissues. NcRNAs can influence chemotherapy-induced toxicity by interacting with various signaling pathways. For instance, miRNAs can target components of the AKT/PI3K, MAPK, and NF-κB pathways to modulate cellular responses to drug-induced stress. Similarly, lncRNAs can affect drug toxicity by regulating the expression of genes related to key signaling pathways, including those involved in apoptosis and cell differentiation.

Conclusion: NcRNAs play a critical role in the toxicity of chemotherapy drugs, acting as key regulators of cellular processes. Targeting specific ncRNAs represents a promising therapeutic strategy to reduce drug toxicity and improve the efficacy of chemotherapy treatments. For example, using antagomiRs to inhibit miRNAs associated with drug resistance is a hopeful approach in this area. Understanding the molecular mechanisms of ncRNAs can lead to the development of new therapeutic strategies to reduce the side effects of chemotherapy and improve the quality of life for cancer patients. However, further research is needed to gain a deeper understanding of the complex interactions between ncRNAs and various signaling pathways.

Keywords: Non-Coding RNAs, Chemotherapy, Drug Resistance, Chemotherapy Drug Toxicity

136.

The Role of Probiotics in Inducing Apoptosis and Regulating Apoptosis-Related Gene Expression in Gastrointestinal Cancer Therapy (Review)

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Introduction: Apoptosis, or programmed cell death, is a crucial mechanism that maintains cellular homeostasis by eliminating damaged or abnormal cells (1). In cancer, particularly gastrointestinal cancers, the disruption of apoptotic pathways allows cancer cells to evade death, leading to uncontrolled proliferation (2). Recent studies suggest that probiotics, such as Lactobacillus and Bifidobacterium species, can trigger apoptosis in cancer cells by modulating various molecular and genetic pathways (3). This article reviews the potential of probiotics to induce apoptosis in cancer cells and their effects on the expression of apoptosis-related genes.

Methods: The study is based on a comprehensive review of research focused on the interaction between probiotics and apoptosis in gastrointestinal cancer cells. Specifically, studies analyzing the effects of probiotics on key apoptotic markers such as p53, Bax, Bcl-2, and caspase activity were included. Data on the molecular pathways involved in apoptosis induction, such as the mitochondrial and death receptor pathways, were also considered.

Results: 1. Activation of the Mitochondrial Apoptosis Pathway: Probiotics have been shown to induce apoptosis via the intrinsic mitochondrial pathway. For example, Lactobacillus acidophilus enhances the expression of pro-apoptotic proteins such as Bax while reducing anti-apoptotic proteins like Bcl-2 , leading to mitochondrial membrane permeabilization and the release of cytochrome c. This release triggers the activation of caspases, particularly caspase-9 and caspase-3, culminating in cancer cell apoptosis (4, 5). 2. Influence on the Death Receptor Pathway: The death receptor pathway is another key apoptotic route that probiotics can modulate. Studies show that Bifidobacterium longum can upregulate death receptors like Fas and TRAIL on the surface of cancer cells, making them more susceptible to apoptosis. This effect promotes the activation of caspase-8, further enhancing the apoptotic cascade (6). 3. Regulation of Tumor Suppressor Genes:

Probiotics are known to regulate crucial tumor suppressor genes involved in apoptosis. For example, Lactobacillus casei has been shown to increase the expression of p53, a tumor suppressor that plays a central role in promoting apoptosis in response to DNA damage. Through this mechanism, probiotics can restore the apoptotic response in cancer cells where p53 activity is otherwise diminished (7). 4. Downregulation of Anti-Apoptotic Genes: In cancer, many cells overexpress anti-apoptotic genes, allowing them to evade apoptosis. Probiotics such as Lactobacillus rhamnosus GG have been reported to downregulate anti-apoptotic genes like Bcl-2 and Bcl-xL, which are commonly overexpressed in gastrointestinal cancer cells. This reduction in anti-apoptotic signals facilitates the initiation of the apoptotic process, leading to cancer cell death (8). 5. Caspase Activation and Apoptotic Cascade: Caspases are essential executors of apoptosis, and probiotics have been shown to activate caspase enzymes directly. Research indicates that Bifidobacterium bifidum can trigger the activation of both initiator caspases (such as caspase-8 and caspase-9) and executioner caspases (caspase-3), leading to efficient and irreversible apoptosis in cancer cells (9). This suggests that probiotics may serve as a natural trigger for the caspase-dependent apoptotic pathway in gastrointestinal cancers.

Conclusion: Probiotics have demonstrated significant potential in inducing apoptosis in gastrointestinal cancer cells by regulating various apoptotic pathways and gene expressions. By targeting the mitochondrial and death receptor pathways, probiotics can influence key regulators such as p53, Bax, Bcl-2, and caspases, effectively promoting programmed cell death in cancerous tissues. The ability of probiotics to modulate these molecular mechanisms positions them as promising adjunctive agents in cancer therapy. Future studies should focus on clinical trials to better understand the full therapeutic potential of probiotics in inducing apoptosis and inhibiting cancer progression. 1. Kari S, Subramanian K, Altomonte IA, Murugesan A, Yli-Harja O, Kandhavelu M. Programmed cell death detection methods: a systematic review and a categorical comparison. Apoptosis. 2022;27(7):482-508. 2. Wang H, Liu M, Zeng X, Zheng Y, Wang Y, Zhou Y. Cell death affecting the progression of gastric cancer. Cell death discovery. 2022;8(1):377. 3. Nowak A, Paliwoda A, Błasiak J. Anti-proliferative, pro-apoptotic and anti-oxidative activity of Lactobacillus and Bifidobacterium strains: A review of mechanisms and therapeutic perspectives. Critical reviews in food science and nutrition. 2019;59(21):3456-67. 4. Taheri F, Moazamian E, Mahdavi M. Lactobacillus acidophilus Cytotoxicity Effect and Apoptosis in Human Bladder Carcinoma Cells: An In Vitro Study. Immunoregulation. 2020;3(2):127-34. 5. Yue Y, Wang S, Shi J, Xie Q, Li N, Guan J, et al. Effects of Lactobacillus acidophilus KLDS1.

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Keywords: Probiotics, apoptosis, Gastrointestinal Cancer, p53

137.

The Synergistic Effects of Cisplatin and Probiotics on BAX and Bcl-2 Gene Expression in Breast Cancer Cells (Review)

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Introduction: Breast cancer is a leading cause of cancer-related mortality among women worldwide. Despite advances in treatment, the resistance of cancer cells to chemotherapeutic agents such as cisplatin remains a significant challenge. Cisplatin is a widely used chemotherapy drug that induces apoptosis by forming DNA adducts and activating apoptotic pathways. However, breast cancer cells can develop resistance to cisplatin, limiting its therapeutic effectiveness. Recent studies have suggested that probiotics, particularly strains of "Lactobacillus" and "Bifidobacterium", could improve chemotherapy outcomes by modulating the gut microbiota and immune responses, as well as by enhancing apoptotic signaling pathways in cancer cells. This review focuses on the combined use of cisplatin and probiotics in breast cancer treatment and their effects on the expression of "Bax" and "Bcl-2", two critical genes involved in apoptosis regulation.

Methods: This review examines recent studies from the last five years that have investigated the effects of cisplatin and probiotics on breast cancer cells. A literature search was conducted using databases such as PubMed and Google Scholar, with a focus on studies that assessed the apoptotic response in breast cancer cells treated with both cisplatin and probiotics. Studies analyzing the expression of pro-apoptotic "Bax" and anti-apoptotic "Bcl-2 genes were selected. The included research covered in vitro experiments on breast cancer cell lines, particularly MCF-7 cells, as well as in vivo studies on animal models.

Results: The combined treatment of cisplatin and probiotics demonstrated significant effects on the expression of "Bax" and "Bcl-2" in breast cancer cells. Cisplatin alone is known to induce apoptosis through the upregulation of "Bax" and downregulation of "Bcl-2", tipping the balance toward cell death. In several studies, probiotics, especially strains

like "Lactobacillus rhamnosus" and "Bifidobacterium bifidum", enhanced this effect. In vitro studies on MCF-7 breast cancer cells showed that treatment with cisplatin led to a 2.5-fold increase in "Bax" expression and a 35% reduction in "Bcl-2" levels. When combined with probiotics, "Bax" expression increased up to 4-fold, while "Bcl-2" levels decreased by 60%, indicating a synergistic effect. This shift in the *Bax/Bcl-2* ratio promotes apoptosis, as "Bax" facilitates mitochondrial membrane permeabilization, releasing cytochrome c and activating caspases, while "Bcl-2" acts to inhibit these processes. Further studies demonstrated that probiotics not only enhanced the pro-apoptotic effects of cisplatin but also contributed to reducing inflammation and improving the overall immune response. By modulating the gut microbiome, probiotics may promote systemic immune responses, which could help in identifying and targeting cancer cells more effectively. Animal models of breast cancer corroborated these findings. Mice treated with both cisplatin and probiotics showed a significant reduction in tumor size compared to those treated with cisplatin alone. Tumor tissues from these mice exhibited higher levels of "Bax" and lower levels of "Bcl-2", further confirming the apoptotic effect of the combined treatment.

Conclusion: The combination of cisplatin and probiotics offers a promising strategy for enhancing the effectiveness of breast cancer treatment. By modulating the expression of key apoptotic genes such as "Bax" and "Bcl-2", probiotics help to amplify the pro-apoptotic effects of cisplatin, making cancer cells more susceptible to programmed cell death. These findings suggest that probiotics may serve as a valuable adjunct to traditional chemotherapy, potentially overcoming resistance mechanisms and improving patient outcomes. Future clinical trials are necessary to establish the optimal combination of probiotics and chemotherapy drugs, as well as to confirm these findings in a clinical setting.

Keywords: Probiotic, apoptosis, Bcl-2, bax, breast cancer

138.

The therapeutic functions of bacteriophage in the treatment of colon cancer (Review)

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Introduction: Colon cancer is a prevalent and deadly disease that continues to challenge modern medicine. Bactericidal therapy is emerging as a promising option in the search for innovative treatments. Conventional treatments for cancer, such as surgery, radiotherapy, and chemotherapy, have limitations and side effects. Therefore, modifying or replacing existing strategies to treat cancer is necessary. Recently, bacteria have gained attention for their therapeutic role as emerging novel anti-cancer agents. Bacteriophages, viruses that target and infect bacteria, possess unique therapeutic properties that can radically change the treatment landscape for colon cancer. Bacteriophages can target and eradicate bacteria involved in colon cancer tumor development and progression. Their ability to specifically attack and destroy cancer cells is one of the most essential advantages in treating colon cancer. Bacteriophages destroy malignant cells in colon cancer while protecting healthy cells from damage. Finally, the use of bacteriophages in colon cancer treatment shows promise. They are a valuable addition to the treatment options for colon cancer patients, thanks in part to their targeted approach, anti-cancer properties, and ability to overcome drug resistance. However, it is crucial to emphasize the need for further research to understand and fully utilize their potential. As research in this area progresses, we hope to see widespread and highly effective use of bacteriophages in colon cancer treatment.

Methods: Due to the nascent research stage on phage therapy for colon cancer, the methodology primarily relies on pre-clinical in vitro and in vivo models. Colon cancer cell lines like HCT116 and HT-29 are used to assess the direct cytotoxic effects of phages on cancer cells (These studies evaluate factors like phage concentration, exposure time, and cell viability after phage treatment). Co-culture models incorporate colon cancer cells and specific bacterial strains implicated in CRC, such as Fusobacterium nucleatum. This allows researchers to investigate the ability of phages to target and eliminate the bacteria while assessing their impact on cancer cell growth and viability. Microbiome analysis:

Fecal samples from patients or animal models can be used to analyze the gut microbiome composition before and after phage treatment. This helps determine the impact of phages on the overall bacterial community and identify potential shifts that might influence colon cancer development. Colon cancer cells are implanted into immunocompromised mice to establish tumors. These models allow researchers to evaluate the efficacy of phage therapy in reducing tumor size and improving overall survival. Syngeneic models utilize genetically modified mice that spontaneously develop colon cancer. Phage therapy can be administered, and tumor progression and potential immune responses can be monitored. By employing these rigorous methods, researchers can gain valuable insights into the therapeutic potential of bacteriophages for colon cancer treatment, paving the way for future clinical trials and advancements in this promising field.

Results: Bacteriophages have shown remarkable potential as targeted delivery vehicles. Studies demonstrated that phage-based nanocarriers could enhance the accumulation of chemotherapeutic agents in colon cancer tumors by up to 60% compared to conventional delivery methods. This targeted approach significantly reduced systemic toxicity while improving therapeutic efficacy. The unique properties of bacteriophages allow for improved tumor penetration. Bacteriophages exhibit significant immunomodulatory effects in the context of colon cancer. A study reported that phage therapy stimulated the activation of tumor-infiltrating lymphocytes and enhanced the production of pro-inflammatory cytokines, resulting in a more robust anti-tumor immune response. Emerging evidence suggests that bacteriophages can effectively target colon cancer stem cells, often resistant to conventional therapies. A study reported that phage therapy significantly reduced tumor-associated macrophages and increased tumor-infiltrating T cells, creating a more favorable environment for anti-tumor responses. These results underscore bacteriophages' multifaceted therapeutic potential in colon cancer treatment. The ability of phages to enhance drug delivery, stimulate immune responses, overcome resistance mechanisms, and improve long-term patient outcomes positions them as a promising avenue for future cancer therapeutics.

Conclusion: Exploring bacteriophages as therapeutic agents for colon cancer presents a captivating avenue in the fight against this prevalent malignancy. Their remarkable ability to target and eliminate pro-carcinogenic bacteria within the gut microbiome and their potential for direct anti-tumor activity offers a unique and potentially transformative approach. While preliminary research is encouraging, further investigations are warranted

to delineate the complete safety profile, optimal delivery methods, and long-term efficacy of phage therapy in the context of colon cancer treatment. However, the targeted nature of phages, their minimal impact on healthy tissues, and their potential to circumvent drug resistance paint a promising future for this innovative therapeutic strategy. As research continues to unveil the multifaceted capabilities of bacteriophages, we can anticipate their emergence as valuable tools in the armamentarium against colon cancer, offering hope for improved patient outcomes.

Keywords: Colon cancer, Treatment, Bacteriophage, Chemotherapy

139.

Therapeutic Role of Transforming Growth Factor- β on Cancer (Review)

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Introduction: Transforming Growth Factor-β (TGFβ) is a vast superfamily of cytokines that includes TGF-βs (TGF-β1, -β2, and -β3), activins, inhibins, Anti-Mullerian Hormone (AMH), Bone Morphogenic Protein (BMPs), Growth Differentiation Factors (GDFs), Glial-derived Neurotrophic Factors (GDNFs), and nodal. Transforming growth factor β (TGFβ) plays a crucial role in various processes, such as cell migration and invasion, inhibition of epithelial, hematopoietic, and immune cell growth, epithelial-to-mesenchymal (EMT) transition, and extracellular matrix remodeling. TGF-β exerts its tumor suppressive role by regulating cell proliferation, apoptosis, and immune cell modulation. The absence of TGF-β1 results in severe inflammatory responses by activating the immune cell population and causing the infiltration of lymphocytes and macrophages in various organs. Additionally, its ability to arrest the cell cycle at the early G1 phase and inhibit the growth of various cell types is well documented.

Methods: In this study, keywords including Transforming Growth Factor-β, Cancer, and Treatment were reviewed from the Mesh list and other reputable websites such as PubMed, Science Direct, and Google Scholar, and the data was organized. The searches included all published papers from 2010 to 2023. Full text papers were considered, while those manifesting only as abstracts were excluded. Only full papers focusing on the specific role of transforming growth factor-β in cancer treatment were selected. A total of 50 papers were chosen and studied in this review.

Results: Evidence suggests that TGF-β promotes the activation of tumor suppressor genes such as p15, p21, and attenuates the tumor-promoting gene c-MYC expression, thereby supporting its antitumor effect. Articles also showed that TGF-β limits cancer formation by activating the apoptotic pathway. Downstream targets for the pro-apoptotic functions of TGF include death-associated protein kinase (DAPK), growth arrest, and DNA damage.

Numerous preclinical results from in vitro cell models and in vivo animal models have demonstrated the great potential of anti-tumor therapeutics with TGFβ-neutralizing antibodies and ligand traps that block the interaction of TGFβ with its receptors or selective small-molecule TGFβ receptor kinase inhibitors. Several studies have shown that TGF-β acts as a tumor suppressor by inhibiting proliferation and inducing apoptosis during the early stages of tumorigenesis. Generally, TGF-β inhibits proliferation and promotes apoptosis by overexpressing cyclin-dependent kinase (CDK) inhibitors and downregulating MYC expression. TGF-β mainly regulates cell proliferation by inhibiting cell cycle progression through G1 arrest. In epithelial cells, it executes a coordinated cytostatic program with dual effects by inducing CDK inhibitors p21Cip1 and p15Ink4b to arrest cell proliferation, and suppressing proliferative drivers. Treatment of tumor cells with a combination of vaccines and antisense TGF-β therapy has shown a reduction in tumor size and increased survival benefit.

Conclusion: Anti-TGFβ therapeutic drugs, including TGFβ-neutralizing antibodies, peptide inhibitors, TGFβ receptor kinase inhibitors, antisense oligonucleotides, and TGFβ ligand traps, were developed for the treatment of cancer, fibrosis, and other diseases with aberrant vascular symptoms. TGF-β intervenes in critical processes linked to tumor development and progression, making this factor a promising molecular target in cancer treatment. The enormous variety of molecules involved in TGFβ synthesis, activation, or signal transduction, as well as those capable of indirectly affecting these mechanisms, represent potential therapeutic targets under research.

Keywords: Transforming Growth Factor- β, Cancer, Treatment

140.

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 80 billion neurons firing up to 17.2 trillion synapses every second?!), the “second brain”, a fascinating neural center located in our gut,And, amazingly, over 500 million neurons are located in this area of our body. According to numerous studies over the past twenty years, the gut sends about 400 more messages to the brain, than the brain does to the gut and, almost 70% of our body’s immune system and 95% of Serotonin is actually found in the gut. And, finally our “third brain” is heart where houses more than 39 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 psychophysiological problems are related to our three-brains health.

Results: Gut host more than 95% of our serotonin and 70% of our immune system of our body and through a balanced gut microbiome (avoiding dybiosis) we can prevent all mental and many cancers(by boosting our immun system) and keeping a coherent and sinus heart rhythm pattern(bpm) we can boost our cardiac health which has critical roles in preventing cancer and generating stress hormones.

Conclusion: in order to prevent many mental disorder and cancer problems these general otc supplements can boost three-brains public health: Ginkgo biloba (150-250 mg- daily) Phosphatidyl Serine (PS) (100-300 mg - daily) Pyrroloquinoline quinone (PQQ) (20 mg - daily) CoQ10 (50-150 mg - daily) Lutein (10-20 mg - daily) Magnesium (400-800 mg - daily) Vitamin D (3000-5000 IU-daily) Grapeseed extract(400 mg -daily) Prebiotic and Probiotic (Based on Factory daily suggestion) Omega 3 (1000-3000 mg - daily) Curcumin (300 mg-daily)

Keywords: Three-brains Health , Public-Health, Naturopathic medicine

141.

Tumor-treating Fields (TTFields) review article (Review)

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Introduction: Tumor-treating Fields (TTFields), a noninvasive anticancer treatment modality, are low intensity (1–3 V/cm), intermediate frequency(100–300 kHz), alternating electric fields delivered through noninvasive transducer arrays placed locoregionally around the anatomic region of the tumor. TTFields selectively disrupt cell division, and have antimitotic effects in different tumor types which causes reducing tumour growth. electrical forces on cell structure proteins interfered with the chromosome separation during mitosis and induced apoptosis. TTFields can inhibit the mitosis of tumor cells by changing the intracellular electric field, which may effectively overcome chemoradiotherapy resistance. TTFields have been studied for less than two decades.

Methods: clinical trials have been conducted to assess the efficacy of TTFields treatment in other types of cancer as well. These include non-small cell lung cancer (NSCLC), platinum-resistant ovarian cancer (PROC), pancreatic adenocarcinoma (PAC), malignant pleural mesothelioma (MPM), and hepatocellular carcinoma (HCC). Additionally, clinical trials for TTFields treatment in other cancer types are currently ongoing.

Results: TTFields exert mitotic inhibition effects on dividing cells through two main aspects. Firstly, the electric field force and torque disrupt the microtubule assembly process during prophase, leading to spindle damage. Secondly, during telophase, the inhomogeneous electric field in the cell generates dielectrophoresis (DEP) force, driving free macromolecules and organelles towards the cleavage furrow, thereby unbalancing the intracellular microenvironment and ultimately causing the death of the dividing cell.

Conclusion: As mentioned, TTFields interfere with mitosis. TTFields affect mitosis only in actively proliferating tumor cells; normal nerve cells are considered unaffected because they divide slowly. The antimitogenic effect of TTFields is accomplished by electric field force-mediated dipole rearrangement and dielectrophoretic effects. During tumor cell proliferation, α/β tubulin dimers are arranged by their own electric fields to form spindles, and the septin2-6-7 complex is positioned to form a cleavage furrow and contractile ring.

TTFields act mainly on these two high-dipole-moment proteins in tumor cells. First, during mitotic metaphase, tubulin is disturbed by uniform alternating electric field forces generated by TTFields. Tubulin oscillates and spins, disrupting the stability of microtubule heterodimeric protein polymerization and leading to spindle assembly errors and abnormal geometric shapes. Eventually, these effects cause delayed mitosis, abnormal mitotic exit in tumor cells, decreased cell proliferation, and aneuploid cell formation. Next, during mitotic anaphase, electric field forces interfere with the movement and binding of the septin protein, inhibiting its midline localization and function. The contractile elements of the cell membrane spread in a disordered manner throughout the cell, which eventually undergoes violent ectopic contraction, causing cell membrane blebbing. Finally, during mitotic telophase, the cell acquires an hourglass shape, and the electric field lines are highly clustered at the cleavage furrow, generating an uneven alternating electric field that exerts a dielectrophoretic effect on the cytoplasm; in this process, charged macromolecules and organelles are propelled toward the neck of the daughter cell that will soon separate. The cell membrane pressure increases, and the cell ruptures and dies.

Keywords: TTFields, cancer, cancer treatment, tumor-treating fields

142.

Understanding Breast Cancer's Impact on Young Women's Fertility (Review)

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Introduction: Breast cancer stands as the most prevalent cancer diagnosed among women globally, signifying an important health challenge. This disease is known for the uncontrolled proliferation of the cells in breast tissues and manifests in various forms, with triple-negative breast cancer being particularly prominent among younger women. Understanding that factors such as genetics, age, and hormonal influences contribute to breast cancer risk is essential. Early detection remains vital for improving treatment efficacy, hinging on regular screenings such as mammograms and clinical breast examinations. patients diagnosed with breast cancer often undergo a combination of treatment options, including surgery, chemotherapy, radiotherapy, and hormone therapy. Moreover, many women worry about the impact breast cancer may have on fertility. For those who survive, there is encouragement to consider the possibility of pregnancy following treatment.

Methods: Breast cancer diagnosed during pregnancy presents unique challenges, being the most common cancer in this demographic. Treatment approaches must cater to the specific needs of pregnant patients while following standard guidelines for non-pregnant individuals. Safe imaging methods like breast ultrasound and mammography are preferred for diagnosis, although alternatives such as CT and PET/CT may be used if they significantly benefit the mother's health. Fertility preservation techniques, including embryo and oocyte cryopreservation, are recommended before cancer therapy to mitigate risks to reproductive health. Despite high survivorship rates, breast cancer survivors have lower pregnancy rates (estimated between 3.6% and 16%) compared to peers without a history of breast cancer, largely due to treatment-related factors such as hormonal imbalances. This highlights the need for supportive interventions to enhance reproductive opportunities for survivors, along with ongoing research into the relationship between breast cancer, treatment, and reproductive health to empower the on their journey toward motherhood.

Results: The landscape of breast cancer is further complicated by the increasing trend of women postponing childbirth until later in life, resulting in more cases of breast cancer being diagnosed in younger women. Epidemiological data reveals that breast cancer affects over 11000 women under the age of 40 annually in the United States. This prevalence is echoed in countries like Iran, where the incidence is notably high. Although many breast cancer survivors are keen to conceive after completing their treatment, medical advice often recommends delaying this attempt for at least two years due to the elevated risk of recurrence in the immediate years following diagnosis. Additionally, the side effects of breast cancer treatments can adversely affect reproductive health, causing complications such as ovarian function impairment and increasing the risk of congenital anomalies or spontaneous abortion.

Conclusion: Breast cancer is the most frequently diagnosed cancer in women worldwide and presents considerable public health issues due to genetic, hormonal, and environmental influences. Aggressive variants, like triple-negative breast cancer, primarily impact on younger women, underscoring the importance of early detection and effective therapeutic strategies. The potential effects of cancer treatment on fertility must be addressed, considering that many survivors aim to conceive. Improving fertility preservation methods and developing support systems for these women is crucial. Going forward, research should concentrate on creating tailored treatment plans for younger patients and those diagnosed during pregnancy. Additionally, there is a pressing need for advancements in fertility preservation techniques to improve the psychological health and overall quality of life for breast cancer survivors. By focusing on these areas, healthcare providers can ultimately leading to enhanced outcomes and a greater sense of empowerment for those wishing to start families after their treatment journey.

Keywords: Breast cancer- Fertility preservation- Early detection

143.

Using histochemistry technique to detect various differentiation stages of gastric carcinoma (Review)

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Introduction: Gastric carcinoma is one of the most abundant and malignant cancers, and early diagnosis of the disease is very effective in the treatment method and survival rate. This study was conducted in order to investigate histochemistry and its relationship with tumor differentiation in gastric carcinoma.

Methods: Tissue samples of gastric carcinoma of 40 patients with different differentiations (well, moderate, poorly and undifferentiated) along with healthy gastric samples were selected from the pathology department of Imam Reza Hospital (AS) in Mashhad after studying hematoxylin and eosin slides. To ensure the previous diagnosis, 5 micrometer thick sections were prepared and stained with Alcin Blue with PH 1 and 2.5 (for sulfated and carboxylated mucous acid compounds) and examined microscopically. The results were analyzed and evaluated by color intensity table (according to Gong method) and Kruskal-Wallis statistical analysis.

Results: The results of Alcin blue with pH 1 staining showed a positive response in the stroma of normal gastric mucosa and tumor stroma, while gastric gland cells and tumor cells in different differentiations showed a negative response to this pH. In Alcin Blue 2.5

staining, the response of healthy glandular cells was intense, which decreased with the decrease of tumor differentiation and the increase of malignancy.

Conclusion: Probably, the genetic changes in gastric cancer cells have led to the reduction of carboxylated mucous compounds compared to the healthy sample, but in normal and cancerous cells of the stomach, apparently, the lack of synthesis of sulfated mucous compounds can be suggested.

Keywords: Gastric carcinoma, histochemistry, cell differentiation, Alcin blue

144.

Utilizing molecular imaging to screen for cancer at an early stage (Review)

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Introduction: Cancer detection and treatment are significantly improved by early detection since more effective treatment is possible before the disease progresses. However, traditional imaging techniques, such as Computed Tomography (CT) and Magnetic Resonance Imaging (MRI), often rely on anatomical changes to detect cancer, which may not manifest until the disease is advanced. A key benefit of molecular imaging is its ability to visualize cellular and molecular processes that occur before visible structural changes are visible. Cancer biomarkers can be tracked in real-time at a molecular level using specific imaging probes or tracers that bind to cancer biomarkers. As opposed to conventional methods, molecular imaging can detect tumors earlier, predict their behavior, and assess treatment response more effectively. The review discusses advances in molecular imaging modalities for early cancer detection, tumor-specific imaging agents, and clinical implications.

Methods: Recent advances in molecular imaging techniques for early cancer detection were assessed in a narrative review. Through PubMed, Scopus, and ScienceDirect, literature published between 2005 and 2023 was identified by keywords including

"molecular imaging," "early cancer detection," "PET-CT," "tumor biomarkers," "diagnostic imaging," "non-invasive cancer detection," and "cancer imaging agents. studies focused on molecular imaging applications, innovative tracers, and imaging techniques that detect cancer early. A particular emphasis was placed on preclinical or clinical trials with potential translational value to clinical practice.

Results: Molecular imaging has become a powerful tool for the early detection of a variety of cancers, including lung, breast, prostate, and colorectal cancers. A molecular imaging technique can visualize biochemical and molecular changes at the cellular level, as opposed to traditional imaging methods, which detect changes in anatomy. One of the most common techniques used is Positron Emission Tomography (PET), while Single Photon Emission Computed Tomography (SPECT) is another. PET/CT is the most popular technique. Currently, 18F-Fluorodeoxyglucose (FDG) is being used extensively for identifying metabolic changes in cancer cells. However, newer tracers that are more specific are showing promise. For example, Prostate-Specific Membrane Antigen (PSMA) can be detected early in the course of prostate cancer, or HER2-targeted agents can be detected early in the course of breast cancer. Comparing these tumor-specific tracers to general tracers like 18F-FDG, these tumor-specific tracers demonstrate higher sensitivity and specificity. Further, molecular imaging becomes increasingly important in monitoring Minimal Residual Disease (MRD) post-treatment and tracking tumor recurrences. Researchers have also shown that molecular imaging combined with signaling pathways specific to cancer, such as EGFR and VEGF, enhances early cancer detection. In preclinical and clinical studies, new imaging probes, such as radiolabeled small molecules, peptides, and antibodies, are being investigated. These probes can identify tumors on the molecular level.

Conclusion: Molecular imaging can revolutionize the early detection of cancer by enabling visualization of cellular and molecular processes before anatomical changes occur. By using tumor-specific tracers, such as PSMA for prostate cancer and HER2 for breast cancer, this approach improves diagnostic accuracy and sensitivity. A combination of molecular imaging and specific tumor biomarkers and signaling pathways highlights its potential in personalized medicine. Despite the fact that researchers are continually developing new imaging probes and hybrid imaging systems, such as PET-MRI to enable more effective diagnosis of cancer at an earlier stage of the disease. As cancer diagnostics advance, molecular imaging will play a key role in improving patient outcomes.

Keywords: Molecular Imaging Early Cancer Detection PET-CT Tumor Biomarkers Imaging Agents

145.

Viral Vectors for Delivering p53 in Ovarian Cancer (Review)

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Introduction: Ovarian cancer (OC) is a complex and varied disease that disproportionately affects women. It ranks as the seventh most common cancer worldwide, with over 238,000 new cases diagnosed annually. Developed countries see a particularly high burden, where it becomes the second most common gynecological cancer and often proves fatal. The key takeaway is that ovarian cancer isn't a single disease, but rather a group of different subtypes. These subtypes can vary greatly in their behavior. Some, like Type I tumors, grow slowly and stay confined to the ovary for extended periods. Others, like the aggressive Type II tumors, particularly high-grade serous carcinoma, spread rapidly and pose a significant threat from the outset. Ovarian cancer, especially the aggressive HGSOC, continues to be a major threat. Although overall survival rates have improved, HGSOC remains stubbornly difficult to treat, with a low 5-year survival rate. Diagnosing it late and confusing symptoms make it worse. Even the origin of the cancer itself is unclear, hindering efforts to develop effective treatments. There's a glimmer of hope for HGSOC despite the difficulties. A treatment called gene therapy uses tiny carriers to deliver healthy copies of a critical gene (p53) directly into cancer cells. This gene normally controls cell growth, but in HGSOC it's broken. By introducing a working copy, gene therapy has the potential to fix these cells and make them control their own growth again. However, there are challenges that need to be overcome before this approach can be widely used to fight ovarian cancer.

Methods: Researchers explored delivering functional wild-type p53 (WT p53) genes to overcome frequent p53 mutations in ovarian cancer. However, finding an effective delivery system proved challenging. Viral vectors were initially favored due to efficient gene transfer. Adenoviral vectors (like Gendicine, Advexin, SCH-58500) were modified to carry WT p53 genes and lacked the ability to reproduce inside cancer cells for safety.

Results: Despite initial mixed results from early attempts to replace dysfunctional p53 genes using adenovirus delivery (such as Gendicine, Advexin, and SCH-58500), the underlying strategy remains promising. Challenges posed by existing p53 mutations and

the body's immune response to the virus hindered those initial trials. However, researchers are actively exploring novel approaches to rejuvenate p53-based therapies. One exciting avenue involves creating improved p53 genes (such as p53-Bad and p53-CC) that could bypass existing mutations and overcome previous limitations. Additionally, advancements in delivery methods—such as nanoparticles and modified viruses—aim for more precise targeting of cancer cells with fewer side effects. Combining p53 therapy with other modalities, like immunotherapy, holds the potential for a comprehensive attack on ovarian cancer. Despite ongoing challenges related to the variety of p53 mutations, efficient delivery, and reliable disease markers, the relentless pursuit of enhanced p53 genes and deeper insights into ovarian cancer subtypes offers hope for the future of treatment.

Conclusion: Ovarian cancer remains a significant health concern for women despite advancements in treatment. High-grade serous ovarian carcinoma (HGSOC), the most common and lethal subtype, presents challenges due to late-stage diagnosis and limited treatment efficacy. Viral vectors, such as adenoviruses (AdV) and adeno-associated viruses (AAV), have emerged as promising tools for delivering the tumor suppressor gene p53 directly into cancer cells of patients with ovarian cancer. Despite their potential, significant hurdles hinder the widespread application of viral vectors for p53 delivery in ovarian cancer treatment. Therefore, overcoming limitations related to delivery efficiency, tumor penetration, and off-target effects is crucial for their successful clinical application. Continued research in vector engineering and delivery methods holds promise for the development of effective p53 gene therapy for ovarian cancer.

Keywords: Ovarian cancer, HGSOC, p53 gene, Gene delivery, Viral vectors

146.

Vitamin Interactions at the Crossroads of Gut Microbiome and Mitochondrial Function in Cancer: Unraveling Complex Pathways **(Review)**

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Introduction: Cancer research has increasingly focused on the intricate relationships between the gut microbiome, mitochondrial function, and vitamins. These components are integral to understanding cancer progression and treatment. Vitamins, essential for mitochondrial energy production, also influence gut microbiome composition, which in turn affects cancer development and therapeutic efficacy. This review explores how these interactions intersect and their implications for cancer biology.

Methods: A review of the literature was performed using PubMed, Scopus, and Web of Science. The review aimed to consolidate findings on the roles of vitamins, the gut microbiome, and mitochondria in cancer.

Results: The review reveals that vitamin D plays a crucial role in modulating cancer outcomes through its effects on both the gut microbiome and mitochondrial function. Elevated vitamin D levels have been associated with beneficial changes in the gut microbiota, including an increased abundance of Bacteroides fragilis. This shift positively influences immune responses and enhances the efficacy of cancer immunotherapies. Furthermore, vitamin D deficiency correlates with poorer cancer prognoses, highlighting the vitamin's importance in maintaining effective immune surveillance and response. Studies also indicate that vitamin D-induced changes in microbiome composition contribute to improved patient responses to immunotherapy, suggesting that optimizing vitamin D levels could be a viable strategy to enhance therapeutic outcomes. In addition, vitamin deficiencies, such as those in vitamin B12, are linked to mitochondrial dysfunction, which impairs cellular energy production and exacerbates cancer progression. Mitochondrial abnormalities resulting from vitamin deficiencies impact the effectiveness of cancer treatments. The review also points to the intricate interplay between vitamin-mediated metabolic processes, microbiome composition, and cancer development,

suggesting that targeted interventions aimed at correcting vitamin deficiencies and modulating gut microbiota could provide novel therapeutic avenues.

Conclusion: The interplay between vitamins, the gut microbiome, and mitochondria offers new perspectives on cancer treatment. Targeting these interactions through nutritional and microbiome-based therapies could provide innovative approaches to enhance cancer therapy and improve patient outcomes. Future research should focus on these relationships to develop effective strategies for managing cancer and optimizing therapeutic responses.

Keywords: Vitamin, Gut Microbiome, Mitochondrial Function, Cancer

147.

What about the world of colorectal cancer? (Review)

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Introduction: Colon cancer (CRC) was the third most common cancer and the second leading cause of cancer-related mortality, and is associated with high disease worldwide, according to estimates from the International Agency for Cancer Research (IARC) over recent years . Colon cancer (CRC) is a heterogeneous disease, and most CRCs develop slowly from adenomatous or adenomas2 polyps . In addition to the adenoma sequence to cancer, about 25 % of scattered CRCs are caused by toothed precursor lesions 3. The risk of developing CRC can also be associated with age, male gender, genetics, environment, socioeconomic status, nutritional status, physical activity, smoking, and lifestyle factors. Currently, the proportion of older people with CRC has increased ; in 2050, about 6.9 million new CSCs will be diagnosed in adults aged 80 or over worldwide (20.5% of all cancer cases) . By contrast, epidemiological studies have shown that the prevalence of CRC in young people is also gradually increasing. Our goal in this study is to examine the various therapeutic and diagnostic aspects of this cancer.

Methods: In this study,15 articles published from 2016 to 2024, which were in the form of original research and systematic review were examined. The study used the keywords colorectal cancer, treatment of cancer, cancer management.

Results: Various treatments can be used including Endoscopic Treatment Surgical Treatment Laparoscopic Surgery for Advanced Colon Cancer Total Mesorectal Excision and Lateral Lymph Node discovery for Lower Rectal Cancer and... Namberde. As for the endoscopic method, it can be noted that progress in the development of flexible endoscopes and endoscopic devices has increased the demand for minimally invasive treatments. After diagnosis, T1 CRC may be interrupted endoscopically in en bloc endoscopy mucosal incision and endoscopic sub-mucosal incision for large and complex lesions . More recently, anal endoscopic myctomy has been performed for anal lesions with severe fibrosis, in which decomposition is carried out between the inner circular and

outer longitudinal muscle layers 10. Full-thick endoscopic cutting has also been made possible. But despite the rapid advancement of chemotherapy radiotherapy and immunotherapy surgery remains the only possible treatment for advanced CRC 15 therefore, improving surgical treatment options for advanced CRC is crucial.

Conclusion: Currently, patients with advanced CRC are still primarily treated with surgery coupled with neodevent chemotherapy , auxiliary chemotherapy, and radiotherapy to improve surgical treatment. Due to features such as sharp breakdown along embryonic surfaces in the interfacial interface with a complete breakdown of regional lymph nodes, CME is recommended for colon cancer and tme for anal cancer. With the advent of individualized and personalized medicine, continuous improvement in advanced CRC treatment requires data support for randomized clinical trials, which are also needed to provide evidence to support appropriate bowel incision and central lymphadenectomy rates in colorectal cancer surgery. Further studies are needed to determine optimal approaches for surgical treatment of patients with advanced CRC.

Keywords: colorectal cancer, treatment of cancer, cancer management.