Abstract Book

1st International Congress of Biomarkers (ICB)

Urmia University of Medical Sciences-2023

Department of Clinical Biochemistry & Applied Cell Sciences

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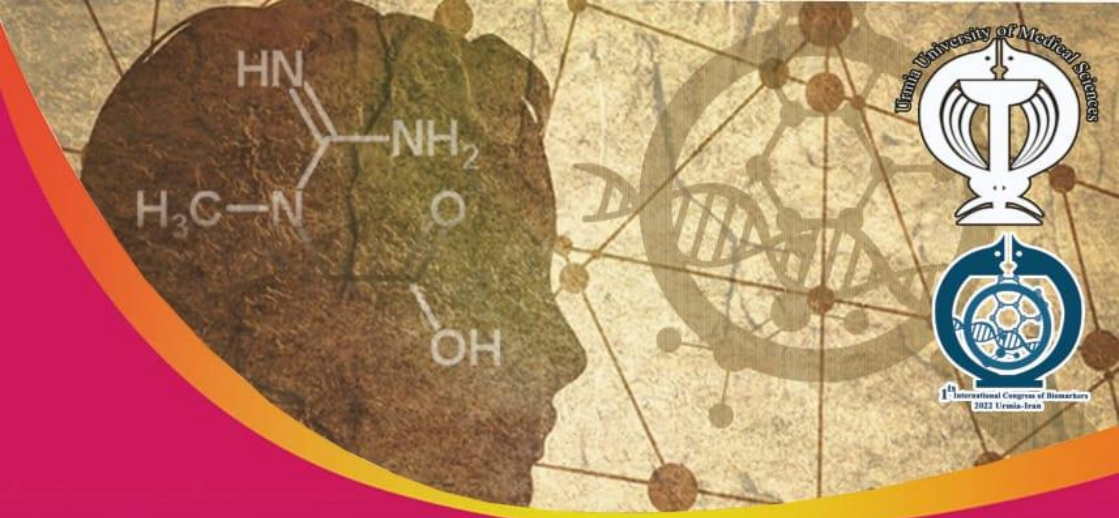

1st International Congress of Biomarkers (ICB)

22-24 February . 2023 Urmia, Iran

Topics:

- Biomarkers in cancer
- Emerging biomarkers
- Immune system biomarkers and graft rejection
- Biomarkers in personalized medicine
- Biomarkers in neurodegenerative diseases
- Biomarkers and epigenetic diseases
- Biomarkers and stem cells

Biochemical monitoring in severe covid- 19

Special Topic: Biomarkers in COVID-19

Abstract Submission Deadline: August 31, 2022

Continuing Medical Education (CME)

Addresse: Djahad Ave, P.O.Box 1138 Urmia, Iran 57147-83734

In The Name of God

Almighty and most merciful God, we approach Thy presence this day to thank Thee for Thy past mercies. We are delighted to have the opportunity to hold a more rewarding and glorious congress than before. In this regard, the 1st International Congress of Biomarkers will be held in October 2022 with the presence of our national respected researchers, and guests from foreign countries in the beautiful city of Urmia. Despite the obstacles and challenges, the medical community of the country has kept up with the advanced world through progressing medical knowledge and providing services to patients. The wise and sincere efforts of researchers to advance the goals of the congress are commendable. It is hoped that with the attendance and participation of you knowledgeable professors, the transfer of experiences and presentation of research conducted in recent years will lead to the promotion of scientific knowledge and skills in the field of basic medical sciences and improving the quality of diagnostic and therapeutic services.

Finally, I would like to express my sincere gratitude to all the colleagues who have spared no effort for the glory and advancement of the university and have rendered valuable collaboration for holding the congress.

Dr. M. Amin Valizad
Chancellor of Urmia University of Medical Sciences
President of the Congress

Dear Colleagues

Urmia University of Medical Sciences is proud to host valuable researchers of the 1st International Congress of Biomarkers in October 2022. The main purposes of holding this congress are to update information, exchange views, and get acquainted with scientific advances in the field of diagnostics and biomarkers. We invite all active and interested researchers in the field of diagnostic biomarkers to accompany us in this field; we can strengthen our scientific relations in Iran and with the scientists of the world by exchanging experiences and benefiting more from the knowledge of specialties.

This congress will focus on different areas of biomarkers including different working groups such as cancer, neurodegenerative diseases, epigenetics, stem cells, person-centered medicine, and disciplines such as biochemistry, applied cell sciences, molecular medicine, biotechnology, immunology, hematology, pathology, medical genetics, laboratory sciences, and all disciplines related to medical sciences that face challenges will be discussed.

It is hoped that this congress will provide an opportunity for experts, and researchers to intercommunicate and present key issues in this field, and its results will pave the way for planning and promoting the health of the people in Iran and the world. I wish everyone success and pride from God Almighty.

Dr. Yousef Rasmi
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Abstracts of 1st International Congress of Biomarkers (ICB)
12-14 Oct. 2022 Urmia, Iran

Biomarkers of different cell types during differentiation from mesenchymal stem cells

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Mesenchymal stem cells (MSCs) also known as mesenchymal stromal cells have the ability to self-renew and differentiate into different cell linages. MSCs have been isolated from various tissues and body fluids. These cells are multipotent cells with highly specific characteristics in terms of morphology, immunological and biological functions.

In our laboratory, we could isolate MSCs with differentiation potential from different sources, including, bone marrow, adipose tissue, cord tissue, cord blood and Warton's jelly. Hepatocyte-like cells, endothelial cells, adipocytes, osteocytes, insulin-producing cells and neuronal cells were the biologically active cells differentiated from MSCs in our lab. Monitoring of such markers is useful for better understanding growth, maturation and biological activities of cells differentiated from the stem cells.

In case of hepatocytes, in addition to morphological changes, biological variations were evaluated by monitoring hepatic markers such as, drug metabolizing enzymes, albumin α-fetoprotein and factors related to metabolism of hepatocytes. In case of differentiated endothelial cells, Von Willebrand (vW) factor, vascular endothelial growth factor receptor (VEGFR2) are used to prove endothelial differentiation. β-cells differentiated from MSCs were evaluated by measuring insulin and pancreatic β-cell markers. Morphological changes observed during differentiation of MSCs into neuronal-like cells is a reliable marker, however such changes are confirmed by changes in pax-6, neuN and, neurofilaments (NfL) which are markers for growth and maturation of neurons.

In conclusion, biochemical and molecular markers are reliable variables for monitoring the efficacy of stem cell differentiation. These information are implicated in identification of different cell lineages and their therapeutic application and regenerative medicine.

Proteomics applications in biomarker discovery

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The potential application of proteomics in clinical research to elucidate disease pathogenesis and discover clinical biomarkers is enormous. The proteomics investigation involves the detection, identification, and characterization of proteins, making it favorably promising for biomarker discovery across many diseases. The most common approach toward biomarker discovery in proteomics involves assessing relative differences in proteins between cases and controls. The most common methods for protein separation are gel-free and gel-based methods and for protein identification, use mass-spectrometry. The biomarker discovery process can be divided into three steps; Discovery, verification, and validation. However, there are several limitations in this field; proteomic technique in combination with other omics data and analysis via bioinformatics methods could be helpful in biomarker discovery.

Keynote Speaker

1st International Congress of Biomarkers

An Overview on Application of Biomarkers in Medicine:

Possible New Insight on Computational Biology Approaches

Nosratallah zarghami

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There are numerous ways that investigation and use of biomarkers can aid the practice of medicine. By definition biomarker is a biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease. A biomarker may be used to see how well the body responds to a treatment for a disease or condition. Also called molecular marker and signature molecule. The first cancer biomarker ever reported was the light chain of immunoglobulin in the urine, as identified in 75% of patients with myeloma in an 1848 study. The test for this marker is still employed by clinicians today, but with use of modern quantification techniques

The time line for biomarker discovery have been shaped by advances in technology, biology, and data science. In the past, biomarker discovery relied heavily on manual methods such as microscopy, histopathology, and immunohistochemistry. Today, modern technologies such as genomics, proteomics, and metabolomics allow for the identification of potential biomarkers at a much faster rate. In the future, advances in data science and machine learning will continue to provide insights into the biological processes involved in diseases and improve the accuracy of biomarker discovery. Additionally, the development of novel biomarkers, such as those based on innovative technology, will continue to expand the range of biomarkers available for use in clinical practice.

Biomarker discovery is an essential component of medical research, as it allows scientists to identify, validate, and apply biomarkers to diagnose and treat various diseases. The timeline for biomarker discovery typically involves identifying potential biomarkers, validating them, and testing them in clinical trials. Biomarkers have the potential to greatly improve the accuracy and reliability of diagnosis and treatments, leading to better outcomes for patients.

Computational biology approaches can be used to help identify and validate potential biomarkers for a given topic. These approaches involve using data-driven methods, such as machine learning algorithms, to analyze large datasets of genomic, proteomic, and other types of data. Using these methods, it is possible to identify patterns in the data that can be used to identify potential biomarkers and to validate their accuracy and reliability. Additionally, these methods can be used to develop new models and to assess the impact of variables on the results.

Viewpoint: BQ COVID-19 Variants

Reza Nassiri

International Institute of Health, Michigan State University, East Lansing, MI 48824, USA

COVID-19 moved at a rapid pace after omicron surfaced in the US toward the end of 2021 and spread exceedingly fast. Since then, multiple omicron subvariants have emerged. Two subvariants, BQ.1 and BQ.1.1 became the dominant strains in the U.S. in mid-November 2022, overtaking BA.5, which was thought to be a relatively mild version of the virus. The BQ strains are thought to be efficient than BA.5 at evading immunity from vaccination or previous infection. The two subvariants, BQ.1 and BQ.1.1 are causing 55% (or more) of new infections in the U.S., according to data published by the CDC two weeks ago. The omicron BA.5 subvariant, once dominant, now makes up only a fifth of new Covid cases. The BQ subvariants are more immune evasive and likely resistant to key antibody medications, such as Evusheld (tixagevimab and cilgavimab), and bebtelovimab, used by people with compromised immune systems, according to the National Institutes of Health (NIH). This includes organ transplant and cancer chemotherapy patients. There are currently no replacements for these drugs. As Pfizer's antiviral Paxlovid remains questionable due to rebound virus (stats not fully available), organ transplant patients often cannot take the pill because of the way it interacts with other medications they need. The more immune-evasive XBB (Gryphon) subvariant is also circulating in numerous countries, which comes from the BA.2 sub-lineage (a hybrid version of two strains of the BA.2 form of Omicron). The WHO and CDC are closely monitoring the spread of XBB, which is poised to trigger a wave of new COVID-19 infections this winter. The expression "old is gold", the face masks are yet effective minimizing the risk of exposure. The natural immunity with XBB and the interval between infection and reinfection warrants clinical investigations.

Role of biomarkers in toxicology studies: Better tools for better Prevention, Diagnosis and treatment

Hassan Malekinejad [1,2]

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Biomarkers as measurable indicators are developed and used for different purposes including: prediction of health condition, diseases prevention, treatment and health materials promotion. In toxicology field like others and sometimes even much urgently, having such indicators to make a correct decision about the poisoned person or contaminated food and medicine is definitely required. Moreover, these biological markers are helping to have the reliable response of the intoxicated person to the specific protocol of treatment, too. In this article, the effectiveness of some biomarkers in the prevention, diagnosis and treatment of some environmental hazardous poisonings and in various acute and chronic forms will be presented.

Bimarkers in delayed graft function

Pedram Ahmadpoor

Associate professor of nephrology

By increasing the prevalence of obesity, hypertension and diabete mellitus in our societies, the number of CKD and ESRD patients are increasing. Improvement of standard of care leads to longer survival on renal replacement therapies (chronic hemodialysis and peritoneal dialysis). Renal transplantation is associated with better quality of life, improved survival and lower long term costs in ESRD patients. In order to manage the burden of dialysis patients every country needs to establish an active and efficient renal transplantation program. Indeed to reduce the long waiting list, it needs not only to increase the incident renal transplantation activity but also to improve graft survival. Delayed graft function is a complication that may impact graft survival. The highlights of this presentation is focused on prevalence and risk factors of DGF and discussing about prognostic and predictive biomarkers of delayed graft function.

Insight to emerging biomarkers for early disease diagnostics

Ghazala Ashraf

College of life science, Huazhong university of science and technology, Wuhan, China

For applications ranging from accurate disease diagnosis to the decoding of complex life processes, methods that detect multiple classes of biomarkers from biological samples are essential. Theoretically, it is challenging to generalize a single recognition system to a variety of targets due to differences in target detection, instrumentation, and signal transduction. We provide a thorough overview of recent advancements in the detection of prominent biomarkers using electrochemical sensing techniques. We go over the variety of these sensing platforms for the development of reliable sensory interfaces, as well as their characterization, operation, and analytical capabilities. The endogenic small biomolecules that are clinically relevant are covered, including neurotransmitters, cancer biomarkers, and more. The identification of a wide variety of biomolecules for *in vitro* and *in vivo* analysis is presented. We also emphasize the biosensor's capability to detect analytes in complex matrices or those built using novel nanoarchitectures. The pros and cons along future possibilities are also discussed.

Bio-nanotechnological advancement in drug, cell, and gene therapeutic applications

Hani Al-Salami

School of Pharmacy, Curtin Health Innovation Research Institute, Curtin University, Bentley, Perth, Western Australia, Australia

More than half of pharmaceutical therapeutics require specialised delivery systems to enable optimum stability, safety, targeted delivery, and improved efficacy profiles. Therapeutic encapsulation with polymers and hydrogels were pioneered in the 1960s and 1970s at McGill University, to protect enzymes and other therapies from the body's immune response. Since then, such encapsulation technology has expanded significantly to encompass encapsulation of small molecules, enzymes and hormones, viable cell transplantation, and gene-based therapies. The technology also encompass food bioencapsulation and biopreservation processes. Collaborating with researchers and clinicians in Australia, NZ and the EU, recent advancement led by the team at Curtin University and Ear Science to develop new platforms for therapeutic delivery, using human-bile acids. Bile acids are endogenously produced enzymes in humans and have many unique features such as improving the pharmaceutical properties of formulations, the ability to act as permeation enhancers, and their own pharmacological effects when given in sufficient amount. The team examines bile acid-based nano delivery systems in the context of brain, ear and oral delivery of pharmaceuticals. Overall, our findings showed that in oral and ear delivery of therapeutics, secondary bile acids showed significant useful effects such as permeation enhancing and improved rheological measurements, while for brain delivery unconjugated bile acids showed significant cell protective and endocrinological pharmacological effects, suggesting the importance of bile acids in bio-nanotechnology and their wider potential applications to advance current therapies.

Oxidative stress and inflammation biomarkers as emerging targets of Nutraceuticals

Imtiyaz Murtaza

Division of Basic Sciences and Humanities, Shere Kashmir University of Agricultural Sciences and Technology of Kashmir, J&K, 190025, India

In the present era, the universal trend has shifted from synthetic to food based medicine due to their lesser side effects. It has been found that fruits like apple, pear, berries, cherries, peaches, plums nuts and green leafy vegetables, tomato, turnip, cucumber etc. are treasure of pharmaceutically significant nutraceuticals particularly caretonoids, alkaloids, glycosides, phenolics, flavonoids, volatile oils, steroids etc. In order to capture the pharma market share, such potential nutraceutical should be evaluated thoroughly through sufficient preclinical and clinical tests to develop a well-established nutra-pharmaceutical that can in turn help to address health insecurity related problems due to potential nutritional, safety and therapeutic effects, as compared to synthetic therapeutic agents. We have reported mechanism of action of several fruit and vegetable based bioactive nutraceuticals like quercetin, fisetin, lupeol, delephidin, phenolic enriched fenugreek plant extracts etc against oxidative stress related diseases like colon cancer, prostate cancer, pancreatic cancer, diabetes etc. These bioactive compounds need further investigations including efficacy evaluation under both in vitro & in vivo, animal toxicity, dosage and bioavailability testing, product formulation for clinical investigations before recommending them as alternate medicines against various oxidative stress and inflammatory related degenerative diseases in humans.

Epoxyeicosatrienoic acid (EET), an arachidonic acid derivative governs hepatic insulin signaling

Kakali Ghoshal

Postdoctoral Researcher, Vanderbilt University Medical Center

Cytochrome P450 (CYP) epoxygenases metabolize arachidonic acid to four epoxyeicosatrienoic acid (EET) regioisomers having several biological activities. We observed deletion of *Cyp2c44,* a major EET producing enzyme in mice makes them insulin resistant. Although EETs are highly bioactive, it is the target of soluble epoxide hydrolase (sEH) and forms less biologically active DHETs. EET analog or EET-A are water soluble, functional analog of biological EETs, having similar functions but does not get affected by sEH activity. This led us investigating whether administration of EET-A could restore insulin signaling *in vivo* in *Cyp2c44(-/-)* mice and the underlying mechanisms by which this effect is exerted. *Cyp2c44(-/-)* mice treated with the analog EET-A for 4 weeks improved fasting glucose and glucose tolerance compared to *Cyp2c44(-/-)* mice treated with vehicle alone. This beneficial effect was accompanied by enhanced hepatic insulin signaling, decreased expression of gluconeogenic genes and increased expression of glycogenic genes. Mechanistically, we show that insulin-stimulated phosphorylation of insulin receptor β (IRβ) is impaired in primary *Cyp2c44(-/-)* hepatocytes and this can be restored by cotreatment with EET-A and insulin. Plasma membrane fractionations of livers indicated that EET-A enhances the retention of IRβ in membrane rich fractions, thus potentiating its activation. We identified that EETs govern hepatic insulin signaling by stabilizing activated membrane-associated IRβ and potentiating insulin signaling. Thus, we provide evidence that Cyp epoxygenase derived EETs are major regulators of hepatic insulin signaling.

Inflammatory Markers in Hospitalized Covid Patients leading to Sepsis – An age-dependent or age-independent perspective.

Laiqha Khadri

Founder at Immune Inspired Health Consulting in Diabetes & Cancer (COVID), India

Classically, sepsis has been characterized by an exuberant immune response, reflected in many-fold higher levels of inflammatory and hemostasis markers. sepsis in the elderly is driven by an age-related increase in inflammation. Recently it has been hypothesized that sepsis may also be characterized by an exuberant anti-inflammatory or immunosuppressive phase that occurs after the initial inflammatory burst. Age-related differences in inflammatory and coagulation responses are affected through the continuum of healthy state, before infection occurs, to severe sepsis and recovery. There are several explanations for a persistent pro-inflammatory state following sepsis. First, resolution of inflammation is an active and highly regulated process that may be age-dependent. Anti-inflammatory mechanisms are activated within the first few hours of acute inflammation. Prostaglandin-derived lipoxins and resolvin D2 induce apoptosis in neutrophils and help stem the inflammatory response from sepsis. These systems may be impaired with age. For example, aging is associated with diminished lipoxin levels. If so, the profound inflammation and coagulation that occurs during sepsis may in fact persist at a lower level for months after apparent recovery. Additionally, patients with severe sepsis and acute respiratory distress syndrome have been found to have deficient glucocorticoid mediated down-regulation of inflammation, despite elevated levels of circulating cortisol. Second, sepsis may accelerate cellular senescence in older adults. Cellular senescence is triggered by a wide range of stimuli, including DNA damage and oxidative stress, both of which are hallmarks of sepsis, associated with secretion of several pro-inflammatory molecules, such as IL-6, IL-8, and IL-1. This unintentional deleterious effect is proposed to be a contributor to the chronic inflammatory state of aging, and may be further exacerbated after critical illness.

The mechanism of MBNL family of alternative splicing factors in colorectal cancer

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Alternative splicing (AS) allows generation of different protein isoforms from initially identical transcripts. Recent studies indicate that dysregulation of alternative splicing has been implicated in the pathogenesis of several diseases, including cancer and muscular dystrophies. AS is known as a versatile and powerful mechanism which is tightly regulated by splicing regulatory proteins. One of the trans - acting splicing regulatory factors are proteins of muscleblind-like (MBNL) family which consist of three members, namely MBNL1, MBNL2 and MBNL3. Primarily, MBNL proteins function as key regulators of AS during mRNA maturation. Our project is focused on gene expression level of MBNL family as key regulators of alternative splicing in colorectal cancer. In addition to MBNL genes, we analyzed selected alternatively spliced isoforms that were confirmed to be regulated by MBNL to evaluate change in MBNL activity, and expression of cancer-related CD44 variants 3 and 6 as a relevant model of alternative splicing.Samples were collected within 20 min after the removal of the tumor tissue from the patient, and small pieces of tumor samples and healthy mucosa were immediately frozen and archived. RNA isolation was done by TriReagent (MRC) and cDNA was synthetized by First Strand cDNA Synthesis kit (Fermentas). Relative gene expression was tested by quantitative real-time PCR. Results were analyzed and basic statistical analysis was carried out using the Bio-Rad CFX Manager software. In the present study, we analyzed the expression of selected gene set on 108 patients. All genes show statistically significant deregulation between tumor and healthy tissue. Our data suggest that MBNL1, MBNL3, and alternative splicing of FOXP, CD44 and EPB41L3 could be deregulated. It is estimated that

the expression profile of three MBNL paralogs and their correlated effect with the set of transcription factors might alter multiple splicing event. Our data show the change in the MBNL expression and also corresponding changes in expression of splice-variants that are known to be regulated by MBNL. Marginally significant correlations were observed among expression of studied genes and T, N, M, G and UICC clinical factors, with minute differences in gene expression among individual groups.

Exosomes and Recent Advances in Biomarker Platforms for Early Diagnosis of Cancer

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Cancer is a complex disease related to genetic abnormalities and subsequent cellular and non-cellular host responses. Cancer causes the death of millions of people each year, mostly in developing countries, and can be prevented by early detection and effective treatment strategies. Cancerous cells release small vesicles from cells with different characteristics to the surrounding biofluids to maintain cancer-specific signaling networks and ensure cellular transduction. These cells create a dynamic environment of interaction by producing and modifying the contents of extracellular vesicles (EVs), such as exosomes, microvessels, and apoptotic bodies. Exosomes are small EVs that are increasingly recognized for their role in carcinogenesis and their potential as cancer biomarkers. They are nearly ubiquitous in biological fluids, and contain tumor-derived materials such as DNA, RNA, proteins, lipids, sugar structures, and metabolites. The almost ubiquitous finding of exosomes in all biological fluids suggests that most cells have the ability to produce exosomes, as well as being an essential component of cell-cell communication. Exosomes carry molecules on their surface that provide information about their origin and allow sorting of vesicle types and accumulation of signatures of tissue-specific origin. Exosomes renew their contents in response to metabolic processes in which the cell is involved, reflecting the heterogeneous biological changes associated with growing tumors. In this context, exosomes derived from cancer cells are potential candidates to be used as reliable next-generation biomarkers for noninvasive early cancer detection, prognosis, and evaluation of therapeutic efficacy.

Micro RNAs as Biomarkers & Therapeutic Tools

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We have studied the role of miRNAs in several clinical scenarios as biomarkers and therapeutic agents. In contrast, failed regeneration in a similar cohort is associated with distinct miRNA enforcing cell cycle inhibition and DNA methylation. Also enforced changes in expression of two miRNA recapitulating changes observed in failed regeneration led to complete growth inhibition of multi-lineage cancers in vivo. Selected miRNAs may serve as intragraft and serum biomarkers for recurrent HCV after LT and help to distinguish between ACR and recurrent HCV. We continued to evaluate whether the serum expression of this regeneration-linked miRNAs signature is associated with clinical outcomes in acute and chronic liver diseases. Patients were grouped depending on their clinical outcome. Global serum miRNA expression was analysed using PCR arrays and selected miRNA expression using targeted PCR. We demonstrate that specific regeneration-linked miRNAs discriminate outcomes in both clinical scenarios. Based on our extensive studies we aimed to use this microRNA signature to develop outcome prediction models for APAP (acetaminophen) induced ALF. We show that blood test markers that measure the potential for liver recovery may help improve identification of patients unlikely to survive ALF who may benefit from a liver transplant. In our latest study, we have performed the largest study of miRNA expression across the full clinical spectrum of decompensated CLD (Chronic Liver Disease). We have demonstrated that miRNA associated with systemic inflammation discriminate between compensated and decompensated CLD states and may have a role in predicting future decompensation. In summary using different clinical scenarios we showed that miRNAs can be used as biomarkers to diagnose or predict the outcome of disease. Also these small molecules can be utilised as new therapeutic tools for a wide range of diseases including cancer.

An Innovative Aryl Hydrazonal Derivative Drug Candidate For Breast Cancer Immune Types

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There is still no specific drug for the survival of triple negative breast cancer patients. Further, anti ER2+ drugs are unable to improve the overall response to patient treatment and relapse in ER2+ breast cancer patients are an important clinical problem. Besides, some breast cancer patients resist drug treatment, making it much more difficult to control the disease. Novel salicylate and indazole derivatives from aryl hydrazonal compounds were synthesized. The compounds were tested on a set of breast cancer immune subtypes and its resistant forms. Anticancer effects and cancer pathways of the compounds were determined by array and flow cytometric methods. A compound that suppress doxorubicin resistant cell line and an effective compound for triple negative and ER+ form were determined. The effect of compound at molecular level searched with array and the compound is effective to drive cells to apoptosis.

MUC13- A novel cancer biomarker for early pancreatic cancer diagnosis

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By 2030, pancreatic cancer (PanCa) is projected to be the second leading cause of cancer related deaths. The early diagnosis of PanCa remains a clinical challenge, predominantly due the lack of effective diagnostic biomarkers. Therefore, the scientific community is making tremendous efforts toward identification of novel early diagnostic markers, as existing biomarkers, including CA19-9 have yielded only suboptimal efficacy in early-stage detection. Mucins are high molecular weight glycoproteins found in mucus that play an important role in diverse biological functions, such as differentiation, cell adhesion, immune response, and cell signaling. Altered mucin expression can be seen in a variety of diseases, including cancer. Recent studies have suggested that high expression of MUC13, a newly identified epithelial cell surface mucin, in PanCa and the overexpression of MUC13 in PanCa cells leads to enhanced tumorigenic and metastatic phenotypes. These characteristics of PanCa cells are mediated by physical interactions between MUC13 and HER2/Neu. Additionally, MUC13 expression inversely correlates with the expression of the tumor suppressor microRNA-145 (miR-145). In addition to our previous studies, the potential role of MUC13 in pancreatic pathophysiology has also been recognized by other institutions. In this lecture, we will provide a comprehensive investigation of MUC13 expression using our newly generated anti-MUC13 monoclonal antibody (MAb) in a large cohort of human PanCa tissue samples. The expression pattern and subcellular localization of MUC13 will be discussed to demonstrate its correlation with early PanCa diagnosis, patient's clinical course, and prognostic significance. We will discuss how MUC13 expression can be useful to discriminate low and high malignant potential early lesions of PanCa (such as PanIns, IPMNs, MCNs). Additionally, we will provide information how MUC13 expression can be useful for developing advanced, targeted molecular therapeutics for the effective PanCa treatment.

Biomarkres in Digestive Tract Neoplasia: Current Status and Future Directions

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More than 50 biomarkers are mentioned in the book of World Health Organization (WHO) classification of tumours Digestive System Tumours. These markers are important for clinical management of patients with cancer in terms of subtyping, prognostic, and prediction of responses to therapy. Major markers of clinical uses include Her-2 in adenocarcinoma of oesophagus and stomach, microsatellite instability (MSI) in gastric adenocarcinoma, MSI, RAS and BRAF mutations in colorectal carcinoma. Studies show that there are potential actionable biomarkers. Awareness of application of the new technologies such as whole slide imaging, tissue microarray, liquid biopsies increase the potential of detection and application of biomarkers in digestive tract neoplasia.

Multiple Epitope-based Vaccine Targets Against Emerging Variants of SARS-Cov-2

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The SARS-CoV-2 virus has infected over 607,888,815 people worldwide since its emergence in Wuhan, China, in 2019. Although 63.4% of the world's population has been fully immunized against the virus, a significant number of new cases is reported every day. Countless efforts have been made in the past two years to prevent, manage, and treat COVID but the virus's quick and constant evolution enables it to survive all the therapeutic efforts. SARS-Cov-2's variants like alpha, beta, gamma, delta, omicron, and the recent-most subvariants of omicron (BA.4#, BA.5#, BA.2.12.1, and BA.3.75***) require one-for-all solution and to this end, this study focuses on the prediction of multiple-epitopes-based vaccine targets against the existing, emerging, and potential SARS-Cov-2 variants. Immunogenic surface proteins, conserved in all variants of SARS-Cov-2, were selected from its genome. B-lymphocytes-specific epitopes, MHC-I-restricting epitopes, and MHC-II-restricting epitopes in the target proteins were screened according to their antigenic potential, non-allergenicity, non-homology to the human host, and an adequate elicitation of IFN-gamma by MHC-II epitopes. The short-listed epitopes were fused together with different linkers (EAAAK, AAY, GSSS) along with a 50S-ribosomal protein adjuvant to ease the vaccine candidate's entry into the host cell and induce a strong HTL response. The secondary and tertiary prediction of the candidate elucidated a soluble and thermostable structure. Immune simulations, molecular docking with TLR-2, and the docked complex's molecular dynamics simulations validated the construct's potential to stimulate a long-lasting immune response. The homology analysis of the vaccine candidate with all SARS-Cov-2 variants further confirmed its potential against all variants;

AMH: hormone on ovarian reserve

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To date, AMH is best known as a serum marker for ovarian function, in terms of diagnosing ovarian reserve and polycystic ovary syndrome (PCOS). In the ovary, AMH is produced by the granulosa cells of developing small follicles including primary to small antral follicles (up to 8 mm in diameter). Therefore, the serum level of AMH is strongly related to the number of developing follicles. In order to check ovarian function, other than AMH, various indices such as number of antral follicles (AFC) through ultrasound and levels of FSH, LH, inhibin B and estradiol are also used. However, considering the cycle-dependent changes in the levels of FSH, LH, inhibin B and estradiol, these are not of much interest regarding ovarian function evaluation. Further, in the case of AMH, these changes are negligible and it has been proven that AMH is not expressed in follicles larger than 8 mm and it is also not present in the corpus luteum; today, AFC and AMH levels are used to assess ovarian function. However, there are some factors that can affect the level of AMH and they should be taken into consideration. The majority of women at childbearing age use hormonal contraceptives or IUDs, which can have an effect on AMH levels; there are conflicting reports in this field. Other factors that can cause changes in AMH levels include endometriosis, cystectomy for the treatment of endometrioma, PCOS, autoimmune thyroid disease and chemotherapy and radiotherapy in cancers. Body mass index and vitamin D levels are also effective in AMH levels.

Most of the studies have shown that AMH levels are the best available measure for evaluating ovarian reserve in clinical situations such as infertility treatments (especially IVF), ovarian dysfunction (especially PCOS), gonadotoxic cancer treatment or ovarian surgery. Ovarian response prediction is effective in controlled ovarian stimulation protocols and prediction of normal and abnormal menopause age. However, there are concerns about the performance of AMH assay under different conditions and internal and external factors affecting AMH levels that should be considered.

Biomarkers of glycation and aggregation

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The toxicity of sugars is realised during the prolonged hyperglycemia. The carbonyl groups of sugars react with the amino groups of proteins and other biomolecules resulting in the formation of heterogeneous groups of deleterious compounds collectively known as advanced glycation end products (AGEs). Some of the important glycation products are methylglyoxal, carboxymethyl lysine (CML), carboxyethyllysine (CEL), pentosidine etc. Another very good marker for glycation in the blood of diabetics is glycated hemoglobin (HbA1c), measured in the blood to assess the duration of hyperglycemic situations. Glycation also leads to aggregation and glycoxidation causing the functional loss of biomolecules especially proteins and DNA. The generation rate of reactive oxygen species is also observed to be increased during the glycation and its downstream processes. The assessment of these products is essential for the disease management and treatment approaches. Spectroscopic, fluorimetric, chromatographic and electrophoretic techniques are used for the analysis of these products and markers in the body fluids.

Fluorescence based nanobiosensors for cancer detection

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Cancer, as a complex disease, is one of the major leading cause of death around the word. The main reasons for high mortality rate of this disease is lack of efficient methods for the diagnosing cancer at the early stages. The detection of cancer biomarkers significantly improves diagnosis and monitoring as well as evaluation of the relevant therapeutic. The approved tests for cancer biomarkers suffer from some limitations such as insufficient sensitivity, high price, time consuming and complicate procedures, etc. Therefore, the design and development of simple, sensitive, and cost-effective methods for early diagnosis and treatment of cancer are so important, and lots of efforts have been made for this purpose. Recently, nanobiosensors have attracted tremendous attention for early cancer diagnosis due to their potential to develop sensitive, cost-effective, reliable, and rapid strategies for detecting cancer biomarkers. Various sensing systems including electrochemical, optical, mass, and calorimetric methods have been applied for designing such biosensors. In this presentation, fluorescence based nanobiosensors and their application in cancer diagnosis will be discussed. After a brief introduction to the nanobiosensors, bioconjugation strategies and fluorometric detection methods will be explained. At last, some recent advances in the field of cancer fluorometric biosensors will be presented.

The role of biomarkers in prediction of drug resistance

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As biomarkers we characterize quantitatively measurable indicators of biological processes and once validated can play a critical role in disease diagnostics, the prediction of disease progression, and monitoring of the response to treatment. More specific biomarkers, play a vital role in biomedical research including the drug discovery and development, including: i) their use as diagnostics to prove the presence of a disease, ii) predicting disease progression and the characterization of disease severity, iii) assessing as well as predicting the clinical benefit or the developed toxicity resulting from a therapeutic procedure, iv) predicting and monitoring treatment response. Biomarkers apart from their use to better understand disease mechanisms and to identify novel disease targets are important of a personalized medicine approach to customize treatment to the specific characteristics of each patient. For the development of clinical important biomarkers is important to explore the effect of inter-individual genetic differences on the pharmacokinetics, pharmacodynamics, efficacy, and safety of drug treatments. The personalized, genetic-based approach that will optimize therapeutic outcomes is the future of the disease therapy.

Epigenetic biomarkers in neurodegenerative disease

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In the recent years, the increase in the number of epigenetic-related diseases such as non-infectious inflammation, cardiovascular diseases, cancer, dementia, and Alzheimer's has led scientists to use epigenetic biomarkers for the early diagnosis of these epigenetic diseases. The reversibility of epigenetic marks raises further interest in this topic. For this purpose, a good understanding of the epigenetic mechanisms underlying aging is crucial. Epigenetic clocks have been successfully designed to monitor these mechanisms and the influence of the environmental factors. Further studies on age-related diseases should be performed to determine the epigenetic signature, as well as to detect the defect in the epigenetic mechanism, thereby identifying potential therapeutic targets. Uncovering the molecular mechanisms involved in aging is essential for prolonging lifespan. As for the duration of health, a better understanding of the mechanisms involved in age-related pathologies is crucial. Epigenetic clocks can also be used to monitor and predict age-related diseases, thus enabling treatment at a very early stage. In the last few years, published studies have been describing age reversal techniques. Early rejuvenation methods involving loss of cell differentiation were replaced by epigenetic reprogramming to prevent any possible tumor development. The fact that the epigenetic clock can be used in the early diagnosis of cancer and neurodegenerative diseases that increase with age has increased attention on the epigenetic clock. The presence of epigenetic factors in the mechanisms of dementia and Alzheimer's, which comes with age and increases rapidly in the last century, and the use of epigenetic markers in their early diagnosis is important in terms of preventing the progression of these diseases. We know that early detection of such neurodegenerative diseases, increase the chances of success. We think that special epigenetic clocks can be developed in the future for the early diagnosis of the of the diseases by changing the epigenetic mechanisms of patients were affected by the negative changes on their epigenetic mechanisms who are affected by the environmental conditions, therefore the diagnosis with epigenetics will be more important than genetics.

MicroRNA-217: a therapeutic and diagnostic tumor marker.

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Cancer as one of the great etiologies of death has considers health challenges in the world. Since, the identification of cancer cells in the early stages can significantly decrease mortality and morbidity rates; it is needed to find novel early detection cancer methods and markers. MicroRNAs (miRNAs) have critical roles in regulation of cell cycles, migration, apoptosis, and cancer progression. Moreover, due to the good stucture of MicRNAs than mRNA in body fluids, they can be considered as non-invasive diagnostic or prognostic markers in cancer patients. In this lecture I have reviewed the role of miR-217 during Cancer progressions. It was observed that *miR-217* mainly exerts its function by regulation of the transcription factors during tumor progressions. The WNT, MAPK, and PI3K/AKT signaling pathways were also important molecular targets of *miR-217* in different type of cancer solid tumors. The present review introducing miR-217 as a non-invasive diagnostic marker and therapeutic target in cancer therapy.

Biomarkers in diagnosis and treatment of parasitic disease

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Treatment and diagnosis are key factors in controlling invasive transmission of the parasitic disease. However, traditional methods of detecting and treating parasites are becoming increasingly ineffective in reducing the transmission of parasitic diseases. The purpose of this study is to investigate the role of biomarkers in early diagnosis or their use as a target in the treatment of parasitic disease. Data for this review were obtained from a database search using a combination of the following terms: parasitological diagnostics, biomarkers, treatment, and microRNAs. A review of various studies showed that miRNAs have a high diagnostic and treatment potential for parasitic diseases. For example, establishes miR-197-5p as a miRNA inhibitor for Plasmodium. Inhibition of miR-548d-3p reduced Leishmania braziliensis growth. Also, miR-155 inhibitor and miR-15a mimic in L. major can induce apoptosis and decrease parasite burden. Studies revealed that parasitic miRNAs including egrmiR-71 and EGR-let-7 as biomarkers can be detected in human plasma and could be used as a new method in the rapid diagnosis and monitoring of hydatidosis. The use of biomarkers, especially micro RNAs, can be used as pioneering and new methods in the treatment and diagnosis of parasitic diseases, and the future is predicted to be very promising. The utilization of biomarkers in basic & clinical research has become so common that as primary endpoints in clinical trials are now accepted.

Assessment of the Level of Interleukin-12 in Gingival Crevicular Fluid of a Group of Patients with Aggressive Periodontitis and a Group of Healthy Subjects

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Aggressive periodontitis (AgP) is a type of periodontal disease that is relatively prevalent among Sudanese population. The disease generally affects younger individuals and might lead to tooth loss if undetected early, leading to costly and long periodontal treatment. Until today, no reliable detection tool is present, so diagnosis is confirmed only after periodontal tissue loss has already occurred. Interleukin-12 (IL-2) has both proinflammatory and immune-regulatory effects and it has been implicated in the pathogenesis of other inflammatory diseases such as rheumatoid arthritis. However, it was not studied extensively in Sudanese population. Therefore, the aim of this study was to measure and compare the level of IL-12 in the gingival crevicular fluid (GCF) of patients with AgP and healthy subjects without periodontitis.

In this study, 30 patients with AgP and 30 healthy subjects were recruited. The periodontal parameters included bleeding on probing (BOP), periodontal pocket depth (PPD), and clinical attachment level (CAL). GCF levels of IL-12 were measured.

A total of 60 participants were enrolled in this study with female predominance of 83% and males comprising 17%. The results of this study showed slight elevation in the level of IL-12 in the GCF in AgP group with a mean value of (60.7) and a mean value of (52.7) in the healthy subjects group; however, the difference was not statistically significant (p-value = 0.120). Also, no statistically significant correlation was found between the level of this interleukin and periodontal parameters with slight elevation in AgP group. The p-value for BOP, PPD, and CAL was 0.369, 0.985, and 0.797, respectively. The slight increase in the level of IL-12 in GCF of AgP patient and slight elevation in sites with attachment loss suggest a possible role of this cytokine in the pathogenesis of AgP. More studies are required to determine the exact role of this cytokine in AgP.

Oral Presentation

1st International Congress of Biomarkers

PN: 1004

Serum Concentrations of Thyroid-stimulating Hormone, Triiodothyronine, and Thyroxine in Outpatients Infected with SARS-CoV2 in Khuzestan Province, Iran: A Disease Clinical

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ABSTRACT

The virus SARS-CoV2, which causes COVID-19, affects the endocrine system. This study investigated serum concentrations of the thyroid-stimulating hormone (TSH), triiodothyronine (T3), and thyroxine (T4) in 53 outpatients infected with SARS-CoV2 and 53 non-infected matched participants in Khuzestan Province, Iran. We also examined the possible association of clinical symptoms progression and disease severity with serum concentrations of TSH, T3, and T4. Materials and Methods: A checklist was applied to collect demographic and clinical data. Blood samples were taken for biochemical analysis of serum concentrations of TSH, T3, and T4. Clinical symptoms of the infected outpatients were monitored weekly for 28 days. Our results indicated that, as the severity of the disease increased, the respiratory and pulse rates raised significantly. Additionally, disease severity was significantly different between genders. Specifically, 79.5% of the asymptomatic/mild, and 38.5% of moderate outpatients were men. We also found significantly lower serum T3 but higher T4 in infected outpatients, compared with controls. However, serum TSH did not significantly differ between the two groups. The generalized estimating equation (GEE) analysis revealed no relationship between clinical symptoms progression and disease severity with serum concentrations of TSH, T3, and T4 in our study population. Additionally, GEE analysis showed that the odds ratio of neurological symptoms among women was 2.5 times that of men, the odds ratio of neurological symptoms in illiterates was 10 times higher than that of those without a high-school diploma, and the chance of developing pulmonary symptoms in those without highschool diploma was about 21 times higher than illiterates. In conclusion, this study showed that infected outpatients had significantly lower serum T3 but higher T4 than non-infected participants. There was no relation between symptom progression and disease severity with serum concentrations of TSH, T3, and T4, but educational status and sex significantly affected the chance of neurological and pulmonary symptoms occurring over 28 days. Our results may be used to develop potential therapies to treat COVID-19 disease.

Keywords: Clinical symptoms; COVID-19; SARS-CoV2; T3; T4; TSH

Oral Presentation

1st International Congress of Biomarkers

PN: 1012

Oxidative Stress and Inflammatory Status in COVID-19 Outpatients: A Health Center-Based Analytical Cross-Sectional Study

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ABSTRACT

The antioxidant system can be critical in reducing exacerbated inflammation in COVID-19 (1). This study compared the antioxidant and inflammatory responses between COVID-19 outpatients and seemingly healthy individuals.This descriptive-analytical cross-sectional study was conducted on 53 COVID-19 outpatients and 53 healthy individuals as controls. The serum concentrations of amyloid A (SAA), total antioxidant capacity (TAC), superoxide dismutase (SOD), and glutathione peroxidase (GPx) were measured and compared between COVID-19 patients and controls using the independent sample *t*-test before and after controlling for dietary supplement use**.** A generalized estimating equation (GEE) regression model, limited to COVID-19 patients, was used to evaluate the odds ratios (ORs) and 95% confidence intervals (95% CIs) of disease symptoms on days 1, 7, 14, 21, and 28 after the disease onset. Serum concentrations of SOD ($p \leq 0.001$) and GPx ($p = 0.001$) were significantly higher in COVID-19 patients than in controls before adjustment for dietary supplement use**.** GPx remained significantly higher among COVID-19 patients than in controls after adjustment for all dietary supplements ($p = 0.005$)**.** Moreover, serum concentrations of GPx ($p = 0.003$), SOD ($p = 0.022$), and TAC ($p = 0.028$) remained significantly higher among COVID-19 patients than in controls after adjustment for vitamin D supplementation. This study showed higher GPx in COVID-19 outpatients than in controls after adjustment for dietary supplement use. Moreover, elevated SOD, GPx, and TAC concentrations were shown in COVID-19 outpatients compared to controls after adjusting for vitamin D supplementation. These results may provide a useful therapeutic target for treating oxidative stress in COVID-19 disease, which may help ameliorate the pandemic.

Keywords: COVID-19; oxidative stress; total antioxidant capacity; serum superoxide dismutase; glutathione peroxidase

Oral Presentation

1st International Congress of Biomarkers

PN: 1023

Theranostic effects of chemotherapy drug-loaded magnetite nanoparticles on glioblastoma cancer cells

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ABSTRACT

Surgery followed by radiation therapy (RT) with adjuvant chemotherapy are the main approaches for cancer treatment but their prognosis remains ineffective. Recently, the development of new strategies to enhance the efficacy of cancer treatment and its diagnosis have got renewing interest for researchers. The aim of the present study was to investigate the radiosensitizing effects and diagnostic properties of Temozolomide-loaded magnetite nanoparticles (TMZ-MNP NPs). Nanoparticles were synthesized and characterized for hydrodynamic diameter, zeta potential, and morphology. To examine the diagnostic properties of the nanoparticles, glioblastoma cancer cells treated with different concentration of nanoparticles were assessed by magnetic resonance imaging (MRI). To evaluate the radio-sensitization effects of nanoparticles, glioblastoma cancer cells were treated with NPs and exposed to ionizing radiation. After treatments, the therapeutic efficacy was evaluated using the intracellular ROS generation, clonogenic assay, and flow cytometry analysis. MRI scanning indicated that TMZ-MNP NPs could serve as an effective T2-weighted MRI contrast agent and nanoparticles accumulated in cancer cells could be tracked by MRI. Colony formation assay proved that TMZ-MNP NPs improved the radiation effects with a dose enhancement factor of 1.65. All results showed that the combination of nanoparticle and radiotherapy caused a higher anticancer efficacy than radiotherapy alone. The nanoparticles synthesized in this study can be proposed as the promising theranostic platform for the diagnosis and radiosensitizing of cancer cells.

Keywords: Radio-sensitizer; Nanoparticle; Radiotherapy; Magnetic resonance imaging

Oral Presentation

1st International Congress of Biomarkers

PN: 1044

Evaluation of inflammatory and anti-inflammatory cytokine gene expression levels (IL-10, TNFα, IL-6 and MIF) in patients with Covid-19 (between acute and mild phase groups)

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ABSTRACT

Since inflammatory factors are important factors involved in inflammation and aggravation of lung diseases and are also important factors related to cytokine storm in SARS-COV2, in this study, the expression level of inflammatory and anti-inflammatory genes including IL-10, TNF-a, IL-6 and MIF were discussed in the disease of COVID-19 as a global epidemic. In this study, the population of patients with Covid-19 disease were classified into two groups: mild phase (phase zero and phase one) and severe phase (phase two and three as PCR positive with acute pulmonary symptoms and inflammation). Then the demographic, clinical and paraclinical characteristics of the individuals were collected based on a pre-prepared checklist. To evaluate the gene expression, RNA total was isolated from all samples according to the protocol of Trizol kit. Then, the extracted product was analyzed by Real-time PCR for target gene expression. Finally, the data were analyzed by SPSS software. The results revealed that there is a significant difference between the two groups of mild and severe phases in terms of smoking, cough, and ESR and HCT factors ($P<0.05$). While the values of gender, BMI, weight, oxygen saturation, fever, sore throat and levels of WBC, RBC and CRP had no statistically significant difference ($P>0.05$). Also, the average gene expression of IL-10, IL-6, TNFα and MIF was 0.54 ± 2.01, 0.38 ± 1.94, 0.45 ± 1.84, and 0.65 ± 2.42 in the mild group and 1.77 ± 0.4, 1.74 ± 0.63, 2.1 ± 0.28 and 3.89 ± 0.86, respectively in the group of acute patients, Statistically, IL-10, TNFα and MIF had a significant relationship between the two groups ($P<0.05$). TNFα and MIF expression increased in the acute phase group, while IL-10 decreased in the acute phase group, but the mean IL-6 gene expression did not show a significant difference between the two groups ($P>0.05$).This study determined that the expression levels of inflammatory genes such as TNF increased significantly in people with severe inflammation compared to those with mild inflammation, while the interleukin-10 gene as an anti-inflammatory factor decreased in the severe group. Maybe by conducting more studies it can be said that inflammatory factors can be used as diagnostic biomarkers.

Keywords: Inflammatory factors; Biomarkers; Cytokine Storm; IL-10; IL-6; TNF; MIF; corona

Oral Presentation

1st International Congress of Biomarkers

PN: 1047

The N-acetylgalactosamine-transferase11 (GALNT11) activation in leukemia and the role of cyclophosphamide and cytarabine in the expression of this enzyme

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ABSTRACT

We investigated the activation of N-acetylgalactosamine-transferase11 (GALNT11) and the role of cyclophosphamide and cytarabine in the expression of this enzyme in AML and CML patients. GALNT11 activity and expression levels were evaluated in human chronic myelogenous leukemia cells (K562) and human acute monocytic leukemia cells (THP1) after incubation with different concentrations of cyclophosphamide (Cyclo) and cytarabine (Cyta). Anti-proliferative effects of Cyclo and Cyta were examined by MTT assay. Real-time PCR and ELISA assays were applied to investigate the expression and activity of GALNT11, respectively.

The IC50 values for Cyclo were 34.73±0.12 μM for K562 and 36.16±0.23 μM for THP1 cells. These values for Cyta were also 0.38±0.15 μM for K562 and 0.52±0.18 μM for THP1 cells.

The activation and expression of GALNT11 increased in acute and chronic leukemia as glycosylation disorders which shows the importance of this enzyme as a potential and possible biomarker. Also ,cyclophosphamide and specially cytarabine cause a significant increase in activation and expression of GALNT11 ,inhibiting glycosylation and tumorogenesis-dependent signaling pathway.

Keyword: Cyclophosphamide; Cytarabine; Leukemia; N-acetylgalactosamine-transferase11

Oral Presentation

1st International Congress of Biomarkers

PN: 1059

Investigation of the P16 and Ki67 predictive effect on the progression of cervical intraepithelial neoplasia -1 in Shahid Motahari Hospital of Urmia

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ABSTRACT

Cervical cancer is a common neoplasm among women, and the role of the HPV virus in the development of precancerous and cancerous cells has been demonstrated. There are different types of HPV virus with different roles. In the high-risk types of HPV, the p16 and ki67 proteins play an important role in regulating of the cell cycle leading to cell proliferation and progression. Considering that these two markers are positive in almost all lesions toward a high degree of malignancy, so they can be discussed and studied as a predictive factor for high-grade malignancy. These two markers, commonly known as oncogenic markers, lead to high-grade malignant lesions in almost all types of low-grade malignancies in accompany with the high-risk HPV virus, and according to studies that have been done so far with measurement of these two markers, expressed positive or negative in low-grade malignant lesions, can be used to predict the progression of these lesions. Therefore, the aim of this study to investigate the predictive effect of P16 and Ki67 on the progression of low grade intraepithelial lesions to high grade malignancy. During this study, the two markers were measured on lesions with a diagnosis of CIN1, and during the average two-year follow-up period, the outcome of positive cases was investigated. In this study, referred patients with the age range of 15 to 75 years were examined in a period from April 2015 to March 2019 and a total of 106 patients were included in the research. In the present study, in the patients with progression of CIN1 to CINII and more severe lesions, P16 protein was positive in 14 cases (60.9%) and there was a significant difference between groups with positive and negative marker in the progression or regression of lesions. The Ki67 protein is more common in the lesions with diagnosis of CIN2 and more severe lesions and in the cases where both markers (P16,Ki67)were positive there was a significant difference. The use of p16 and Ki67 as a predictive markers is still controversial, and in countries like the United States these are not yet used for prediction alone, but can be used in combination altogether . The authors of this study strongly suggest for further studies to be conducted to assess the role of p16 in association with other markers and within a larger population to apply the functional role of p16 and Ki67 in clinic and for prevention.

Keywords: uterian cervical cancer; P16-Ki67-HPV-CIN.

Oral Presentation

1st International Congress of Biomarkers

PN: 1063

Towards clinical and therapeutic approaches in Alzheimer's disease based on neuroimaging, CSF, and blood biomarkers

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ABSTRACT

Biomarkers are measured with the aim of awareness of the physiological and pathogenic processes and responses to a therapeutic intervention. Biomarkers can be classified as a diagnostic, prognostic, predictor, clinical, and therapeutic. In Alzheimer's disease (AD), multiple biomarkers have been reported so far, nevertheless, finding a specific biomarker in AD remains a major challenge. Three databases, including PubMed, Web of Science, and Scopus were selected with the keywords of Alzheimer's disease, neuroimaging, biomarker, and blood. The inclusion criteria were: high-impact articles, peer review journals, and relevant subjects in regard to our work. To distinguish between normal and AD patients, we could detect amyloid-beta$_{42}$ (Aβ_{42}), total-tau (T-tau), phosphor tau (P-tau), and neurofilament light (NFL) as potential biomarkers in cerebrospinal fluid (CSF) as well as serum. Nevertheless, there are more biomarkers whose levels fairly change in the CSF during AD listed as neuron-specific enolase (NSE), Virus-like particles (VLP-1), Heart-Type Fatty Acid-Binding Protein (HFABP), and chitinase-3-like protein 1 (YKL-40). Besides, the LRP1 and soluble RAGE levels decreased in the blood of AD patients. In the neuroimaging aspect, atrophy is an accepted biomarker for the neuropathologic progression of AD. In addition, MRS can be used to detect AD biomarkers, since NAA/Cr and NAA/mI ratios changes correlated with early tau and Aβ accumulation. Finally, in the PET scan, multiple radioactive tracer have been suggested, however, [18F]-Flortaucipir is thought to be the best choice. CSF and blood biomarkers alone are not proper options to detect AD and distinguish it from other diseases. By aiding neuroimaging we could obtain numerous information about the changes that occur during AD and even detect AD before clinical symptoms reveal, hence, we could select the suitable therapeutic option to attenuate disease symptoms and follow up on the efficiency of the prescribed drug.

Keywords: Alzheimer's disease; Diagnosis; Neuroimaging; Biomarker; Prevention.

Oral Presentation

1st International Congress of Biomarkers

PN: 1065

Pharmaceutical modulation of macroautophagy by medicinal products for the treatment of cancers

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ABSTRACT

Macroautophagy, a highly evolutionarily conserved process where intracellular components are recycled for cellular homeostasis. However, its dysregulation is associated with various pathological conditions such as cancer. Thus, modulation of autophagy by natural products may signify a new pharmacologic target for therapeutic intervention of cancers. A sensitive search is developed in Medline, Embase and PubMed to identify all validation studies, reviews, or meta-analyses in which the natural products were the development or validation for anticancer activity mediated by autophagy. A reviewer screened title and abstracts, selected the studies, and collected data concerning validation are used to check the anticancer activity of natural products. Modulation of autophagy using repurposing natural products has shown promise in the treatment of diseases including cancer. There are many natural products can activate autophagy and consequently modulate cancer cells in various models such as initiation stage activators: mTOR inhibitors; polyphenolic compounds; quercetin; magnolol, kaempferol, apigenin; coffee and tea: (−)-epigallocatechin-3-gallate, catechin and epicatechin; genistein; curcumin derivatives; resveratrol; propolis extract: chrysin; fisetin, rottlerin; terpenoids:γ-Tocotrienol. Here, it will be summarized the up-to-date knowledge regarding an overview the mechanisms of actions of natural products that modulate the autophagy process. Interestingly, there is increasing evidence that autophagy proteins activate extracellular vesicles' (EVs) biogenesis. The pathways between autophagy and EVs occur not only in mammalian cells, but also in plants. This can be significant in the context of cancer treatment through the interaction between natural products derived from EVs, which are loaded with oncosuppressive cargoes on mammalian cancer cells. Here, a better understanding of the pharmacology of autophagy modulators through this project may ultimately allow scientists and clinicians to develop autophagy-based therapeutic interventions for several human diseases and to improve human health.

Keywords: Natural products; Autophagy; Cancer treatment; mTOR signaling; Drug discovery and Development.

PN: 1066

Resensitization of antimicrobial resistance (AMR) with the help of repurposing drugs

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ABSTRACT

Infectious diseases cause a major life-threat and mortality. Global-wide AMR crisis represents a major challenge that aggravates the problems posed by microbial infections. Because of AMR, the efficacy of antibiotics are endangering, there are some clinically approved drugs modulate the resistance to antibiotics. When co-administered with an antibiotic, the AMR breakers they may help to either block the main bacterial resistance mechanisms or enhance the antimicrobial action of the drug. The main objective of this research work was to apply repurposing for antibiotic resistance breaker like haloperidol, an antipsychotic drug.We performed antibacterial activity and the minimum inhibitory concentration (MIC) tests against different Gram positive and Gram-negative bacteria. Here, we used several number of antibiotics including azithromycin and ciprofloxacin. The individual antibiotic (20µg), haloperidol (10µg) and their combinations (30µg) were used. Antibiotic-haloperidol combination showed synergistic effect. Azithromycin combination was more prominent effect than azithromycin only. Interestingly in combination with haloperidol, azithromycin caused decrease MIC values likely 2, 4, 4 and 8 µg/ml for *Staphylococcus aureus*, *Pseudomonas aeruginosa, Bacilus cereus* and *E. coli* respectively. High MIC value indicated the less activity and the small MIC value indicated the large activity. Our results suggest that azithromycin and other combination may provide potential antibacterial actions. To confirm this beneficial we need to perform clinical trials on the basis of *in vivo* model data.

Keywords: Antimicrobial resistance (AMR); MDR; haloperidol; azithromycin; drug combination; synergism

PN: 1068

Metabolic deregulation in peripheral blood mononuclear cells reflects the onset of atherosclerosis

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ABSTRCAT

Upregulation of key pathogenic elements in peripheral blood mononuclear cells (PBMCs) including transforming growth factor beta (TGF-β), matrix metalloproteinase-9 (MMP-9), and legumain could be involved in early stages of atherosclerosis in patients with coronary artery disease (CAD), such as recruitment and activation of monocyte in the vascular lesion.

115 Iranian individuals who underwent coronary angiography at the Hajar Hospital, affiliated to the Shahrekord University of Medical Sciences, Chaharmahal and Bakhtiari province, Iran. Serum biochemical parameters was measured. PBMCs were isolated via Ficoll solution. The genes expression of TGF-β, MMP-9, and legumain was measured with Real-time PCR. The Gensini scoring method was used to determine the degree of stenosis in the main coronary arteries, including the left circumflex (LCX), right coronary artery (RCA), and left anterior descending coronary artery (LAD). Student's t-test was carried out to compare the continuous data between the two groups. Moreover, Kendall's tau and Spearman's correlation coefficient analysis was carried out to identify the correlation between study variables'.

Contrary to our expectation, history of smoking and abnormal blood pressure were not correlated to coronary artery stenosis. Among current results, history of Type 2 diabetes and total cholesterol was most strongly correlated with coronary stenosis. As compared to demographic and biochemical data, alteration of cellular metabolite was more correlated to coronary artery stenosis. Genes expression of TGF-β, MMP-9, and legumain were significantly elevated in PBMCs of CAD subjects as compared with Non-CAD subjects ($p \leq 0.05$). LAD stenosis was significant associated with the overexpression of TGF-β, MMP-9, and legumain. Also, RCA and RCX stenosis were significant associated with the overexpression of MMP-9.

Our data presented the evaluation of expression profile changes in PBMCs could be more beneficial biomarker to determine the prognosis of coronary artery events as compared to traditional parameters such as dyslipidaemia.

Keywords: Liegeman; Matrix metallopeptidase-9; transforming growth factor beta; Atherosclerosis; Peripheral blood mononuclear cell.

Oral Presentation

1st International Congress of Biomarkers

PN: 1070

Paper-Based Colorimetric biosensor integrated with Smartphone device for Detection of miRNA-21

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ABSTRACT

MicroRNAs (miRNAs) are known as a reliable important biomarker for disease diagnosis and also clinical examination. It has been considered that inappropriate expression of special miRNAs is closely associated to numerous diseases, especially various types of cancer. Therefore, the development of rapid, highly sensitive, selective, simple and low-cost diagnostic approaches is an crucial need to identify biomarkers for early monitoring of cancer. To address this need, we designed and fabricated a simple, inexpensive, and paper-based colorimetric biosensor to detect miRNA-21 based on peroxidase mimetic activity of DNA-templated hierarchical Au/WO_3 hollow nanoflowers (DNA- Au/WO_3 HNFs), which could catalyze the reaction of H_2O_2 and 3,3′,5,5′ tetramethylbenzidine (TMB), to produce a blue color. Based on the blockage effect of miRNA-21 on peroxidase-like activity, the designed biosensor was capable of quantify miRNA-21 with high sensitivity. Designed colorimetric based biosensor has been integrated with the smartphone-based recorder to correlate change in color with the concentration of miRNA-21 in the human urine samples. Accordingly, the quantification of miRNA-21 was facilely realized based on the color changes, and the detection limits were calculated to be 250 nM for colorimetric methods. Hence, this biosensor can achieve determination of miRNA-21 with the concept of point-of-care testing (POCT). Furthermore, the proposed monitoring platform also displayed satisfactory sensing performance for the miRNA-21 assay in human urine samples. This promising strategy may enable new insights on the fabrication of a POCT platform for selective, sensitive, and valid monitoring of biomarkers for disease diagnosis.

Keywords: Colorimetric, Paper based biosensor, MicroRNA-21, DNA- Au/WO_3 HNFs, Cancer.

Oral Presentation

1st International Congress of Biomarkers

PN: 1072

The effect of dexamethasone on uterine receptivity, mediated by the ERK1/2-mTOR pathway, and the implantation window: An experimental study

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ABSTRACT

The role of glucocorticoids in implantation has been demonstrated.This study aimed to evaluate the effect of dexamethasone on endometrial receptivity. In this experimental study, 40 BALB/c female mice aged eight wk old weighing approximately 25.0 ± 1.4 gr were used. The mice were divided into four groups (n = 10/each) of control, dexamethasone (100 µg/kg, intraperitoneal injection), mammalian target of rapamycin (mTOR) inhibitor (PP242) (30 mg/kg, intraperitoneal injection), and dexamethasone and PP242. The endometrial epithelium of the mouse was separated to measure messenger RNA expression of heart and neural crest derivativesexpressed protein 2 (*HAND2*), Msh homeobox 1 (*Msx-1*), heparin binding epidermal growth factor (*HB-EGF*), microRNA (miRNA) Let-7a, miRNA-145 and miRNA-451, using real-time polymerase chain reaction. Also, protein expression of mammalian mTOR and eukaryotic translation initiation factor 4E-binding protein1 (4E-BP1) was measured using western blot.The results revealed that the expression of *Msx-1*, *HAND2*, *HB-EGF*, miRNA-451, and miRNA-Let-7a was significantly decreased in the endometrium in the dexamethasone group compared to the control, while the expression of miRNA-145 in the endometrium was up-regulated. Additionally, the administration of PP242, known as an inhibitor of mTOR, was associated with significantly reduced expression of *Msx-1*, *HAND2*, *HB-EGF*, miRNA-451, and miRNA-Let-7a, while PP242 induced messenger RNA expression of miRNA-145. It appears that dexamethasone can diminish uterine receptivity during the implantation period, at least to some extent, through the alteration of particular genes that impact endometrial receptivity. Furthermore, the mTOR pathway seemingly showed an essential role in endometrial receptivity.

Keywords: Dexamethasone, ERK1/2-mTOR pathway, implantation

Oral Presentation

1st International Congress of Biomarkers

PN: 1075

Imprinted polymers: Synthesis, characterization and their applications to the analysis of protein biomarkers

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ABSTRACT

Imprinted polymers are a type of artificial polymer, which have complementary cavities that are designed to bind a specific target molecules with a high degree of selectivity. Due to their effectiveness and stability, imprinted polymers have found their way into many applications in medicine, chemistry, analysis and sensing fields. One of the most important modern uses of imprinted polymers in the recognition of biological molecules of medical significance, which are named “biomarkers”. The application of imprinted polymers enables easy and fast extraction and detection of these biomarkers from different biological matrices. In this presentation, I discuss imprinted polymers in detail including their different types, method of synthesis, characterization methods, in addition to their applications in various fields with focus on their use in the analysis of protein biomarkers.

Keywords: Imprinted Polymers‹Biomarkers‹Cancer

Oral Presentation

1st International Congress of Biomarkers

PN: 1101

Preoperative Hypoalbuminemia and Development of Surgical Site Infection and Anastomotic Leakage in Emergency Colorectal Surgery

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ABSTRACT

Malnutrition is a major cause of morbidity, mortality, and increases the length of hospital stay. Hypoalbuminemia is a well-known indicator of malnutrition, and its occurrence before surgery is predictive of postoperative complications including surgical site infection (SSI) and anastomotic leakage (AL) in gastrointestinal surgery. In this study, we investigate the association between preoperative serum albumin and development of SSI and AL in emergency colorectal surgery. A total of 156 patients who underwent emergency colorectal surgery during 17 months, were enrolled in this study. Albumin level was measured before surgery, and patients were followed for one month after surgery to identify development of surgical site infection (SSI) and anastomotic leakage (AL). Preoperative albumin level in patients with infection was significantly lower than those without infection (P = 0.017). However, the difference of preoperative albumin level between patients with anastomotic leakage and patients without anastomotic leakage was not statistically significant (P = 0.561). An inverse weak but significant correlation was observed between age and albumin level (r = - 0.169, P = 0. 035). Mortality rate was significantly higher in hypoalbuminemic group (p = 0.009). It seems that low preoperative albumin level is an independent risk factor for development of surgical site infection, and increases mortality rate.

Keywords: anastomotic leakage; surgical site infection; colorectal surgery.

Oral Presentation

1st International Congress of Biomarkers

PN: 1105

Memantine, an N-methyl-D-aspartate receptor antagonist, attenuates VEGF level in DMH-induced colon cancer: An *in vivo* study

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ABSTRACT

Glutamate levels are significantly higher in colon cancer cells than in normal cells. Increased expression of N-methyl-D-aspartate (NMDA) receptors has been observed in tumor cell lines that cause angiogenesis. Vascular endothelial growth factor (VEGF) promotes proliferation and endothelial migration through the calcium influx. As a result, NMDA receptors may be a therapeutic target of cancer, and inhibition of these receptors may reduce tumor growth. In this study, the effects of memantine, an NMDA receptor antagonist, on histology, tumor size, and number, as well as VEGF level in 1, 2 dimethylhydrazine (DMH)-induced colon cancer in rats were investigated. Thirty male Wistar rats were divided into three groups: the control group, the colon cancer group (30 mg/kg of DMH solution was injected subcutaneously twice a week for 24 weeks), and the memantine group (20 mg/kg). The results showed that the injection of DMH induced colon polyps ($P<0.001$) in the colon cancer group, but memantine 20 mg/kg showed protective effects and reduced the number and size of colon polyps ($P<0.001$). The level of VEGF also increased significantly ($P<0.05$) in the colon cancer group compared to the control group. Treatment with memantine 20mg/kg/day reduced VEGF level significantly ($P<0.01$) in comparison to that of the colon cancer group. The present in vivo study, for the first time, showed the anti-cancer effects of memantine in colon cancer, which can be attributed partially to a reduction in VEGF level.

Keywords: NMDA receptor; Memantine; Colon cancer; VEGF; DMH.

Oral Presentation

1st International Congress of Biomarkers

PN: 1117

Investigation Impact of the B12, Vitamin D, Folic Acid and Anemia In Hashimoto's Thyroiditis

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ABSTRACT

Hashimoto's thyroiditis (HT) is the most common autoimmune thyroid disease and approximately 20-20% of the causes are genetic predisposition and loss of immunological tolerance due to environmental conditions. Anti-TPO,is an essential biomarker since it is seen in more than 90% of patients and the presence of TPO antibodies in blood, suggests that the cause of thyroid disease is an autoimmune disorder, such as Hashimoto's disease or some other diseases.Thyroid disorders may occur in deficiencies of iodine,selenium,iron,zinc,minerals and vitamins A,C,B6,B5,B12 and D, which are necessary for the synthesis and metabolism of thyroid hormones.Therefore, evaluation of the frequency of B12,vitamin D (vit-D),folic acid and iron deficiency, which play a role in the pathophysiology of HT. Age, gender, thyroid stimulating hormone (TSH), free-T4 (FT4), free-T3 (FT3) andvit-D among 30 HT patients and 37 non-HT patients admitted to the outpatient clinic between January-December 2021. Anti-TPO and Anti-Thyroglobulin iron,vit-D,ferritin,B12 and folic acid parameters were obtained from the patients having routine blood test results, datas were statistically evaluated by using SPSS software version24. When the vit-D levels of 30 patients with HT and 37 patients without a diagnosis of HT were compared, vit-D levels showed a difference between them. A negative correlation was found between the blood, vit-D level and Anti-TG (as the vit-D value increases, the Anti-Thyroglobulin value decreases) ($r=-0.417;p=0.001;p<0.01$). There was a statistically significant and weak correlation between blood vit-D measurements and Anti-TPO measurements ($r=-0.341;p=0.005;p<0.01$). Evaluation of Hemoglobin, FT3, FT4, TSH, Ferritin, B12, and Folic acid between patients with and without a diagnosis of HT, their measurements did not show a statistically significant difference ($p>0.05$). Importance of vit-D deficiency in the physiopathology and treatment of HT, elimination of vit-D deficiency have actually been shown how important in the treatment process of HT.

Key words: Hashimoto's thyroiditis (HT); otoimmun disease; Vitamin D (vit-D); anti-TPO; Ferritin; Vitamin B12.

PN: 1125

Swimming and its effects on Survival biomarkers, miRNA-126, miRNA-124, in the hippocampus of orectomized Diabetic rats.

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ABSTRACT

The beneficial effects of exercise on the prevention of brain inflammation and survival increasing in ovariectomized rats have been studied. Our study aimed to examine the effects of swimming training on brain expression of miRNA-124, miRNA-126, Igf1 levels, and Nf-kB and Bcl-2 protein changes in the hippocampus of ovariectomized diabetic rats.

In this study we had fifty animals, they were separated into five groups as a sham, ovariectomy (OVX), ovariectomized diabetic group (OVXD) ovariectomized group with 8 weeks swimming training (OVXE), and ovariectomized diabetic group with 8 weeks swimming training (OVXDE). Training effects were evaluated by measuring, miRNA-124, miRNA-126 expression levels, and Nf-kB and Bcl-2 protein changes in the hippocampus tissue. Grafts were analyzed by reverse transcription-polymerase chain reaction for miRNA-124, miRNA-126, and by Western blot for Bcl-2 and Nf-kB protein. Ovariectomy down-regulated Bcl-2, miRNA-124, and miRNA-126 expression levels and up-regulated Nf-kB in the hippocampus tissue, and swimming training up-regulated the expression of Bcl-2, miRNA-124, and miRNA-126 and downregulated Nf-kB as an inflammatory marker.

This study suggested that regular exercise as a physical replacement therapy can have a prevention and improvement effect of estrogen deficiency in the brain.

Keywords: Swimming training; Survival biomarkers; Hippocampus; Ovariectomy.

PN: 1134

Effects of cannabinoid system components, 2-arachidonoyl glycerol and Tetrahydrocannabinol, in cultured mouse Sertoli cells: role of Caspase-3 and FGF-b as apoptotic and growth biomarkers

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ABSTRACT

The 2-arachidonoyl glycerol (2-AG) is a prominent endogenous member of the cannabinoid system. The presence of endogenous cannabinoids (EC) and their receptors in male reproductive tracts is suggestive of their involvement in vital physiological processes such as spermatogenesis. Tetrahydrocannabinol (THC), the most important exocannabinoid and the principal psychoactive substance in marijuana, impairs testicular cell activity and causes apoptosis. THC may also disrupt the physiological activity of EC and so affect male fertility by interfering with the endogenous cannabinoid system. This study aimed to determine through which mechanism(s), an alteration of Sertoli cell death occurs as a result of 2-AG and THC exposure and investigate critical biomarkers that link cannabinoid system components to apoptotic pathway activation. TM4 Sertoli cells were cultured and investigated in four groups: control, 2-AG (2µM, concentration in which the best cellular viability was obtained), 2-AG (3µM, a sub-cytotoxic concentration), and THC (50µM, a highly toxic concentration). Then, gene expression levels of caspase3 (as a cell apoptosis biomarker) and fibroblast growth factor-b (FGF-b, as a potential biomarker of Sertoli cells growth and development) were determined by qRT-PCR. THC and 2-AG (3µM) both significantly increased caspase-3 gene expression ($P<0.05$, $P<0.001$, respectively), whereas 2-AG (2µM) decreased caspase-3 expression level. In contrast, THC markedly decreased the gene expression of FGF-b ($P<0.001$), whereas 2-AG (2µM) demonstrated considerably higher FGF-b expression ($P<0.001$). 2-AG (3µM) had no impact on FGF-b expression statistically. 2-AG has a hormesis effect on Sertoli cell apoptosis. 2-AG at concentrations around its physiological level shows an anti-apoptotic effect by decreasing caspase3 and increasing FGF-b gene expression, whereas, at high concentration promotes apoptosis. THC causes apoptosis, over expression of caspase3 and down-regulation of FGF-b expression in Sertoli cells which may be a reflection of THC-induced testicular toxicity, and a suggestive mechanism in infertility associated with Marijuana abuse.

Keywords: 2-AG; Caspase-3; FGF-b; THC.

Oral Presentation

1st International Congress of Biomarkers

PN: 1156

Biomarkers in Parkinson's disease

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ABSTRACT

Research has shown that biomarkers development is more challenging in Parkinson's disease (PD) compared to other neurodegenerative diseases like AL (Alzheimer's disease). No radioligand exists for the detection of alpha-synuclein, the hallmark protein in PD, and to date, no specific blood or CSF biomarkers are used in the clinical diagnosis or management of PD. Understanding the mechanisms involved in PD pathogenesis and identifying useful, easy, available and economical biomarkers are necessary. In recent years, several study populations have been done about NFL (neurofilament light chain) role as a biomarker for neurodegenerative disease. NFL is a neuron-specific cytoskeletal protein that is released into the extracellular fluid following axonal injury. Research demonstrated that NFL levels in serum samples are increased in PD. Longitudinal analyses performed that plasma and CSF NFL levels correlated substantially (spearman $r = 0.64$, $P<0.001$). NFL is known to be the first blood-based biomarker candidate to support disease stratification of PD versus other cognate/neurodegenerative disorders. Though more extensive research is needed, plasma NFL is believed to be a useful prognostic biomarker for PD, predicting clinical conversion to mild cognitive impairment or dementia.

Keywords: Parkinson's disease (PD), biomarkers, neurofilament light chain (NFL), diagnosis

PN: 1159

Alteration of serum matrix metalloproteinase-9 (MMP-9) and legumain as novel biomarkers for estimating severity of coronary artery stenosis

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ABSTRACT

We aimed to investigate the association between alteration of serum level of the cysteine protease legumain and matrix metalloproteinase-9 (MMP-9) with severity of coronary artery stenosis in patients with clogged coronary arteries.

100 Iranian individuals underwent coronary angiography at the Hajar Hospital, affiliated to the Shahrekord University of Medical Sciences, Chaharmahal, and Bakhtiari province, Iran made up the study population. Serum biochemical parameters was measured. Serum levels of matrix MMP-9 and legumain protein were measured by western blot and ELISA techniques. The Gensini scoring method was used to determine the degree of stenosis in the main coronary arteries, including the left circumflex (LCX), right coronary artery (RCA), and left anterior descending coronary artery (LAD). Student's t-test was carried out to compare the continuous data between the two groups. Moreover, Kendall's tau and Spearman's correlation coefficient analysis was carried out to identify the correlation between study variables'.

Serum levels of MMP-9, and legumain were significantly elevated in serum of CAD subjects as compared with Non-CAD subjects ($p \leq 0.05$). Severity of stenosis of LAD artery was significant associated with increase in serum levels of legumain. Also, severity of stenosis of LCX, LAD, and RCA arteries were associated with increase in serum levels of MMP-9. Among biochemical data, prehistory of hyperglycaemia was most strongly correlated with coronary artery stenosis. As compared to demographic and biochemical data, increased serum level of MMP-9, and legumain was more correlated to coronary artery stenosis.

Our data showed that Serum levels of MMP-9 and legumain were significantly elevated in CAD patients as compared to Non-CAD subjects. Also, increased serum level of legumain and MMP-9 protein levels were significantly associated with the severity of coronary artery stenosis. Consequently, these factors besides prehistory of hyperglycaemia maybe consider as a novel biomarker for estimating severity of coronary artery stenosis.

Keywords: Legumain; Matrix metallopeptidase-9; Coronary artery disease; Coronary stenosis.

PN: 1160

Alantolactone enhances Cisplatin sensitivity of Ovarian Cancer Cells through the reactive oxygen species-mediated the Phosphatidylinositol 3-Kinase (PI3K)/Akt and NF Kb

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ABSTRACT

Ovarian Cancer (OC) is one of the frequent gynecologic malignancies which is the fourth most fatal disease among women. a major problem in the treatment of ovarian cancer resistance to cisplatin -based chemotherapy which results in early recurrence and death. In the present study, it was examined whether ALT and ZnO NPs may enhance the sensitivity of SKOV3 ovarian cancer cell line to cisplatin and then the underlying mechanisms were investigated. To evaluate the viability of SKOV3 cells and assess the IC50 of ALT, and ZnONPs, MTT assay was used. Expression of Akt, VEGF (vascular endothelial growth factor) and NF-κB mRNA and proteins was analyzed by real-time PCR method and western blotting, respectively. Anti-oxidant capacity was also assessed. Finally, the statistical analysis of the obtained values was analyzed by SPSS software. Results showed significant differences between mono- and double therapy ($p < 0.05$). Combination of cisplatin with ALT resulted in synergistic effect (Combination Index <1). Among double combination groups cisplatin /ALT (1×IC50 and 0.5×IC50) resulted in down-regulation of Akt, NF-KB and VEGF mRNA expression, respectively. Moreover, a significant decrease of genes expression in our triple combination group cisplatin /ALT/ZnO NPs (1×IC50 and 0.5×IC50) was obtained. cisplatin /ALT (1×IC50 and 0.5×IC50) double combination groups resulted in down-regulation of p-Akt, NF-KB and VEGF protein levels, respectively. cisplatin /ALT/ZnO NPs (1×IC50) decreased p-Akt and NF-KB protein levels in our triple combination group, however, the cisplatin /ALT/ ZnO NPs (0.5×IC50) combination was not notably affected. Taken together, these results suggest that ALT alone or in combination with zinc oxide can increase the therapeutic effect of cisplatin on OC cells. Therefore, this kind of treatment can be considered a new therapeutic strategy for OC.

Keywords: Ovarian cancer; Anti-angiogenesis; Oxidative stress, (PI3K)/Akt and NF-κB pathway.

Oral Presentation

1st International Congress of Biomarkers

PN: 1180

Inflammatory Mediator IL-6 as Salivary Biomarker for chronic periodontitis and Oral Squamous Cell Carcinoma

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ABSTRACT

Saliva is a useful as a liquid biopsy for the diagnosis of various oral or systemic diseases such as periodontal disease and oral squamous cell carcinoma (OSCC). Periodontal disease is an inflammatory disease affecting periodontal tissue such as gingiva, periodontal ligament and alveolar bone. Periodontal disease is linked to many systemic diseases. Recently a link between periodontal disease and cancer is suggested. Early detection and prevention of oral cancer is important, salivary cytokines expression, specifically of Interleukin-6 (IL-6) and Tumor necrosis factor (TNF-α), does contribute to the pathogenesis of cancer and these cytokines serve as potential biomarkers. Their excessive production plays a role in cancer progression and establishment of angiogenesis. Saliva samples were collected from three groups: Chronic Periodontitis (n=32); OSCC with chronic periodontitis (n = 22); and healthy controls (n = 30).periodontal parameters were measured and IL-6 concentrations (determined by enzyme-linked immunosorbent assays) was determined using total salivary protein–standardized levels to validate the data. There was a statistically significant difference between groups for all clinical periodontal parameters detected by student T test. A highest reading of IL-6 concentration was shown in group B OSCC patient (mean and SD 346.3 ±199.5) comparing to (mean andSD59.29+128.34) in chronic periodontitis group and (mean and SD18.85+6.26) in healthy control group.Salivary IL-6 levels were significantly higher in patients with OSCC than in patients with CP ($P < 0.001$) and healthy controls ($P < 0.001$). Salivary IL-6 may be a strongbiomarker in the detection of Oral Squamous Cell Carcinomaun-confounded by Chronic Periodontitis.

Keywords: IL-6, Salivary Biomarker, chronic periodontitis, Oral Squamous Cell Carcinoma

Oral Presentation

1st International Congress of Biomarkers

PN: 1192

Detection of Disease-Associated Biomarkers Using Nucleic Acid-Based Aptamers For Dual Antibody-Based Proximity Ligation Assay

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ABSTRACT

Many diseases, including cancer, are there where timely detection is of utmost importance for treating the ailment before it becomes incurable. There are several biomarkers present in the blood/Serum of the patients, which may be used in a non-invasive manner to diagnose the disease. Biomarkers for any disease can be circulating cell-free ribonucleic acids (ccfRNAs), including messenger RNA (mRNA) and miRNA, circulating cancer cells, unusual metabolites, unusual quantities of metabolites, specific antigens etc. These biomarkers may be detected in the serum, plasma, saliva, urine, and lymph. Aptamers are highly organized, single-stranded DNA/RNA molecules of 20-100 bp length and affinity for the target molecule. Since aptamers can tolerate a wide range of temperature, ionic conditions, and pH variations, these are robust choices for diagnosis. Aptamersbind with a high affinity and specificity to a wide range of molecules, including proteins, nucleic acids, cells, and tissues. Aptamers to Ligand are selected through enrichment of aptamers from a random library called Systematic evolution of ligands by exponential enrichment (SELEX). Variants of SELEX are available for screening aptamers, including High-Throughput SELEX, Cell SELEX, and Microfluidic SELEX. Aptamers can be easily chemically modified and conjugated with chemicals or biological molecules, including fluorophores, quantum dots, and nanoparticles, for detection purposes. Dual antibody-based proximity ligation assay (PLA) is a technique that uses co-detection of two markers present over the surface of a single cancer exosome. A connector probe joins two biomarkers and enhances specificity. The method is useful for enhancing specificity and sensitivity.

Keywords: Aptamers; Biomarkers; Cancer detection; SELEX.

PN: 1193

Diagnostic efficacy and development of microRNA biomarkers for early detection of gastric cancer

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ABSTRACT

Even though most gastric cancers (GC) are detected at advanced stages, they have a dismal prognosis. Given this clinical issue, identifying non-invasive biomarkers for early diagnosis is critical. The goal of this study was to create a non-invasive, liquid-biopsy-based technique for the early detection of GC utilizing Micro RNAs (miRNAs) as molecular biomarkers. Used GC and surrounding normal mucosa-matched tissue specimens to undertake comprehensive biomarker identification and validation of candidate miRNAs. Following that, transferred the identified miRNA-based biomarker panel into blood samples from GC patients (n = 240) and non-disease controls (n = 80) and assessed their diagnostic performance. Furthermore, we examined the expression of miRNAs in serum samples from pre- and post-surgical GC patients. And assessed the specificity of the miRNAs biomarker panel in comparison to other gastrointestinal (GI) cancers. The finding of 8-miRNAs was followed by confirmation of GC tissue specimens. Created an 8-miRNA-based risk-prediction model for the diagnosis of GC using patient training. Notably, the biomarker panel could reliably detect even early-stage GC patients, independent of tumor histology (diffuse vs. intestinal). miRNA expression was reduced in post-surgery serum specimens, indicating tumor-specificity and a possible source of origin in the systemic circulation. A panel of 5-miRNAs was found as non-invasive, liquid-biopsy biomarkers that might serve as possible diagnostic biomarkers for the early diagnosis of GC.

Keywords: MicroRNAs; Gastric cancer; Biomarker; Early detection.

Oral Presentation

1st International Congress of Biomarkers

PN: 1201

Time-restricted eating, regulation of circadian rhythm and metabolic biomarkers

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ABSTRACT

The circadian system regulates metabolism on a 24-hour cycle, creating rhythms in energy expenditure, appetite, insulin sensitivity and other metabolic processes. Disturbance of the circadian rhythm and irregular food patterns, such as eating for a long time during the day and odd timing of food, has been shown to cause the occurrence and exacerbation of metabolic diseases. Time-restricted eating (TRE) is a diet that restricts the daily eating window to 4-12 hours per day, which can improve metabolic biomarkers. We searched five public databases and six nutrition journals for words circadian rhythm, time-restricted eating, and metabolic biomarkers to identify all studies published between January 2015 and July 2022 that evaluated the effects of TRE on human populations. In general, 8 to 16 weeks of TRE with different windows of 4 to 12 hours causes an average weight loss of 3-4% and a decrease in fat mass without calorie restriction in people. Furthermore, TRE produced beneficial metabolic effects independent of weight loss, indicating an intrinsic impact on feeding and circadian clock re-regulation. TRE reduces fasting insulin and improves insulin sensitivity in people with prediabetes and obese people. In addition, TRE enhances glucose tolerance and reduces serum glucose levels. The observed effects of TRE on plasma lipids were highly variable among studies, but it significantly reduced systolic and diastolic blood pressure independently of weight loss. TRE is a simple and tolerable diet. Preliminary data suggest that TRE induces mild weight loss and may improve some aspects of metabolic health by reducing blood pressure and insulin resistance. However, further research is needed to determine the effects of TRE on metabolic biomarkers.

Keywords: Metabolic biomarkers; Circadian rhythm; Time-restricted eating.

Oral Presentation

1st International Congress of Biomarkers

PN: 1203

Effect of bone marrow mesenchymal stem cells transplantation on CX3CR1/CX3CL1 axis in the cuprizone model

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ABSTRACT

Multiple sclerosis (MS) is a kind of autoimmune and demyelinating disease with pathological symptoms such as inflammation, myelin loss, astrocytosis, and microgliosis. Mesenchymal stem cells (MSC), with neuroprotective and immunomodulating properties, could improve numerous diseases. We evaluate the immunomodulating effects of MSC on microglia through CX3CR1/CX3CL1 in a cuprizone model of MS. The fifteen male C57BL/6 mice (8 weeks old) were divided into 3 groups include control, cuprizone and MSC. For inducing the chronic demyelination model, C57BL6 mice were given a diet with 0.2% CPZ for 12 weeks. In the MSC group, cells were cultured and labled by DiI and then they were transplanted into the right lateral ventricle of mice. The microglial population was measured using Iba-1 marker by immunohistochemistry. The expression of targeted genes include CX3CR1 and CX3CL1 was assessed by real-time polymerase chain reaction. Data were analyzed using GraphPad Prism and SPSS software. The results showed that the MSC transplantation significantly ($p \leq .001$) reduced microglial cells compared to cuprizone model. According to the results, MSC transplantation increased the expression level of anti-inflammatory microglia (M2) messenger RNA (CX3CR1) in comparison to the CPZ group. In addition, MSC treatment significantly increased the CX3CL1 expression level in comparison with the CPZ group. The results showed that MSC transplantation decreased microglial population in MS. This change was accompanied by upregulation of CX3CR1 as anti-inflammatory microglial biomarker and CX3CL1 as MSCs secreted factor. Therefore, MSC therapy can be appropriate approach for preserve of immunomodulation in MS via CX3CR1/CX3CL1 axis maintain.

Keywords: Microglia; Mesenchymal stem cells; Multiple sclerosis; CX3CR1/CX3CL1.

Oral Presentation

1st International Congress of Biomarkers

PN: 1204

Association between the Expression of Annexin A6 with Estrogen, Progesterone and HER2 Receptors in Metastatic Breast Cancer

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ABSTRACT

Breast cancer (BC) is the most common invasive cancer in women and accounts for 22.9% of invasive cancers. Annexin A6 (ANXA6), a member of Ca^{2+}-dependent membrane-binding annexin proteins, was shown to be down-regulated in various diseases including heart failure, melanomas, and ductal breast cancers. The well-known importance of hormonal receptors including estrogen (ER), progesterone (PR), and human epidermal growth factor receptor-2 (HER2) in BC staging and prognosis led us to investigate the association between ANXA6 with ER, PR, and HER2 as a marker of BC diagnosis and treatment. Forty-eight healthy and invasive ductal BC tissue samples were obtained from the pathology ward of Imam Khomeini hospital. Monoclonal antibodies of ANXA6 and the patients' records containing immunohistochemistry (IHC) and demographic results were used to assess the difference in the expression of ANXA6 in the tissue samples as well as its relationship with ER, PR, and HER2 and lymph node involvement. The results of the present study revealed a direct correlation between ER expression and ANXA6 ($P < 0.001$). Evaluation of IHC and ANXA6 results indicated that in triple-negative (ER/PR -, HER2 -) and ER/PR -, HER2 + samples there was a significant decrease in ANXA6 expression ($P<0.05$). Besides, ANXA6 expression in patients with less than 10 involved lymph nodes was significantly lower than the patients with 10 or more involved lymph nodes ($P=0.004$). This study showed the possible association of ANXA6 expression with the hormonal status in poor prognosis subtypes of BC. Our findings implied that the lower expression of ANXA6 could be a marker of metastasis likelihood in BC-bearing women.

Keywords: Breast cancer; Annexin A6; ER; PR; HER2.

Oral Presentation

1st International Congress of Biomarkers

PN: 1206

Potential Therapeutic Effect of Primed-Mesenchymal Stem Cells in Lessening Kidney Damages in Rat Model of Diabetic Nephropathy by modulation of inflammation

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ABSTRACT

Prolonged hyperglycemia leads to severe damages to kidney tissue in diabetic conditions. One of the most progressive microvascular complications of diabetes is diabetic nephropathy (DN) that frequently leads to end stage renal disease (ESRD) in individuals with diabetes, with no so far available effective treatment methods. Recently, MSC-based therapeutic approaches have been considered for the treatment of various diseases, such as DN. In this study, we investigated the influence of Toll-like receptor 4-primed mesenchymal stem cells (TLR4-primed MSCs) on the kidney injury in streptozotocin (STZ)-induced diabetic nephropathy rats. STZ-induced diabetic rat models were divided into five different subgroups including 1) DN group, 2) DN group received insulin treatment, 3) DN group received human foreskin fibroblast cells (DN-HFF), 4) DN group with administration of one dose of 1 × 106 MSCs and 5) DN group received one dose of TLR4-primed MSCs. In order to assess the efficiency of the new treatment strategy, the biochemical, histological and also molecular analysis was carried out on DN-model groups. By using qRT-PCR method, we clarified that the mRNA levels of the pro-inflammatory cytokines such as tumor necrosis factor α (TNF-α) and transforming growth factor-β (TGF-β) was significantly down-regulated in DN group that received TLR4-proimed MSCs. The histopathological observations also showed that TLR-4-primed MSCs can reform pro-inflammatory cytokines production as a marker of inflammation modulation, prevent hyperglycemia-mediated inflammation by modulation of inflammatory mediators and exhibited a significant instructive effects on renal protection by alleviate renal injury of DN in rats. In conclusion, the results of this study may support a growing evidence that primed-MSCs transplantation could have a critical role in MSC-based immune-modulating therapy and a novel potential therapeutic strategy for the diabetes mellitus and especially for DN and could serve as a novel monitoring bio-markers for management of DN in future.

Keywords: MSCs; Diabetic nephropathy; Inflammation; Toll-like receptor.

Oral Presentation

1st International Congress of Biomarkers

PN: 1207

The effects of creatine on the PI3-AKT-mTOR signaling pathway in hippocampus during chronic stress

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ABSTRACT

Chronic stress leads to cellular metabolism changes, which diminish the cell's energy status and the intensity of anabolic reactions. Hence, searching for substances that can prevent these processes during stress is important. Our attention was drawn to creatine. It is endogenous in mammals, also given as a supplement during strenuous physical exertion, and is believed to have a therapeutic effect in certain neurodegenerative diseases. Our experiments showed that intraperitoneal injections of creatine during the prolonged disruption of circadian rhythm activate. Mitochondrial enzymes involved in energy metabolism in the hippocampus. From the investigation of the PI3K-AKT-mTOR pathway under chronic stress and administration of exogenous creatine, we inferred that creatine increases the amount of phosphorylated mTOR and its activator AKT, which is initially decreased due to stress, weakening energy metabolism. This inference was strengthened by data on the upregulation of PTEN, a negative regulator of AKT. Hence, it is proposed that the diminishing energy metabolism under chronic stress is due to downregulation of the PI3K-AKT-mTOR pathway; exogenous creatine counters the diminution by increasing the activity of energy metabolism enzymes, which may be directly related to upregulation of the PI3K-AKT-mTOR pathway.

Keywords: Creatine; PI3-AKT-mTOR; Hippocampus; Chronic stress

PN: 1208

The mechanism of MBNL family of alternative splicing factors in colorectal cancer

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ABSTRACT

Colorectal cancer (CRC), one of the most frequently detected cancers in digestive tract, remains the third leading cause of cancer-related death in the world. Alternative splicing (AS) allows generation of different protein isoforms from initially identical transcripts. Recent studies indicate that dysregulation of alternative splicing has been implicated in the pathogenesis of several diseases, including cancer and muscular dystrophies. AS is known as a versatile and powerful mechanism which is tightly regulated by splicing regulatory proteins. One of the Trans - acting splicing regulatory factors are proteins of muscleblind-like (MBNL) family which consist of three members, namely MBNL1, MBNL2 and MBNL3. Primarily, MBNL proteins function as key regulators of AS during mRNA maturation. Disruption of the normal activity of the MBNLs has been identified in cancer progression. Our project is focused on gene expression level of MBNL family as key regulators of alternative splicing in colorectal cancer. In addition to MBNL genes, we analyzed selected alternatively spliced isoforms that were confirmed to be regulated by MBNL to evaluate change in MBNL activity, and expression of cancer-related CD44 variants 3 and 6 as a relevant model of alternative splicing. Samples were collected within 20 min after the removal of the tumor tissue from the patient, and small pieces of tumor samples and healthy mucosa were immediately frozen and archived. RNA isolation was done by TriReagent (MRC) and cDNA was synthetized by First Strand cDNA Synthesis kit (Fermentas). Relative gene expression was tested by quantitative real-time PCR. Results were analyzed and basic statistical analysis was carried out using the Bio-Rad CFX Manager software. In the present study, we analyzed the expression of selected gene set on 108 patients. All genes show statistically significant deregulation between tumor and healthy tissue. Our data suggest that MBNL1, MBNL3, and alternative splicing of FOXP, CD44 and EPB41L3 could be deregulated in tumor tissue. It is estimated that the expression profile of three MBNL paralogs and their correlated effect with the set of transcription factors might alter multiple splicing event. Our data show the change in the MBNL expression and also

corresponding changes in expression of splice-variants that are known to be regulated by MBNL. Marginally significant correlations were observed among expression of studied genes and T, N, M, G and UICC clinical factors, with minute differences in gene expression among individual groups.

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Keywords: MBNL family; colorectal cancer; Alternative splicing

PN: 1212

Comparison of CD44 and CD24 expression levels in vivo model of 3D and 2D breast cancer

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ABSTRACT

The two-dimensional (2D) models of breast cancer still exhibit limited success. Whereas, three dimensional (3D) models provide more similar conditions to tumor for growth of cancer cells. Identification of breast cancer stem cell (BCSCs) is mainly based on CD44 + and CD24- phenotypes. The aim of this study is to investigate these markers in the modeling of breast cancer in 2D and 3D .In this regard we design a 3D in vivo model of breast cancer using 4T1 cells and chitosan based thermosensitive hydrogel. Chitosan/β-glycerol phosphate hydrogel was prepared with final ratio of 2 and 10 %. The hydrogel properties examined by FTIR, MTT, PH, SEM and biodegradability. 3D model of breast cancer induced by injection of 1×106 4T1 cells in 100 µl hydrogel and 2D model 1×106 4T1 cells in 100 µl Phosphate-buffered saline (PBS) subcutaneously. After 3 weeks induced 3D tumor was evaluated by size and weight determination, ultrasound, H&E and Masson trichrome staining and evaluating of stem cells with CD44 and CD24 markers. The two-dimensional (2D) models of breast cancer still exhibit limited success. Whereas, three dimensional (3D) models provide more similar conditions to tumor for growth of cancer cells. The results showed that hydrogel with physiological pH had no toxic effect. Results showed that in 3D model, tumor size and weight increased more in comparison with 2D model. Histological and ultrasound findings showed malignancy in the 3D tumor model. CD44 and CD24 expression in the 3D model suggested the presence of cancer stem cells in that tissue**.** In present study we were reported expression of the CD44+/CD24-/low in 3D breast cancer model. In fact, in 3D model increased malignancy phenotype, which was aligned with other research and other findings in this analysis.

Keywords: Cancer stem cell, CD44, CD24, Breast neoplasm, 2 and 3dimensional

Oral Presentation

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PN: 1215

Trimethylamine N-Oxide: New Potential Biomarker for Cardiovascular events

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ABSTRACT

The crosstalk between food, health and disease have attracting considerable attention recently. The potential role of the gut microbiota in the pathogenesis of some chronic diseases such as cardiovascular disorders has been demonstrated in recent investigations. Trimethylamine N-Oxide (TMAO) is generated from choline, betaine, and L-carnitine via gut microbial metabolism. Plasma TMAO is suggested as a candidate biomarker for cardiovascular diseases (CVDs). In this review we summarized recent reports regarding the potential utility of TMAO as a novel biomarker with therapeutic target in CVDs. A comprehensive search was carried out in PubMed/MEDLINE, Scopus, google scholar, and Web of Sciences up to July 2022. Full texts of related articles were reviewed in terms of the inclusion/exclusion criteria. Based on some observational studies, red meat consumption is a leading cause of increased plasma and urine levels of TMAO. Strong evidence suggests an association between a high level of TMAO, inflammation and the risk of developing CVDs. TMAO can be considered as an atherogenic factor that can lead to alterations in cholesterol and bile acid metabolism, promotion of inflammatory pathways, and activation of foam cells formation. In summary, TMAO can be considered as a potential biomarker for predicting the prevalence of adverse cardiovascular events, including myocardial infarction, stroke, and death.

Keywords: Trimethylamine N-Oxide; Cardiovascular Diseases; Biomarker; Gut Microbiota

Oral Presentation

1st International Congress of Biomarkers

PN: 1221

Bioactive compounds from functional foods as biomarkers

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ABSTRACT

Functional foods and their bioactive compounds have been extensively studied as a food group of high importance due to their rich amount in compounds such as anthocyanins, proanthocyanidins, flavan-3-ols, flavonols, phenolic acids, stilbenes, and dietary fibers, which provides a wide variety of potential biological activities. Nowadays, many *in vitro*, animal, clinical, and epidemiological studies support that consuming functional foods within a balanced diet may significantly contribute to reducing disease risks. This effect can be measured by biomarkers such as lipid profile, endothelial function, platelet activation, hemostasis, inflammation, type 2 diabetes, and glucose metabolism, among others. Also, there has been a trend to use gut microbiota as a biomarker. Furthermore, several functional bioactive compounds can significantly affect disease prevention and treatment, affecting the levels of those biomarkers beneficially. Therefore, adopting a diet rich in several functional foods, such as fruits, vegetables, whole grains, flaxseed, nuts, fishes, olive oil, beverages, and fortified foods, may play an essential role in preventing diseases affecting these biomarkers.

Keywords: Functional foods; Phenolic compounds; Metabolic biomarkers; Gut microbiota

Oral Presentation

1st International Congress of Biomarkers

PN: 1223

Metformin modulates Shh/Gli1 pathway to increase the chemosensitivity of gastric cancer cells to docetaxel and 5-flourouracil

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ABSTRACT

Gastric cancer (GC) is a crucial cause of cancer-related death characterized by poor prognosis. Docetaxel and 5-fluorouracil (5-FU) are approved for the treatment of GC, but chemo-resistance limits their application for GC. Metformin, a popular anti-diabetic drug, has been proven to have potent anticancer effects on gastrointestinal cancers. In this study, we investigated the roles of metformin in the chemo-sensitivity of GC cells by targeting Shh/Gli1 Pathway**.** The anticancer effects of metformin, 5-FU, docetaxel, and their combination on the AGS gastric cancer cells were evaluated by clonogenic assay and DAPi staining. We used immunocytochemistry assay to assess the expression of the Shh protein.Then, the expression of Gli1, Gli2, and TWIST1 mRNAwas determined using real-time PCR in these cancerous cells. All data were analyzed using SPSS V.21 software (SPSS Inc., USA). The significant differences were determined using Student's t-test and one-way ANOVA followed by the Tukey post hoc comparison test ($P<0.05$). Our results demonstrated that metformin increases the sensitivity of GC cells to chemotherapy by enhancing the apoptosis rate and inhibiting colony formation ($p<0.05$). The co-treatment of GC cells with metformin, 5-FU, and docetaxel attenuated the expression of Shh protein ($p<0.05$). We also found that the combination of metformin with docetaxel significantly down-regulated the mRNA levels of Gli1, Gli2, and TWIST1 in the AGS gastric cancer cell line compared to docetaxel alone ($p<0.05$). Overall, our data strongly support an important role for metformin as an enhancer of the efficacy of chemotherapeutic agents against GC via modulating Shh/Gli1 biomarkers.

Keywords: Gastric cancer; Metformin; Docetaxel; 5-fluorouracil; Cancer biomarkers

PN: 1225

High levels of miR-155 as a key regulator for Th17/Treg imbalance in severe condition COVID-19 patients

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ABSTRACT

Since the beginning of the SARS-CoV2 (SARS-CoV2) pandemic, a series of experiments have been employed to understand the different angles of the virus' impact on immune responses. One of the regulators of acute respiratory syndrome coronavirus 2 (SARS-CoV2) is miRNAs. Inflammation-related miRNAs like miR-155 can affect host immune responses to SARS-CoV2 infection. A total of 80 individuals (40 confirmed COVID-19 patients and 40 healthy controls) were enrolled in this study. After blood sampling, peripheral blood mononuclear cells (PBMCs) were isolated by Ficoll gradient centrifugation. The frequency of Th17 and Treg cells was evaluated by flow cytometry. Gene expression of miR-155, signal transducer and activator of transcription 3 (STAT3), suppressor of cytokine signaling (SOCS-1), and Fork Head Box Protein 3 (FoxP3) was measured using quantitative real-time PCR. Western blotting was assessed to further evaluation of RORγT, FoxP3, and STAT3 at the protein level. The serum concentration of IL-21, IL-17, TGF-β, and IL-10 were measured by the ELISA method. The frequency of Th17 and Treg cells showed a significant increase and decrease in COVID-19 patients compared to controls, respectively. COVID-19 patients had elevated expression for RORγT and STAT3 at mRNA and protein status. Whereas, FoxP3 has decreased expression at both mRNA and protein levels in these patients. miR-155 and SOCS-1 have increased and decreased mRNA expression in COVID-19 patients, respectively. Our study showed a significant reduction in TGF-β and IL-10 and an increase in IL-21 and IL-17 serum levels in the patients' group compared to healthy controls. miR-155 can affect the balance of Th17/Treg in COVID-19 patients and therefore could be considered an important diagnostic and prognostic factor in COVID-19 patients.

Keywords: miR-155; T lymphocytes; COVID-19; Immune system

PN: 1227

Effects of zinc supplementation and treadmill exercise during pregnancy on prenatal stress-induced anxiety-like behaviors and neuro-inflammatory biomarkers in adolescent female rat offspring

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ABSTRACT

Many studies have shown the deleterious influence of prenatal stress (PS) on neurological and behavioral manifestation in offspring, however, little is known about how to minimize these negative effects. The present study examined the effects of prenatal intervention of physical activity and zinc on PS-induced anxiety and neuro-inflammatory biomarkers in adolescent female rat offspring. Pregnant rats were divided into 5 groups: control, stress, stress + exercise, stress + zinc, and stress + exercise + zinc. The stress groups were exposed to the restrain stress for 5 consecutive days (G15-19). Rats in the exercise and zinc groups were subjected to either forced treadmill exercise (30 min/daily), or zinc sulfate (30 mg/kg/orally), or both throughout the pregnancy and similarly exposed to the stress. At postnatal day 25-27 anxiety-like behaviors of offspring were recorded using elevated plus maze and the gene expression of interleukin-1β (IL-1β) and tumor necrosis factor-α (TNF-α) were measured in the prefrontal cortex. Anxiety- like behaviors significantly increased in the stress group. Prenatal zinc, but not exercise, reversed PS-induced behavioral impairments. RT-PCR analysis showed that the TNF-α and IL-1β gene expression was significantly increased in offspring of the stress group ($p<0.05$). Prenatal zinc supplementation, but not exercise, downregulated the mRNA level of the both neuro-inflammatory biomarkers to around control levels. TNF-α and IL-1β expression did not differ in pups prenatally exposed to both exercise and zinc. Prenatal zinc supplementation improved PS-induced behavioral impairments partly through triggering the anti-inflammatory properties. Intensive involuntary exercise was not be able to prevent PS-induced behavioral deficits and neuroinflammatory responses. It seems that strenuous exercise increases the amount of brain pro-inflammatory cytokines which may mask or conceal the direct influence of the exercise under consideration. How exercise may positively modulate PS-induced changes, further research is needed to elucidate these effects.

Keywords: Anti-inflammatory responses; Anxiety; Physical exercise; Prenatal stress; Zinc.

Oral Presentation

1st International Congress of Biomarkers

PN: 1228

Analysis of lncRNA expression according to COVID-19 severity in blood

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ABSTRACT

WHO declared a pandemic and "international public health emergency" in 2019 due to an emerging disease. There is increasing evidence that long noncoding RNAs (lncRNAs) play a critical role in virus infections and antiviral immune responses. Analysis of lncRNA profiles of COVID-19 patients at different stages of disease progression are crucial to understanding the pathogenicity of SARS-CoV-2 and establishing effective therapies.

In this study, we compare the 3 lncRNAs profile expression of 120 blood samples of Covid-19 severity (asymptomatic, mild, moderate, severe/acute) with 120 healthy samples in order to find the differential lncRNAs in Covid-19 patients.

There was a significant up-regulation of lncRNA metastasis-associated lung adenocarcinoma transcript 1 (*MALAT1*) in both mild and severe/acute blood patients. It has also been observed that mild patients have an up-regulation of nuclear paraspeckle assembly transcript 1 (*NEAT1*). The inflammation-modulating lncRNA (Differentiation Antagonizing Non-Protein Coding RNA (*DANCR*) is down-regulated in severe/acute blood patients.

In COVID-19, *NEAT1*, *DANCR*, and *MALAT1* appear to be potential immune dysregulators, which may be used as biomarkers for predictive severity or therapy of COVID-19.

Keywords: Covid-19 Severity; *NEAT1*; *DANCR*; *MALAT1*.

Oral Presentation

1st International Congress of Biomarkers

PN: 1231

Mesenchymal stem cells conditioned medium treated with Morphine promote cancer stem cell populations of murine 4T1 cell line

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ABSTRACT

Mesenchymal stem cells (MSCs) are a group of non-hematopoietic adult stem cells with capacity for self-renewal and differentiation. They are an important component of the tumor microenvironment and recruited by cancer cells to similarly promote tumor growth and progression. Morphine, an opiate-based agent is widely used for management of severe pain associated with cancer metastasis. Many tumors, including breast cancer, consists of undifferentiated slow-cycling cells with self-renewing capacity which maintain tumor growth called cancer stem cells (CSCs). These cells are identified with $CD44^+$ /$CD24^-$ cell surface markers. An increasing amount of evidences indicate a possibility that morphine causes immunosuppression on the hosts. This survey was designed to determine the effect of morphine on the interaction of MSCs and 4T1 cells that may promotes CSCs populations. MSC was isolated by flashing the Tibia and femur bones of mice. After 14 days, MSCs were incubated for 24 h with 0 and 10 µM of Morphine. Then cells were cultured without serum for 24h and the conditioned medium (CM) was isolated. 4T1 cells were incubated for 2 weeks in a medium with isolated CM (50%) and FBS. The medium was changed every 2 or 3 days. Cells were then harvested and incubated with antibodies against CD44 and CD24 for detection of CSCs. Flow cytometry analysis indicated that the CM of MSCs treated with 10 µM of morphine could significantly increases the number of CSCs within murine mammary tumor 4T1 cell line. Percentage of 10 µM is almost two times higher than percentage of control group. This data clearly showed that treatment with CM of morphine treated MSCs results in enrichment of cancer stem cell populations within 4T1 cells.

Keywords*:* Mesenchymal Stem Cells; Conditioned Medium; Morphine; Cancer Stem Cells; Flow Cytometry.

Oral Presentation

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PN: 1241

Effect of cold plasma on skin stem cells

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ABSTRACT

Wound healing is a major problem for many older and young individuals. Furthermore, chronic, non-healing skin ulcers are a majer source of health care costs and patient morbidity and mortality. The use of Cold Atmospheric Plasma (CAP) has recently received more attention which can accelerate the natural healing process and be more effective in maintaining the appearance of the skin after healing. This study showed recent advances in CAP therapies for skin stem cells and skin proliferation and implicated future strategies for increasing effectiveness or broadening clinical indications. Epidermal stem cells were cultured in 25-T flask in DMEM supplement without FBS and 1% Pen/ Strep and incubated at 37◦C with 5% co2. The culture medium was changed two times per week. Cultured stem cells were exposed to Cold atmospheric plasma after two weeks and evaluated Integrin alpha 6/CD49f, CD 34, and integrin β1 expression as stem cell markers. Statistical analysis was performed using t-test with GraphPad Prism statistic software. A significant rise was perceived in integrin α6 and β1 compared to the control group ($P \leq 0.001$). The currently used therapeutic strategies for skin repair are skin grafts and skin substitutes; however, there is still a lack of comprehensive in vivo and clinical treatment that emulates the complex regenerative process. In addition to overcoming the difficulty of enrichment of renewable sources of EPSCs in large quantities, major advances in both knowledges of the biology of EPSCs and the development of tissue engineering scales will finally allow the widespread application of CAP on EPSC-based tissue-engineered skin for tissue repair and regeneration.

Keywords: CAP, Skin, Stem cells

Oral Presentation

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PN: 1251

Endosomal and Cytoplasmic Cell Surface PRRs as Novel Clinically Biomarkers of cardiovascular risk in Stable Coronary Artery Disease

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ABSTRACT

Coronary artery disease (CAD), or "atherosclerotic heart disease", is a serious disease and known as an inflammation-based condition that caused by the formation of plaque in the coronary arteries. Cell surface and endosomal innate pattern recognition receptors (PRRs), have recently been shown to play a crucial role to modify cell function in various immune and non-immune cell types such as endothelial cells. In this study, using qRT-PCR, we examined the expression levels of cytoplasmic and endosomal PRRs, their related cell signaling pathways, and associated inflammatory mediators in peripheral blood mononuclear cells (PBMNCs) in patients with varying degrees of coronary artery atherosclerosis. In mononuclear cells, the expression levels of TLR3, TRIF, and TAK1 were meaningfully down-regulated. On the other hands, the mRNA expression levels of TLR4, MyD88, NF-kB, IL-1β, IL-6, IL-8, and TNF-α were significantly increased in patients with coronary artery stenosis compared with controls. On the other hands, serum levels of IL-1β, IL-6, and TNF-α was significant upregulated and there was noticeable down-regulation in IL-10 in patients with diverse CAD. This study validates differential expression of endosomal PRR (TLR3) and cytoplasmic cell surface PRR (TLR4) at the mRNA level in both mononuclear cells and serum of patients with stable CAD compared with the control group. The expression of TLR4 and TLR3 strictly interrelated with the severity of coronary artery disease. In this regard, TLRs and other related cell signaling pathways may be roles as a novel clinically useful biomarker and therapeutic targets in coronary atherosclerotic disease and other related complications.

Keywords: PRRs; TLR3; Coronary artery disease; Biomarker

Oral Presentation

1st International Congress of Biomarkers

PN: 1255

Biomarkers in diagnosis and treatment of parasitic disease

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ABSTRACT

Treatment and diagnosis are key factors in controlling invasive transmission of the parasitic disease. However, traditional methods of detecting and treating parasites are becoming increasingly ineffective in reducing the transmission of parasitic diseases. The purpose of this study is to investigate the role of biomarkers in early diagnosis or their use as a target in the treatment of parasitic disease.Data for this review were obtained from a database search using a combination of the following terms: parasitological diagnostics, biomarkers, treatment, and microRNAs. A review of various studies showed that miRNAs have a high diagnostic and treatment potential for parasitic diseases. For example, establishes miR-197-5p as a miRNA inhibitor for Plasmodium. Inhibition of miR-548d-3p reduced Leishmania braziliensis growth. Also, miR-155 inhibitor and miR-15a mimic in L. major can induce apoptosis and decrease parasite burden. Studies revealed that parasitic miRNAs including egrmiR-71 and EGR-let-7 as biomarkers can be detected in human plasma and could be used as a new method in the rapid diagnosis and monitoring of hydatidosis. The use of biomarkers, especially micro RNAs, can be used as pioneering and new methods in the treatment and diagnosis of parasitic diseases, and the future is predicted to be very promising.The utilization of biomarkers in basic & clinical research has become so common that as primary endpoints in clinical trials are now accepted.

Key words: Parasite, Biomarker, miRNA, Diagnosis, Treatment

Oral Presentation

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PN: 1261

Biomarkers in Upper Gastrointestinal cancers: What we can learn from Systems Biology and Multi-Omics Data Integration

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ABSTRACT

Upper gastrointestinal (GI) cancers, including esophageal, gastric, and pancreatic cancers, are a major medical and economic burden worldwide. Despite significant advances in radiotherapy, chemotherapy, and targeted therapy for upper GI cancers in the past decade, GI cancer is characterized by a high recurrence rate and poor prognosis. This trouble is rooted in the current diagnosis methods and the lack of adequate and reliable diagnostic/prognostic biomarkers. The diagnosis of almost every disease of the upper GI tract still depends on invasive investigations such as endoscopy of the upper GI tract, manometry of the stomach and esophagus, or radiography. Although cancer was considered a single disease in the organ of origin in the past, today, it is accepted that cancer is a heterogeneous disease assuming the same organ of origin. Therefore, it seems necessary to have suitable biomarkers to make an accurate diagnosis, appropriate patient classification, prognosis assessment, and drug response in cancers. Systems biology and multi-omics research are strategies adopted to provide genetic and molecular biomarkers in cancer. Toward studying complex biological processes, multi-omics data analysis provides an opportunity to gain a deeper and more comprehensive understanding of cancer development and progression. Multi-omics approaches are new frameworks that integrate omics datasets, including genome, epigenome, transcriptome, proteome, metabolome, and metagenome, across multiple studies and multiple 'omes generated on the same set of samples to better understand the molecular and clinical characteristics of cancers. Therefore, in this review, we focus on the integrated multi-omics studies conducted on esophageal, gastric, and pancreatic cancers and discuss the results regarding diagnostic and prognostic biomarkers, as well as biomarkers that determine the response to treatment.

Keywords: Gastrointestinal Cancers, Biomarkers, Systems biology, Multi-omics data integration, Personalized Medicine

Oral Presentation

1st International Congress of Biomarkers

PN: 1264

Residual methylation of tumor suppressor gene promoters, RASSF6 and RASSF10, as novel minimal residual disease markers in acute lymphoblastic leukemia

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ABSTRACT

Aberrant promoter methylation of RASSF6 and RASSF10 occurs at a high frequency in acute lymphoblastic leukemia (ALL). Because of the complexity of the current minimal residual disease (MRD) detecting-methods, the DNA methylation status of the RASSF6 and RASSF10 genes could potentially become biomarkers for the assessment of MRD levels in ALL patients. The promoter methylation status of RASSF6 and RASSF10 was assessed by using methylation-specific PCR (MSP) in the DNA isolated from 280 peripheral blood (PB) samples taken at the time of diagnosis, day 14, 28, and from the subsequent 30-month follow-ups of 45 adult ALL patients. The relative methylation level obtained during the follow-ups by MSP was compared to the MRD results obtained by the amplification of IG/TCR clonal rearrangements using the allele-specific quantitative PCR (ASOPCR) assay. Frequently, RASSF6 was methylated in B-ALL, and RASSF10 was methylated in T-ALL. The applicability and accuracy of the assays were increased when these markers were combined (91.1% and 93.8%, respectively). When a cutoff was defined for the PCR-MRD level, results of the 30 months of MRD detection showed a significant correlation between the PCR and MSP techniques ($r = 0.848$; $p < 0.001$). Due to the high applicability, the non-invasiveness, and promising prospect of longitudinal assessment, the DNA methylation status of the RASSF6 and RASSF10 genes could be potential biomarkers for the assessment of residual disease in PB of patients with ALL.

Keywords: Minimal residual disease; RASSF6; RASSF10; Acute lymphoblastic leukemia; DNA hypermethylation; Tumor suppressor gene.

Oral Presentation

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PN: 1267

Role of CD133 in Tissue Engineering and Regenerative Medicine

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ABSTRACT

Stem cells are essential for tissue engineering and regeneration and are a prospective source of cells for cutting-edge treatments. At least in part because of their paracrine activity, which includes soluble substances and extracellular vesicles, adult stem cells have positive effects when exposed to injured tissue (EVs). Human mesenchymal stem cells (hMSCs) and CD133+ cell-derived EVs have been evaluated in several disease models and proven to repair damaged tissues due to the diversity of signals carried by these vesicles through the horizontal transfer of functional molecules. Since its discovery in 1999, the pentaspan membrane glycoprotein known as CD133 has been utilised as a stem cell biomarker for the separation of stem-like cells from a variety of normal and diseased tissues as well as cell lines. The function of CD133 has been the subject of recent research. Recent advances in our understanding of CD133 regulation and its function in metabolism, differentiation, autophagy, apoptosis, and cell self-renewal, cancer, metastasis, resistance, and regeneration. In this review, we highlight recent developments in CD133 regulation as well as CD133's roles in cell self-renewal, differentiation, and regeneration.

Keywords: Biomarker, CD133, Tissue Engineering, Regenerative Medicine

Oral Presentation

1st International Congress of Biomarkers

PN: 1271

Human Cardiac Organoids and microRNAs; An Overview

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ABSTRACT

Due to the main limitations of animal models for investigating and the conventional 2D cell culture, human cardiac organoid technologies were developed recently. The development of tissue-engineered organoids (organ mimics) is a necessary technology for personalized disease modeling and drug discovery. Small regulatory microRNAs (miRNAs) play key roles in vast biological events including cardiovascular development. This review is summarized scientific evidence in terms of critical cardiac-specific miRNAs.

By searching in the electronic databases including PubMed/Medline, Scopus, Web of Science, and google scholar from 2010 to August 2022, all related articles were included based on eligible criteria. MiRNAs are non-coding RNAs with a crucial role in controlling gene expression involved in various biological processes including pluripotency maintenance and embryonic development. Based on the literature review, some miRNAs be involved in the development human heart such as miR-1, miR-21, miR-421, and miR-181. Some of these miRNAs are effective in the differentiation of cardiac progenitors to cardiomyocytes and be potential molecular modeling to renew the cardiac progenitor niche for regeneration. In summary, some miRNAs may be considered useful biomarkers in different cardiovascular diseases including ventricular septal defect and myocardial infarction.

Keywords: Tissue-engineered organoids; microRNAs; cardiovascular diseases; personalized disease modeling

Oral Presentation

1st International Congress of Biomarkers

PN: 1273

A Simulation study of β-*Amyloid* Aggregation in A Variable Height Capillary Microfluidic Device for Early Diagnosis of Alzheimer's Disorder

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ABSTRACT

Among all neurodegenerative diseases, Alzheimer's Disorder (AD) is a severe neurological disability. Due to the substantial economic and social burden of clinical procedures, efforts have been continued toward early diagnosis methods of AD. Biologically, AD is defined by the presence of ***β-amyloid-containing aggregates*** which is postulated as a potential biomarker. This study introduces microfluidic technology as the detection method and investigates the time and accuracy by novel architecture-multi-channel with variable heights.The first step to design the microfluidics is simulation. So, we simulate microchip with five different heights and define the material and dimensions of micro-chip and sample containing β-amyloid using COMSOL MULTIPHYSICS software. Simulation was performed with five percentages of the media included Phosphate buffered saline (PBS) and deionized water (DIW) (respectively 1/0,2/4,3/4,5/5,0/1) and the process repeated to every channel to obtain the best design.

In this study, a capillary microchip with five different parallel channels introduces to examine different concentration of samples. As the height of channel increases, the biomarker aggregation grows faster. Also, there are differences between channels with varying concentrations so we can find a new way on prediction of particle behavior. Development of POCT tests is crucial in early diagnosis. One of the emerging methods for this purpose is microfluidics due to their portability, fast response, and low-cost process. As we investigate, variable heights can be considered an effective parameter for accomplishment of fast detection of β-amyloid with feasible fabrication process.

Keywords: Alzheimer; Biomarkers; Capillary microfluidic; β-amyloid

Oral Presentation

1st International Congress of Biomarkers

PN: 1290

Study of prognostic significance of immune check points and tumor infiltrating lymphocytes in glioblastoma patients and their relation to MMR system

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ABSTRACT

Glioblastoma is a grade IV brain tumor with a median survival time of 14 months. Besides molecular alteration in WHO classification in defining diagnostic markers, additional biomarkers are urgently needed to distinction of clinically and biologically different glioblastoma tumors. Biomarkers that can predict outcomes will improve the treatment efficacy of glioblastoma patients. Also, these markers can help to choose appropriate treatment based on tumor status and sensitivity to improve patients' outcomes. In this study, we aimed to investigate the prognostic effect of TILs, PD1, PD-L1, CD45RO, Ki-67 and MMR deficiency on these patients. Using immunohistochemical analysis, we measured the incidence of selected markers expression in FFPE tissue blocks of 61 glioblastoma patients. An expert pathologist blinded to the patient's outcome evaluated immunostained slides. Chi-square test was employed for studying the association of the studied markers with clinicopathologic disease features. Univariate Cox regression analysis was conducted to study the prognostic effect of the markers on patients' OS. High infiltration of TILs was associated with vascular infiltration of CD45RO+ cells (P=0.050) and higher expression of Ki-67 (P=0.030). In univariate analyses, IDH mutation had a significantly positive effect on patients' OS (HR=7.584, P=0.001). Higher expression of TC-PDL-1 and PD-1 in patients with high infiltration of TILs had a negative prognostic impact on patient's outcome (HR= 3.268, P=0.036 and HR=3.024, P=0.036). In addition, in patients with a high level of PDL-1 expression and high infiltration of TILs, MMR deficient patients have a worse OS than MMR proficient patients (HR=5.990, P=0.037).

Results of our study showed that immune-related markers in glioblastoma patients could predict patient's outcome when tumor microenvironments have high infiltration of TILs. Also, our results offer a subgroup of patients with high infiltration of TILs, TC-PDL-1 high, and MMR deficient as an appropriate target therapy for immune-checkpoint inhibition.

Keywords: lymphocytes; glioblastoma patients; MMR system

Oral Presentation

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PN: 1297

Comparison of the Sperm Tail Proteome in Asthenozoospermic and Normozoospermic Patients Reveals the Role of DDX3 Induced Stress Response in Loss of Motility

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ABSTRACT

Asthenozoospermia which is characterized by low sperm motility is one of the most common causes of male infertility. While many intrinsic and extrinsic factors are involved in etiology of asthenozoospermia, the molecular basis of this condition still remains poorly understood.

Aims: Since sperm motility is the result of a complex flagellar structure, an in-depth proteomic analysis of sperm tail can uncover mechanisms underlying the asthenozoospermia. So, the aim of this study was to perform the detail proteomic analysis of sperm tail. We quantified the proteomics profile of 40 asthenozoospermiac sperm tails and 40 controls using TMT-LC-MS/MS. Overall, 409 differentially expressed proteins were quantified in sperm tails of which, 250 were up regulated and 159 down regulated in asthenozoospermia. Further bioinformatics analysis revealed that several biological processes including mitochondrial related energy production; citric acid cycle, oxidative phosphorylation, cytoskeleton, protein metabolism and stress response are changed in asthenozoospermic sperm tail samples. Remarkably, we identified the involvement of ATP-dependent RNA helicase DDX3 induced stress response in asthenozoospermic sperm samples. Our findings reveal the importance of mitochondrial energy production and DDX3X/DDX3Y induced stress response as potential mechanisms involved in loss of sperm motility in asthenozoospermia.

Keywords: Asthenozoospermia, Sperm tail; TMT proteomics; Mitochondrial energy production & Stress response

Oral Presentation

1st International Congress of Biomarkers

PN: 1307

TLR3 Priming Influence Epigenetic Plasticity of MSCs and Facilitate Cardiomyocyte Differentiation

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ABSRACT

Cellular plasticity is known as a main characteristics of tissue biology and alterations in the epigenetic landscape of cells are happen in order to let typically restricted cell fate transitions. In this regard, DNA methylation and histone modifications play an important role in regulating such plasticity. Priming approaches are proposed to increase the therapeutic effectiveness of MSCs and pre-conditioning of MSCs with pattern recognition receptors (PRRs) ligands has recently received more attention. The preliminary results of our laboratories and others have reported on the effects of innate immune priming on the reduction of chromatin resistance which refer to epigenetic plasticity. The main purpose of the current study is to investigate of Poly(I:C) priming on expression levels of DNMT1, DNMT3A, HDAC and cardiac lineage genes. In this regard, several pulse preconditioning of ASCs with TLR3 agonist along with 5-azacitidine(5-Aza) accelerates the subsequent cardiac differentiation of MSCs in compare to 5-Aza alone. The results of the recent study shown that the co-administration of 5-azacytidine, a DNA methyltransferase inhibitor, and Poly(I:C), a TLR3 agonist, can increase the capacity of MSC differentiation into cardiomyocyte lineage and can be served as novel biomarkers in following of cardiomyocytes differentiation processes.

Keywords: PRRs; TLR3; Cardiomyocytes; Epigenetic plasticity

Oral Presentation

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PN: 1310

Frequency spectrum analysis of the arterial blood velocity waveforms as a novel biomechanical technique for vascular evaluation

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ABSTRACT

In an attempt of developing modern, accurate and non-invasive methods for early diagnosis of cardiovascular degenerative, ultrasound is a promising imaging modality which provides dynamic imaging of different cardiovascular pathologies as well as arterial blood velocity from which the initial biomechanical changes could be extracted. Vascular blood flow waveform has been noted to fluctuate throughout the arterial tree to modulate the arterial pressure. However, a complete evaluation of these fluctuations has not been investigated as a biomechanical marker. The goal of this study is to extract and compare the blood flow spectrum in frequency domain for elastic and conduit arteries.

Duplex ultrasound images of the common, internal and external carotid arteries as well as brachial and abdominal aorta arteries of 14 healthy participants (20-50 yrs) were recorded. Images were processed to remove the grain noise and low intensity edges. The envelope profile of the Doppler spectrums was resulted for all arteries using a dedicated written algorithm. By applying the Fast Fourier Transform (FFT) on the resultant profiles, frequency spectrum of the blood velocity waveforms were extracted and compared. The present study showed that there were significant differences in frequency domain spectrums of elastic and conduit arteries, including frequency distribution, number of significant harmonics as well as main harmonic magnitude of arteries throughout the arterial tree. Moreover, harmonics with magnitude larger than 20% of that of the first harmonic appear just in brachial and abdominal aorta arteries for which, ratio of the third and fifth harmonics' magnitudes were the highest. In addition to peak forward blood velocity as the most common vascular assessment using duplex ultrasound, frequency domain analysis of blood velocity fluctuations may expand our insight into the human physiological modulations and provide an biomechanical diagnostic technique.

Keywords: Vascular evaluation; Velocity waveform; Frequency spectrum; Image processing.

Oral Presentation

1st International Congress of Biomarkers

PN: 1313

Effect of Vitamin D3 on the cell proliferation, differentiation markers and self-renewal in colorectal cancer stem-like cells

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ABSTRACT

Colorectal cancer (CRC) is the most common cancer in the world with resistant to the majority of the current treatments. Different studies have shown that colorectal cancer stem cells (CRCSCs) are responsible for resistance to conventional therapies. Therefore, effective targeting of CRCSCs is of great importance in CRC treatment. These cells are small subpopulation of tumor cells that possess rapid proliferation and poor differentiation. With these in mind, finding a safe compound with the ability to target cell proliferation, self-renewal and differentiation markers, has high value and may provide more sensitivity of CRCSCs to chemotherapy. In this study, we evaluated the effect of Vitamin D_3 as a safe compound on the cell proliferation, self-renewal capacity and differentiation markers in CRC stem-like cells. CRC stem-like cells (Caco2) were treated with different concentrations of Vitamin D3 after which cell proliferation rates, self-renewal capacity, cytokeratin 20 (Ck20), Mucin 2 (Muc2) and CD133 expression as differentiation markers were evaluated with MTT assay, colony-forming assay and real-time RT-PCR method respectively.

48 h post-treatment with 0.1□to 1 nM Vitamin D_3 resulted in 28.2 % to 66.4 % decreases in cell proliferation rates followed by remarkable decreases in self-renewal capacity ranged from 95- to 0 colonies per well after 2 weeks. Treatment with 1 nM Vitamin D3 dramatically increased the expression level of Ck20 and Muc2 by 2.9- and 2.6 fold respectively followed by a remarkable decrease in CD133 expression level by 0.35 fold of the untreated control cells. Vitamin D3 targeted CRC stem-like cells and successfully inhibited cell proliferation rate in these cells. Differentiation markers Ck20, Muc2 and CD133 appear to be promising targets of Vitamin D3. Our results may open up avenues for treatment of CRC patients using Vitamin D3-based differentiation effects on the CRC stem-like cells with lower toxicity on normal cells.

Keywords: Colorectal cancer; Colorectal cancer stem cells; Differentiation markers; Vitamin D3

PN: 1317

Expression of DNMT1, DNMT3a, and DNMT3b in Radiotherapy Resistance and Sensitive Colorectal Cancer Cell Lines

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ABSTRACT

Radiotherapy (RT) is one of the main treatments for colorectal cancer (CRC), a highly prevalent neoplasm among Iranian patients. Unfortunately, the radioresistance of colorectal tumors leads to failure of treatment and more toxic effects of ionizing radiation. Promoter hypermethylation contributes to the epigenetic modulation of radioresistance-related genes. To evaluate the contribution of DNMTs, as leading factors in regulation of DNA methylation process, expression in development of radiotherapy resistance of CRC, the present study was designed. In this study, the expression of DNA methyltransferase 1, 3A and 3B (DNMT1, DNMT3A, and DNMT3B) at mRNA and protein levels in radio-resistance colorectal cancer cell line with its parental radio-sensitive cell line was compared by real time RT-PCR and Western blotting methods.The expression of DNMT1 in radio-resistance cells was statistically higher than radio-sensitive cells at mRNA and protein levels. No significant differences were observed in the expression of other DNMTs between two cell lines. Our data for the first time suggest that DNMT1 could be an effective factor in development of radiotherapy resistance in colorectal cancer.

Keywords: Colorectal cancer‹Epigenetic‹Radiation resistance

Poster Presentation

1st International Congress of Biomarkers

PN: 1001

Circular RNA's as new biomarkers in Glioma

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ABSTRACT

Primary brain tumors are a different group of tumors from CNS (central nervous system) cells. Glioma is 75% of malignant primary brain tumors in adults. Glial or precursor cells of neuroectoderm are the origin of Glioma tumors and include oligodendroglioma, astrocytoma, and ependymoma, and there are limited options for treatment. Significantly circRNAs are enhanced in the brain and are repetitively expressed. Previous studies have stated that definite circRNAs are differentially expressed in Glioma and regulate apoptosis, metastasis, cell proliferation, and oncogenesis of Glioma. The object of this review was to review the importance of circRNA research in Glioma tumors and discuss the diagnostic and prognostic values of circRNAs in Glioma. The present review established on published studies were studied from Scopus, PubMed, and Google scholar, and retracted articles were excluded. Circ-FBXW7 and circ-AKT3 are down-regulated and function as a tumor suppressors but following circRNAs are up-regulated in Glioma circ-SMO as tumorgenicity, circ-0014359, circ-PTN as including Proliferation, circ-CPA4 as proliferation and prognoses markers, circ-MAPK4, has-circ-0037251and circ-RNA-104075 apoptosis inhibitor, circ-002136, circ-DICER1and circ-ATXN1as angiogenesis inducer, circ-SMAD7, circ-POSTN, has-circ-0034642 and circ-DENND2A as migration and invasion marker, circ-0079593 and circ-CDC45 as prognoses marker, circ-CEP128 as drug resistance, circ-ATP8B4 as radiosensitivity, circ-NFIX as targeted therapy. Glioma is a malignant tumor and there are limited options for treatment but with circular RNA and their prognostic value we can have a specific treatment plan based on circular RNA biomarkers and these findings will help patients to have an accurate and specific treatment with better outcomes but the study in this field should continue to have new and more specific biomarkers for Glioma and more biomarkers for personalized therapy.

Keywords: Glioma; Circular RNA; Biomarkers

Poster Presentation

1st International Congress of Biomarkers

PN: 1002

The Prognostic Value of Hematological Parameters in the Setting of COVID-19 Severity

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ABSTRACT

Recently, a new emerging viral infection induced by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was named coronavirus disease-2019 (COVID-19) with high morbidity and mortality on a global scale. Here, we exclusively aimed to evaluate distinct laboratory biomarkers to predict disease severity, classified as moderate, severe, and critical forms, in patients with SARS-CoV2 infection. Following COVID-19 diagnosis, all consecutive patients with confirmed SARS-CoV-2 infection were included since September 2020 for one year. Data were collected using electronic medical records. For further analysis, SPSS *ver.*20 was used. Based on our results, the mean age was 47.96 ± 4.91 years amongst 685 patients, of whom 339 were male (49.5%), and 346 were female (50.5%). In addition, 41 included patients were smokers (6%). The mean length of hospital stay in hospitalized patients was 6.87 ± 4.55 days. Also, 62 (9.1%) patients required mechanical ventilation, and 59 (8.6%) patients expired, finally. There was a positive correlation regarding the mean length of hospital stay in both genders with higher NLR and LDH serum levels (P value = 0.01). Moreover, the 28-day mortality rate and mechanical ventilation (MV) required in patients with either positive CRP or high levels of LDH were remarkably greater than that of the non-severe group (P= 0.01). Notably, as in-hospital outcomes, the rate of LDH was significantly higher in expired individuals and in those who required MV in the two genders ($p<0.001$). Besides, it has been revealed that the serum level of LDH was positively correlated with the prognosis of the length of hospital stay in both male and female patients with spearman r = 0.29 and 0.27, respectively (P value <0.001). Together, our findings revealed that high values of NLR, CRP, and LDH can be considered reliable clinical prognostic aids for risk stratification and identification of disease severity.

Keywords: Covid-19, Mechanical Ventilation, CRP, LDH, NLR

Poster Presentation

1st International Congress of Biomarkers

PN: 1003

Evaluation of liver enzymes, renal and hematological diagnostic markers in patients with epilepsy

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ABSTRACT

Epilepsy is one of the most common neurological disorders that affect approximately 70 million people worldwide. We aimed to assess the changes in liver enzymes, kidney, and blood diagnostic markers in patients diagnosed with epilepsy admitted to educational hospitals in Abadan and Khorramshahr. This was a cross-sectional, retrospective analytical study. The study population was the patients diagnosed with epilepsy admitted to the educational hospitals of Abadan University of Medical Sciences from March 21, 2019, to March 19, 2020. Demographic information including age, sex, and values of blood, liver, and kidney factors of patients was collected by referring to the HIS (Hospital Information System). Data were analyzed by SPSS software. In this study, 100 patients with epilepsy were randomly selected with a mean age of 21.84±23.47 which included 42% female and 58% male. The mean FBS (129.14 ± 55.443) in all patients with epilepsy except 20-39 years was higher than normal. Also, the mean serum ALK level (443.94 ± 218.304) of these patients was higher than normal. The mean of hemoglobin (11.78 ±1.712) was lower than normal in patients with epilepsy, and also decreased MCHC (30.26 ±3.269) was common in all age groups except 40 years. The mean of ESR (17.25 ± 17.676) in all age groups was higher than normal. Decreased MCHC and hemoglobin, and elevated ESR, ALK, and blood glucose levels are common findings in patients with epilepsy. Thus, Hyperglycemia, Iron Deficiency Anemia (IDA), inflammation, and elevated ALK have important roles in the pathogenesis of epilepsy.

Keywords: Epilepsy; Liver enzymes; Renal markers; Hematological markers

Poster Presentation

1st International Congress of Biomarkers

PN: 1005

Biomarkers in patients with symptomatic temporomandibular disorders

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ABSTRACT

Temopromandibular disorder (TMD) is one of the most prevalent causes of orofacial pains and a significant percentage of the population suffer from at least one of TMD symptoms. TMD diagnosis is still a challenge for the clinicians and requires descriptive history, comprehensive clinical examinations and imaging. The complex anatomy and function of temporomandibular joint, different pathologies that involves maxillofacial region resulting in pain and the complicated nature of pain make the need for more definitive diagnosis of TMD by new approaches more crucial. In symptomatic TMD conditions, the role of biomarkers is still vague. Identification of biomarkers related to symptomatic TMD may help in developing new methods for the diagnosis and even treatment of TMD. This review aims to find the potential relationship of biomarkers and painful TMD and categorize such biomarkers. PubMed, Scopus, Cochrane Library and Web of Science databases were comprehensively searched from inception to May 2022. Articles were screened based on the inclusion and exclusion criteria. 43 articles met the inclusion criteria. Serum, saliva, and synovial fluids were investigated to find related biomarkers with TMD. Five categories of associated biomarkers with TMD including molecular biomarkers, neurotransmitters, growth factors, epigenetic biomarkers and biochemical markers were identified. Various biofluids and different biomarkers are investigated to identify the risk factors, progression and treatment outcomes of symptomatic TMD. Since still there is not a standard guideline for definitive TMD diagnosis, defining the related biomarkers to TMD in the domain of diagnosis would help clinicians to a more precise diagnosis and confident treatment. Besides, an important biofluid for biomarker assays is saliva that could be collected noninvasively. Moreover, biomarkers have the potential to diagnose TMD at the early stages when medical interventions are more efficient and noninvasive. The potential biomarkers are needed to be more explored on heterogenous and large-scale sample size populations to reach desirable reliability and practicality and the results could be generalized to the clinic.

Keywords: Biomarkers; Temporomandibular joint; Temporomandibular disorders; Chronic pain.

Poster Presentation

1st International Congress of Biomarkers

PN: 1006

Role of Biomarkers in Risk Assessment, Diagnosis, Response to Treatment, and Prognosis of Multiple Sclerosis

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ABSTRACT

Neurodegenerative disorders are a group of conditions caused by progressive damage to cells and nervous system connections that are necessary for mobility, coordination, strength, sensation, and cognition. Millions of people worldwide are affected by neurodegenerative diseases. Neurodegenerative disorders include Alzheimer's disease, Parkinson's disease, Huntington's disease, Multiple Sclerosis disease, and Prion disease. Multiple sclerosis (MS) is a chronic neurological disease that affects the central nervous system (the brain and spinal cord). There are numerous biomarkers available to aid in the diagnosis of Multiple Sclerosis. Multiple sclerosis biomarkers could help with diagnosis, treatment, and prognosis. Furthermore, these biomarkers are making it easier to diagnose Multiple Sclerosis.

Keywords: Multiple sclerosis (MS); Biomarkers; Neurodegenerative

Poster Presentation

1st International Congress of Biomarkers

PN: 1007

Serum IL-27 concentration in patients with colorectal cancer compared with healthy individuals

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ABSTRACT

Colon cancer is one of the most common cancers worldwide. Numerous studies have shown anti-tumor roles for IL-27, but some evidence has also demonstrated tumor promoting effects for this cytokine. In this study, we compared serum levels of IL- 27 in colorectal cancer (CRC) patients with the control group. In addition, the relationship between serum levels of IL-27 and clinicopathological characteristics of patients was investigated. This study consisted of 70 CRC patients who did not undergo any treatment, including surgery, anti-cancer drugs, or radiation therapy. The control group, including 70 healthy individuals who were matched with the patients in terms of age and sex. Serum level of IL-27 was measured using a commercially reliable sandwich enzyme-linked immunosorbent assay (ELISA) kit, and the results were analyzed using SPSS software. The serum level of IL-27 in controls was significantly higher than in CRC patients ($P< 0.001$). However, we did not find any statistically significant relationship between the serum level of IL-27 and clinicopathological characteristics (stage, grade, lymph nodes involvement, and tumor size) of CRC patients. Based on the ROC curve, the best cut-off point of IL-27 was 57.50 pg/ml, at which the test's sensitivity was 60% with a specificity of 77.1%. Serum level of IL-27 in the control group was higher than in patients with colorectal cancer. According to the ROC curve, serum level of IL-27 could probably be an indicator for colorectal cancer screening. To use IL-27 to diagnose or treat these patients, more studies with larger sample sizes are needed.

Keywords: IL-27; Colorectal cancer; ELISA

Poster Presentation

1st International Congress of Biomarkers

PN: 1008

Evaluating the role of serum level of IL-27 in patients with prostate cancer compared to healthy controls

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ABSTRACT

IL-27 has shown to play a dual role in various cancers, and in some cases, tumor prognosis, metastasis, and tumor angiogenesis are associated with IL-27 expression. Therefore, IL-27 may be a new target for cancer treatment in the future. In the present study, we examine the serum level of IL-27 in high and low-grade prostate cancer. These results will help better understand the role of IL-27 in this cancer. In this case-control study, 69 patients with prostate cancer and 40 men as a control group were included based on inclusion and exclusion criteria. Serum IL-27 was compared in the patients and controls using the sandwich ELISA method. Also, the relationship between serum IL-27 levels in patients based on the clinical and pathological characteristics extracted from their records was investigated. The diagnostic cut-off point of IL-27 was identified for patients with prostate cancer. The mean serum level of IL-27 in patients was significantly higher than controls. We did not find any statistically significant relationship between the serum level of IL-27 and prostate cancer's clinical and pathological features, which included stage, grade, and lymph node involvement. Additionally, the correlation between serum IL-27 level and age and tumor size was not statistically significant. In the present study, the best cut-off point (highest sensitivity and specificity) for using the IL-27 serum level was 83.2 pg/ml, at which the test sensitivity was 84.1%, and its specificity was 75%. Serum IL-27 level in patients with prostate cancer is higher than the control group. Serum IL-27 levels in patients with prostate cancer are not associated with the clinical features of the disease. Serum IL-27 levels may be indicative of prostate cancer screening. Further studies are needed to use IL-27 to diagnose or treat prostate cancer patients.

Keywords: IL-27; Prostate cancer; ELISA

Poster Presentation

1st International Congress of Biomarkers

PN: 1009

Receiver Operating Characteristic curve analysis of interlukine-37 in Iranian patients with breast cancer

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ABSTRACT

Breast cancer is known as the most common cancer and the fifth main cause of death among Iranian women. In Iran, the incidence of breast cancer increased in recent years particularly in individuals less than 40 years. Circulating cytokines have been proposed to simplify and improve cancer detection and prognosis. Interleukin-37 (IL-37) is a newly described member of IL-1 family, and it might be employed as a promising and useful prognostic and/or diagnostic marker for different types of cancer. Receiver Operating Characteristic (ROC) curve is used to graphically indicate the connection or trade-off between two parameters of sensitivity and specificity for each cut-off point value in test(s). The value of such information in patient with breast cancer is currently under investigation. The aim of this study was to determine ROC curve and the area under the curve (AUC) for IL-37 concentration in patients with breast cancer in comparison to healthy individuals in a population from southern Iran. Enzyme-linked immunosorbent assay (ELISA) kit was used to measure IL-37 concentration 60 patients with breast cancer and 30 healthy controls. ROC curve analysis was used to determine the sensitivity, specificity and cut off point of IL-37 concentration in sera. IL-37 ROC curves discovered a good differentiation between patients with BC breast cancer and healthy controls with the area under the curve (AUC) of 0.83. The sensitivity and the specificity were 88.30 and 75.90 at cut- off value more than 37.94 pg/ml. Regarding ROC curve analysis, IL-37 concentration may have some utility in screening tests and/or might be served as a promising candidate biomarker for early detection of breast cancer. However, it is a preliminary study and more trainings with larger sample size are essential to accurately define the clinical role of IL-37 in breast cancer.

Keywords: Breast cancer; IL-37; ROC curves

Poster Presentation

1st International Congress of Biomarkers

PN: 1010

A Case-Control Study of Vitamin D and Zinc Status in Outpatients Infected with COVID-19 and Non-Infected Participants: Association with the Progression of Symptoms during the Clinical Course of the Disease

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ABSTRACT

Vitamin D and zinc are important components of nutritional immunity. This study compared the serum concentrations of vitamin D and zinc in COVID-19 outpatients with those of non-infected participants. Clinical symptoms and associations with vitamin D and zinc status were also examined. A checklist and laboratory examination were applied to collect data in a case-control study conducted on 53 healthy individuals and 53 patients of both sexes. Lower serum concentration of total 25-hydroxyvitamin D [25(OH)D] were observed in patients with moderate illness (18.9±11.5 ng/mL) than in patients with asymptomatic or mild illness (29.2±18.3 ng/mL) ($p=0.054$). Also, infected patients (100.6±17.8 µg/dL) showed lower serum concentration of zinc than non-infected participants (113.8±13.4 µg/dL) ($p=0.013$). Patients with normal and insufficient vitamin D status at the time of admission had decreased odds ratios of general symptoms of COVID-19 (odds ratio, 0.19; $p\leq0.001$ for normal and odds ratio, 0.3; $p=0.007$ for insufficient vitamin D status) compared to patients with vitamin D deficiency. This study revealed the importance of 25(OH)D measurement as a relatively easy option to predict disease severity and the progression of COVID-19 symptoms. Also, this study showed that a poor zinc status of the outpatients might affect the disease onset of COVID-19.

Keywords: Clinical symptoms; Vitamin D status; Zinc status; Sunlight exposure; COVID-19

Poster Presentation

1st International Congress of Biomarkers

PN: 1013

Predictive biomarker for colorectal cancer

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ABSTRACT

Using typical molecular indicator analysis for cancer patient's aids leader directed therapy choices and improvements adapted maintenance for these patients. The current study on improvements in cancer investigation and management additional emphasized the prominence of biomarker analysis (both tissue- and blood-based) in foreseeing the answer, cancer regulator, side properties, and conflict. In the present review, we summarize and critically appraise the most recent advances with emphasizing the predictive biomarker analysis. Trophoblast cell-surface antigen-2 (Topo-1) is a nuclear enzyme that is essential for reproduction and relaxing DNA and stopping dangerous element disruptions. An active component of anti-Trop-2 antibody conjugate, SN-38 is a cytotoxic treatment that disrupts the Topo-1/DNA covalent multifaceted made in the CRC cells. It encourages permanent double-strand breaks, leading to S-phase stop, and cell loss. This is completed by assigning the SN-38 molecule to the multiplexes and prevents upcoming reproduction divergences inhibiting maintenances of double-strand disruptions. This is an opportunity to develop predictive double biomarker testing for optimization of therapy of complex and new generation of highly potent antineoplastic drugs. In conclusion, a more comprehensive and wide-ranging considerate of these multifaceted drugs, comprising the choice of the cell surface marks, antibodies, cytotoxic burden, and the linker knowledge, will certainly improve and augment the effectiveness of these capable anticancer mediators.

Keywords: biomarker, cancer, drug

Poster Presentation

1st International Congress of Biomarkers

PN: 1014

The suppression effect of B7-H7 as a prognostic biomarker on the chemosensitivity of gastric cancer cells to Docetaxel

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ABSTRACT

Gastric cancer (GC) is the leading cause of cancer-related death in the world and drug resistance to conventional therapies is one of the main barriers in GC therapy. B7-H7, as a prognostic biomarker, belongs to the immune checkpoints of the B7 family and is expressed in different types of human cancers. However, the function of B7-H7 on the chemo-sensitivity and aggressiveness of GC still remains unclear. Considering that, this study was conducted to assess the impact of combination therapy of B7-H7 siRNA/ Docetaxel on GC cells. MKN-45 GC cells were transfected with B7-H7 siRNA and treated with Docetaxel individually and in combination. Gene expression was quantified via qRT-PCR. Besides, to investigate cell viability and migration capacity, MTT assay and wound-healing assay were done on GC cells, respectively. We showed that B7-H7 suppression combined with Docetaxel decreased the expression of B7-H7 mRNA in MKN-45 GC cells. Moreover, the obtained results illustrated that siRNA-mediated B7-H7 suppression increased the chemosensitivity of MKN-45 cells to Docetaxel and decreased its efficient dose. It was also indicated that combination therapy of B7-H7 siRNA and Docetaxel decreased cell migration. In conclusion, B7-H7 has an important role in the chemo-sensitivity and pathogenesis of GC. Also, the findings of the current study demonstrated that silencing B7-H7 combined with Docetaxel could be a potent treatment approach in GC targeted therapies.

Keywords: Gastric cancer; siRNA, B7-H7; Docetaxel; Chemo-sensitivity; Combination therapy

Poster Presentation

1st International Congress of Biomarkers

PN: 1015

The role of caspase3 and PDGF-A biomarkers in the protective effect of zinc against tetrahydrocannabinol-induced Sertoli cell apoptosis: from biomarker to therapeutic target

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ABSTRACT

The global rise in marijuana abuse during reproductive years has placed many men at risk for the negative consequences of -9-tetrahydrocannabinol (THC), marijuana's primary active component. It has been reported that THC affects male fertility and causes testicular cell dysfunction and apoptosis. We examined the effects of THC alone and in combination with zinc on cultured Sertoli cells to gain mechanistic insight into the THC-induced testicular toxicity and to evaluate zinc's protective effect. We also measured the protein expression levels of caspase3 (as cell apoptosis biomarker) and PDGF (as mitogenic biomarker) to investigate zinc pretreatment's potential protective role in this testicular toxicity model and underlying mechanisms. The Mus Musculus Sertoli cell line (TM4) was cultured and exposed to THC alone (IC50: 470 µM, 24 h) and co-administered with zinc (8 µM, 48 h) and investigated in three groups: control, THC and THC + zinc. Western blotting was applied to detect protein expression levels of Caspase3, Pro-caspase3, and PDGF-A. THC significantly decreased expression levels of PDGF-A and pro-caspase3 proteins ($p<0.05$ for both), whereas it increased the expression level of cleaved caspase3 protein ($p<0.001$). Pretreatment with zinc reversed THC-induced apoptotic effects and reduced cleavedcaspase3/pro-caspase3 ratio but could not reverse THC-induced reduction of PDGF-A expression level in TM4 cells. The present data suggest that THC induces Sertoli cell damage through a multi-target mechanism. Over-expression of cleaved caspase3 and under-expression of PDGF-A in Sertoli cells exposed to THC may be the underlying cause of THC-induced Sertoli cell apoptosis. Pretreatment with zinc alleviated the THC-induced toxic effects via modulation of caspase3 signaling pathways. These findings suggest the probable clinical importance and therapeutic effects of zinc trace elements on infertility among chronic Marijuana users.

Keywords: Apoptosis; Caspase 3; PDGF-A; Tetrahydrocannabinol; Zinc

Poster Presentation

1st International Congress of Biomarkers

PN: 1016

Multiple Sclerosis Biomarkers

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ABSTRACT

MS is a chronic autoimmune neurological disease with a prevalence of 52 per 100,000 in Iran, with the highest prevalence in Isfahan. Its rapid diagnosis plays an important role in increasing the success of treatment and disease control. Biomarkers are the main factor in prediction, diagnosis, relationship with disease and response to treatment. A variety of methods and biomarkers in MS include NGS, gene translocation, intermediate metabolites, multiple tissue spectrometry, FISH analysis, secretory protein analysis, functional analysis of signal transduction pathways, tissue pathological analysis, protein arrays, non-coding RNA expression profile such as miRNA, investigation of gene polymorphisms, etc. These methods differ depending on the biological nature of the marker (protein, RNA, DNA, metabolites, etc.) and their circulatory or fixed. MRI is the best tool for diagnosing, progressing and checking the treatment process of MS until now, but molecular biomarkers are used more specifically and accurately every day in predicting and diagnosing different stages of the disease and better planning to prepare treatment instructions and type and amount of medicine. Diagnostic biomarkers are more abundant and important than other biomarkers in MS identification. MS biomarkers play a role in designing personalized treatment for patients and significantly reducing the costs of clinical trials, drugs, length of treatment, etc. However, in a complex disease such as MS, a single marker is not effective and there is a need to use a combination of various biomarkers and analyze their profiles for prediction, diagnosis, prognosis, treatment response, etc.

Keywords: Multiple sclerosis; Molecular biomarkers; miRNA; Gene polymorphism

Poster Presentation

1st International Congress of Biomarkers

PN: 1017

Hepatoprotective Effect of *Gongronema latifolium* Benth Leaf Flavonoid-rich Extracts in streptozotocin-induced Wistar Rats via Fetuin-A and Tumor Necrosis Factor-alpha

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ABSTRACT

This study was designed to address the hepatoprotective potential of flavonoid-rich extracts from *Gongronema latifolium* Benth on streptozotocin-induced Wistar rats via Fetuin-A/tumor necrosis factor-alpha (TnF-α). The flavonoid-rich extract from *Gongronema latifolium* leaf was prepared using an established method. To induce diabetes mellitus, 45 mg/kg body weight of streptozotocin was intraperitoneally injected into the experimental animals. The animals were randomly divided into five groups of ten rats each, comprising non-diabetic rats, diabetic controls, diabetic rats treated with low and high doses of flavonoid rich-extracts from *Gongronema latifolium* leaf (FREGL) (13 and 26 mg/kg, respectively), and diabetic rats treated with 200 mg/kg of metformin glibenclamide orally for three weeks. Thereafter, the animals were sacrificed, blood and liver were harvested to evaluate different biochemical parameters, hepatic gene expressions and histological examinations. The obtained results revealed that FREGL (especially the low dose) significantly ($p < 0.05$) reduced alanine transaminase, aspartate aminotransferase, and alkaline phosphate activities, lipid peroxidation level, as well as relative gene expressions of fetuin-A and TNF-α in diabetic rats. Also, diabetic rats given low and high doses of FREGL demonstrated a significant ($p < 0.05$) increase in antioxidant enzymes and hexokinase activities, glucose transporters (GLUT 2 and GLUT 4), and glycogen levels. Added to this, the histoarchitecture of the liver of diabetic rats administered FREGL (especially low dose) was also normalized. Therefore, FREGL (particularly at 13 mg/kg) might be helpful in mitigating the hepatopathy complication linked to diabetes mellitus.

Keywords: Liver; Histoarchitecture; Complications; Low; High

Poster Presentation

1st International Congress of Biomarkers

PN: 1019

Chemotherapy against colorectal cancer cells: delivery of capecitabine by polycaprolactone-polyethylene glycol carrier

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ABSTRACT

Colorectal cancer causes many deaths despite many treatment options. Capecitabine (CAP) uses as the standard chemotherapy regimen for colorectal cancer. However, after a period of administration, the free drug does not induce effective apoptosis due to rapid metabolism. This work aims to encapsulate CAP and evaluates cytotoxic and apoptotic effects on HCT-119, HT-29 colorectal cancer cells, and human umbilical vein endothelial cells (HUVECs). CAP nano-formulation was prepared by triblock (TB) (PCL-PEG-PCL) biodegradable copolymer to improve drugs' bioavailability as an anticancer agent. The nanoparticles were prepared with the Ultrasonic homogenization method. The physicochemical characteristics of nanoparticles were evaluated using FTIR, DLS, and FESEM techniques. The zeta potential, entrapment efficiency, drug release, and storage stability were studied. Also, cell viability and apoptosis were examined by using MTT and acridine orange (AO) and propidium iodide (PI), respectively. The smaller hydrodynamic size (291.1 nm), polydispersity index (0.203), and zeta potential (-20.8 mV) were observed in nanoparticles. Nanoparticles revealed good formulation and storage stability at 25°C than 4°C in 90 days. Despite the increase in IC50 of nanoparticles compared to the free drug, the cytotoxic effect was observed with a slow release of the drug. (p-value < 0.05). In (AO/PI) staining, the percentage of apoptotic cells in the CAP-loaded TB in HUVEC, HT-29, and HCT-116 were calculated as 54%, 51.32%, and 51.22%, respectively. Developed micelles formulation was able to sustain the drug release and entrap the CAP to more apoptosis of cancer cells. The CAP-loaded TB nanoparticles in this research could be an effective strategy for targeted colorectal cancer therapy.

Keywords: Colorectal cancer; Capecitabine; Micelle; Apoptosis

Poster Presentation

1st International Congress of Biomarkers

PN: 1020

MicroRNAs and Drug Resistance in Colorectal Cancer with Special Focus on 5-fluorouracil

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ABSTRACT

Colorectal cancer (CRC) is globally one of the most common cancers in all age groups. The current chemotherapy combinations for CRC treatment include 5-fluorouracil (5-FU)-based regimens; however, drug resistance remains one of the main reasons for chemotherapy failure and disease recurrence. Many studies have determined CRC chemoresistance mechanisms such as drug efflux, cell cycle arrest, DNA damage repair, apoptosis, autophagy, vital enzymes, epigenetic, epithelial-mesenchymal transition, stem cells, and immune system suppression. Several microRNAs affect drug resistance by regulating the drug resistance-related target genes in CRC. These drug resistance-related miRNAs may be used as promising biomarkers for predicting drug response or as potential therapeutic targets for treating patients with CRC. This work reviews and discuss the role of selected microRNAs in 5-FU resistance and their molecular mechanisms in CRC. In this review we searched "MicroRNAs ", "5-FU " and " Colorectal Cancer" as primary terms in three popular search engines in medical sciences including PubMed, Science Direct and Google scholar data bases. Toxicity and drug resistance to 5-FU and other chemotherapeutic drugs are major problems in CRC treatment. Also, numerous studies have demonstrated the importance of miRNAs in the development of drug resistance in CRC through disruption of various cellular mechanisms such as drug efflux, cell cycle arrest, DNA damage repair mechanisms, apoptosis, autophagy, key enzymes, epigenetic, EMT, stem cells, and immune system. Nowadays, delivery systems have been designed that can be effective in treating cancer by specific miRNAs carrier to specific target. These technologies are supposed to be used for the benefit of cancer patients.

Keywords: Colorectal cancer; MicroRNA; Drug resistance; 5-fluorouracil

Poster Presentation

1st International Congress of Biomarkers

PN: 1021

Signaling Pathways Involved in 5-FU Drug Resistance in Cancer

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ABSTRACT

5-fluorouracil (5-FU) is used as an anti-metabolic drug in various cancers in the first stage of treatment. Unfortunately, in some cancers, 5-fluorouracil has low effectiveness because of its drug resistance. Studies have shown that drug resistance to 5-FU is due to the activation of specific signaling pathways and increased expressions of enzymes involved in drug metabolites. However, when 5-FU is used in combination with other drugs, the sensitivity of cancer cells to 5-FU increases, and the effect of drug resistance is reversed. This study discusses how the function of 5-FU in JAK/STAT, Wnt, Notch, NF-κB, and hedgehogs (Hh) in some cancers. We searched “Signaling Pathways ", “5-FU " and " Cancer" as primary terms in three popular search engines in medical sciences including PubMed, Science Direct, Medline, Embase, Scopus, and Google scholar data bases. Title and abstracts, selected the studies, and collected data concerning validation were used to check the anticancer activity of 5-FU in the signaling pathways. The JAK/STAT, Wnt, Notch, NF-κB and Hh pathways, by expressing their specific genes STAT, β-catenin, Notch receptor, IκBα, and Gli, respectively, cause drug resistance and reduce the effectiveness of 5-FU through the increase of anti-apoptotic genes, EMT, N-cadherin, MMPs, VEGF, cell cycle, and tumor cell proliferation. Also, increased expression of enzymes involved in 5-FU metabolites such as DPD, TS, and MTHFR, affects 5-FU action by altering some genes expressions such as EMT and increasing genes methylation that inhibits signaling pathways in patients. There are also several signaling pathways involved in drug resistance in any type of cancer. To deal with drug resistance to 5-FU, it is necessary to design new drugs or a suitable combination therapy that can be more effective in controlling cancer with its multiple functions in the mentioned pathways and increase the quality of life in patients.

Keywords: 5-fluorouracil; JAK/STAT pathway; Wnt pathway; Notch pathway; NF-κB pathway; Hedgehog pathway

Poster Presentation

1st International Congress of Biomarkers

PN: 1024

The effect of miRNAs on female and male infertility: A systematic review

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ABSTRACT

miRNAs are small single-stranded RNAs of 15-23 nucleotides that do not encode proteins, but are involved in regulating gene expression by binding to a protein called AGO and forming a ribonucleoprotein complex called the RNA-induced silencing complex (RISC). This complex binds to`3 utr mRNA of the target gene and disrupts its function. Recent studies prove that MIRs play an important role in infertility with their post-transcriptional settings on 3`utr mRNA. MIR is involved in many stages of mammalian spermatogenesis, as well as testicular growth, sperm maturation, migration, and also it is involved in Ovulation, menstrual cycles, as well as diseases such as endometriosis and PCOS, so changes in the amount may affect each of these processes and cause infertility. In this review article, 172 valid articles from PubMed and Google Scholar databases were examined and the best articles were selected. The search keywords included MIRs in female infertility, MIRs in male infertility, and treatment and diagnosis using miRNAs. This article is a comprehensive review of miRNAs associated with infertility. miRNAs are found in body fluids such as plasma , serum, Follicular fluid , semen , etc. Their availability and cheapness to examine make miRNAs a high-potential biomarker for future diagnosis and novel treatments for most diseases, including infertility. Nowadays, the use of biomarkers is of great interest for the diagnosis and treatment of diseases due to their non-invasiveness. There are many types of coding and non-coding RNAs in the human body, and MIRs are currently the most important in this case, and this It makes them superior in diagnosis and treatment, that's why today, in addition to proteins, investigating the role of miRNA is a new and promising field in the evaluation of infertility in men and women.

Keywords: miRNAs; infertility; PCOS; Endometriosis; Biomarker

Poster Presentation

1st International Congress of Biomarkers

PN: 1027

Retinoprotective Effects of Crocin and Crocetin via Anti-Angiogenic Mechanism in High Glucose-Induced Human Retinal Pigment Epithelium Cells

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ABSTRACT

Diabetic retinopathy (DR) is one of the most common side effects of diabetes. We aimed to investigate the effects of crocin and crocetin (as a deglycosylated form of crocin in blood stream) in gene expression or protein levels of vascular endothelial growth factor (VEGF), vascular endothelial growth factor-receptor1 (VEGFR-1), matrix metalloproteinases2 (MMP-2), matrix metalloproteinases9 (MMP-9) and thrombospondin-2 (TSP-2; as a biomarker for DR) in high glucose cell culture media. The retinal pigment epithelium (RPE) cells were exposed to high glucose (HG, 30 mM glucose concentration) and normal glucose (NG, 24.5 mM mannitol + 5.5 mM glucose) for six days. RPE cells were treated in four treatment groups (crocin, crocetin, Bevacizumab, and crocin + Bevacizumab). Gene expressions were measured using quantitative real-time PCR, and protein levels were evaluated by western blot. Findings showed that VEGF gene expression and protein level significantly decreased in all treatment groups. In addition, reduction in VEGFR1 gene expression was significantly higher in Bevacizumab and crocin + Bevacizumab groups than other groups. Only crocin and crocetin could reduce the gene levels of MMP-2 and MMP-9. In addition, TSP-2 protein levels increased when HG cells were exposed to crocin or crocin + Bevacizumab groups. Our data showed that crocin and crocetin have anti-VEGF function similar to Bevacizumab, act as an anti-angiogenic agent. Also, crocin and crocetin could decrease MMP-2 and MMP-9 gene levels being inflammatory and angiogenesis factors. As a result, crocin and crocetin have protective effects against angiogenesis and inflammation in DR.

Keywords: Anti-angiogenesis; Diabetic retinopathy; VEGF; Crocetin; Crocin.

Poster Presentation

1st International Congress of Biomarkers

PN: 1028

Potential use of biomarkers in the family members of new untreated relapsing remitting multiple sclerosis for early diagnosis of multiple sclerosis

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ABSTRACT

Multiple sclerosis (MS) is a neuroinflammatory autoimmune disorder of the central nervous system. The pathogenic function of Receptor for advanced glycation end products (RAGE), Apolipoprotein-A1 (Apo-AI), and High mobility group box1 (HMGB1) in the breakdown of the blood barrier, and neuroinflammatory diseases such as MS have been reported. Use an enzyme-linked immunosorbent assay to measure plasma levels of S100A12, Apo-A1, and western blot to measure HMGB1plasma levels. Thirty-five new cases of untreated patients with deterministic relapsing-remitting multiple sclerosis (RRMS) according to the McDonald criteria, twenty-four healthy controls (HC), and twenty-six family members of untreated RRMS (termed them as a high-risk group) were entered into the study. In the new cases of untreated RRMS ($P<0.05$; 0.045) and high-risk ($P<0.05$; 0.001) groups, the plasma level of S100A12 was dramatically lower. Although Apo-A1 level decreased markedly in the high-risk group ($P<0.05$; $P=0.003$) compared to the HC group, there was no significant difference in the patients group ($P=0.379$). HMGB1 level was significantly higher in the untreated RRMS patients ($P<0.05$; $P=0.063$) than HC group, but there was no notable difference in the patients group ($P=0.571$). Based on previous studies that have revealed the significance of these biomarkers in the inflammatory processes, by considering the plasma alterations in family members of MS patients, our study suggested they could be one of the contributing factors in the pathogenesis of MS. However, their practical applicability as a prognostic biomarker will take more research and testing.

Keywords: S100A12; Apo-A1; HMGB1; Relapsing-remitting

Poster Presentation

1st International Congress of Biomarkers

PN: 1030

Gastrointestinal disorder biomarkers

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ABSTRACT

Gastrointestinal disorders (GI diseases) refer to conditions involving the gastrointestinal tract, which are ranging from dyspepsia to inflammatory bowel diseases (IBDs) and malignant tumors. Radiology, endoscopy, and serology are common methods employed to diagnose GI diseases. Plus, Biomarkers, which are assessable indicators of the presence or severity of the disorders, are indispensable agents to diagnose GI conditions. Diagnostic biomarkers, including serological biomarkers (C-reactive protein and Erythrocyte Sedimentation Rate), antibodies (Anti-neutrophil cytoplasmic Antibodies, Antifungal Brewer yeast Antibodies, anti-OmpC, Anti-I2 and Antibodies against Fla-X and A4-Fla2 flagellins), Immunological biomarkers (Regulatory T cell and Cytokines), fecal biomarkers (Calprotectin, Lactoferrin, and Pyruvate kinase M2) and genetic biomarkers (Non-encoding RNAs), are investigated and categorized in this review. Furthermore, we have discussed the essential biologic functions and diagnostic roles and the advantages and disadvantages of these biomarkers. Furthermore, novel genetic biomarkers such as miRNA-146a and their role in IG diseases are mentioned.

Keywords: Biomarker; Gastrointestinal disorders; Inflammatory bowel diseases; miRNAs; Crohn's disease

Poster Presentation

1st International Congress of Biomarkers

PN: 1031

Comparison of Anti-Cancer Effects of Platinum Ribovirin and Ribovirin via Telomerase and Bcl-2 Genes Expression

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ABSTRACT

One of the most serious threats to human life is cancer, which has recently become the leading cause of death in many countries. Among the common treatments for cancer, chemotherapy, radiotherapy and surgery have been widely used. The use of effective anti-cancer drugs such as Ribovirin has played an important role in the treatment of cancer. One way to evaluate anticancer effects of drugs or new compounds determining of tumor markers expression such as telomerase and Bcl-2. Hence, this study aimed to evaluating of anti-cancer effects of the newly synthesized platinum compound Ribovirin (Pt-Rb) in comparison with Ribovirin (Rb) via telomerase and Bcl-2 genes expression. In this study cells were cultured and divided into four groups: groups A (HDF cells, human derived fibroblast cells) as healthy or control group and group B (HepG2 cells, hepatocyte G2 cells) were cancerous cells as negative untreated cancer group; groups C and D were HepG2 cancer cells that were treated with Ribovirin (Rb) (group C) and platinum-Ribovirin (Pt-Rb) (group D). After evaluating LC_{50} for the drugs by MTT test, the telomerase and Bcl-2 gene expression were evaluated using real-time PCR (RT-qPCR). The results showed a significant increase in telomerase and Bcl-2 genes expression in group B but there was significant decrease in telomerase and Bcl-2 in treated cancer groups i.e. (group C) and (group D), also there was significant difference between group B with group C and also between group B with group D ($p< 0.05$). In our study, there was significant difference in telomerase and Bcl-2 genes expression between group C and D ($p<0.05$), therefore due to more decreasing of tumor markers in group D (Pt-Rb), it was more anticancer effect than group C(Rb) on HepG2 cells. Our results indicated that Pt-Rb (group D) is more effective drugs in reducing anti-apoptotic factors i.e. telomerase and Bcl-2 on HepG2 cancer cells than Ribovirin (group C). Hence, it is possible to use this compound as anticancer drug, however, for its widespread use in the treatment of cancers such as carcinomas, more studies are required on animal model and finally on human subjects.

Keywords: Ribovirin (Rb); Platinum Ribovirin (Pt-Rb); Telomerase; Bcl-2

Poster Presentation

1st International Congress of Biomarkers

PN: 1034

Swimming Training Modulates Lung Injury Induced by Ovariectomy in Diabetic Rats: Involvement of inflammatory and Fibrotic Biomarkers

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ABSTRACT

In the present study, we evaluated the effects of swimming training on inflammatory and fibrotic biomarkers in the lung of ovariectomized diabetic rats. Forty female rats were randomly assigned into four groups (n=10 in each group): sham; rats underwent surgery without bilateral ovariectomy, OVX: rats that underwent bilateral ovariectomy, OVX.Dia: ovariectomized rats that were fed with high-fat diet, OVX.Dia.Exe: ovariectomized diabetic rats with 8 weeks of swimming training. At the end of experiment, lungs were harvested under anesthesia in all the groups and expression levels of transforming growth factor beta-1, interleukin-1 beta, matrix metalloproteinase-2, B-cell lymphoma 2, caspase3 and extracellular signal-regulated kinase were assessed with western blot. Also, lung sections were subjected to immunohistochemical and hematoxylin eosin staining. There was a significant difference in the protein expressions including TGFβ1, MMP2, IL1β, ERK 1/2, caspase 3, and Bcl-2 between exercise and ovariectomized diabetic groups ($p < .05$). Swimming training ameliorated expression levels of inflammatory and fibrotic biomarkers in the lung of ovariectomized diabetic rats. These data encourage further investigation into the inclusive effects of exercise in menopausal women with diabetes.

Key words: Ovariectomy; Diabetes; Inflammation; Fibrosis;Exercise

Poster Presentation

1st International Congress of Biomarkers

PN: 1035

Investigating the effect of BUN biomarker on non-invasive ventilation failure in covid-19 patients hospitalized in intensive care units

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ABSTRACT

Concerning the high Covid-19 prevalence and mortality among patients with acute respiratory distress syndrome (ARDS) and the overriding importance of using non-invasive ventilation (NIV), the disease treatment is presently a leading challenge, especially among ICU-admitted patients. This way, the present study was conducted to determine the effect of demographic information and clinical variables on the failure rate of non-invasive ventilation in ICU-admitted covid-19 patients. This is a retrospective cross-sectional study (2021) was conducted on 200 Iranian adult Covid-19 patients with acute respiratory failure (ARF) admitted to the ICU (Pao2 < 300 mmHg; PaCO2 < 45 mmHg) who undergo continuous positive airway pressure (CPAP) therapy. Patients' demographic and laboratory data were recorded and analyzed in SPSS-22 software using Mann-Whitney statistical tests, chi-square test (or Fisher's exact test), the significance level was considered as $p \leq 0.05$. The mean age of patients was 63.96 ± 16.23 years. Of all 200 patients, 157 (78.5%) experienced CPAP failure, and the remaining 43 (21.5%) underwent successful CPAP therapy. Among clinical variables such as hemoglobin, creatinine, sodium and potassium electrolytes and blood sugar, only BUN had a significant difference with CPAP failure rate. In other words elevated blood urea nitrogen (BUN) impacted NIV failure rates among patients. Ultimately, the mortality rate was significantly higher in patients with NIV failure. The elevated BUN favor elevated NIV failure rates among patients. The mortality rate is much higher in patients with NIV failure.

Keywords: BUN, biomarker, covid-19

Poster Presentation

1st International Congress of Biomarkers

PN: 1036

Composition, Biogenesis and Role of Exosomes in Tumor Development

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Abstract

The role of exosomes and their mechanism of action at the tumor site has received increasing attention. These microvesicles are produced by a wide range of cells including mesenchymal stem cells (MSCs) and immune cells. In particular, tumor cells release remarkable amounts of exosomes which spread to distant organs through the blood and enhance the possibility of tumor metastasis. In spite of results on tumor promoting properties, there are reports demonstrating the tumor inhibiting effects of exosomes depending on the type of the tumor and cell source. Considering the antitumor effects of exosomes and their capability of easily reaching the bulk of solid tumors, they can be engineered as potential drug delivery vehicles or cell free vaccines providing alternative strategies for exosome-based anticancer therapies. However, due to the dual role of exosomes more detailed studies on these mysterious bullets are undoubtedly needed. This review aims to have a comprehensive appraisal on the biogenesis, composition and isolation of exosomes, and then highlights the current knowledge of their role in cancer progression or inhibition by special focusing on MSC's exosomes (MSC-EXOs).

Keywords: Mesenchymal stem cell; Microvesicles; Exosomes; Cancer progression; Metastasis

Poster Presentation

1st International Congress of Biomarkers

PN: 1038

Evaluation of serum levels of MicroRNA-146a, IL-18 and RANKL genes expression in severe and mild phases of patients with COVID-19

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ABSTRACT

The microRNAs and inflammatory factors play an important role in the level of inflammation in patient with COVID-19. Therefore, in our study, to evaluate the serum level of miR-146a expression in patients with SARS-CoV-2 and investigated their association with the expression of interleukin-18 (IL-18) and receptor activator of nuclear factor kappa-B ligand (RANKL) genes and its relationship with lung damage have been investigated. In this study, the population of patients with covid-19 disease were classified into two groups: mild phase (positive PCR and no symptoms) and severe phase (positive PCR with acute pulmonary symptoms and inflammation). Then, demographic, clinical and paraclinical characteristics of individuals were collected based on a pre-prepared checklist. To evaluate the gene expression, RNA total was isolated from all samples according to the Trizol kit protocol. Then, the extracted product was changed to cDNA then evaluated by real-time PCR technique for the expression of mir-146a and the expression of target genes including IL-18 and RANKL. The mean expression of mir-146a gene in mild and severe patients was 0.73± 0.3 and 1.89 ± 0.52 respectively, which was statistically significant between the two groups. Also, the mean expression of IL-18 gene, which was 1.37 ± 0.38 and 2.83 ± 0.58 in the mild and severe groups of the disease, respectively, showed a significant difference between the two groups. While the expression levels of RANKL gene did not show a significant difference between the two groups. This study showed that the expression levels of target genes, especially IL-18, in patients with severe inflammation were significantly different from those with mild inflammation. And perhaps one of the reasons for this change is the role of microRNAs (mir146a) in regulating gene expression.

Key words: COVID-19, mir-146a, respiratory disease, IL-18, RANKL.

Poster Presentation

1st International Congress of Biomarkers

PN: 1039

Long Non-coding RNAs (lncRNAs); Roles in tumorigenesis and potentials as biomarkers in cancer diagnosis

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ABSTRACT

New research has indicated that long non-coding RNAs (lncRNAs) play critical roles in a broad range of biological processes, including the pathogenesis of many complex human diseases, including cancer. The detailed regulation mechanisms of many lncRNAs in cancer initiation and progression have yet to be discovered, even though a few of lncRNAs' functions in cancer have been characterized. In the present study, we summarize recent advances in the mechanisms and functions of lncRNAs in cancer. We focused on the roles of newly-identified lncRNAs as oncogenes and tumor suppressors, as well as the potential pathways these molecules could play. The paper also discusses their potential uses as biomarkers for the diagnosis and prognosis of cancer.

Keywords: long non-coding RNA; Cancer; Biomarker

Poster Presentation

1st International Congress of Biomarkers

PN: 1040

Inhibition of Telomerase and Mitochondria are biomarkers for the treatment of Triple Negative Breast Cancer

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ABSTRACT

Triple Negative Breast Cancer (TNBC) is as the most invasive breast cancer. TNBC exhibits the properties of cancer stem cells (CSCs) and is resistant to conventional treatment. High telomerase activity and high mitochondrial biogenesis are involved in tumorigenesis of TNBC. Telomerase, especially hTERT subunit, displays several oncogenic functions such as the effect on mitochondria function, gene expression, and apoptosis except telomere protection. Therefore, we assessed the effect of telomerase and mitochondria inhibition on apoptosis and DNMT3a (DNA methyltransferases 3A) and TET2(Ten-eleven translocation proteins) expression in TNBC. MDA-MB-231 and MDA-MB-468 cells were treated with IC50 levels of BIBR1532, Tigcycline, and a combination of them. Then, telomere length, and the expression of DNMT3a, TET2, and hTERT were studied. Finally, apoptosis rate, apoptosis-related proteins, and genes were analyzed. The present results showed that IC50 level of telomerase and mitochondria inhibition induced apoptosis but had no significant effect on telomere length. Data also proposed that telomerase inhibition induced extrinsic apoptosis in MDA-MB-231 while, causing intrinsic apoptosis in MDA-MB-468 cells. Furthermore, it was found that the expression of p53 decreased following telomerase and mitochondria inhibition and was ineffective in the apoptosis of cells. The expressions of DNMT3a and TET2 were increased in cells flowing treatment with IC50 level of telomerase and mitochondria inhibition. In addition, combination treatment was better than BIBR1532 and Tigcycline alone. In conclusion, the inhibition of telomerase and mitochondria caused intrinsic and extrinsic apoptosis and increased DNMT3a and TET2 expression.

Keywords: Telomerase, Mitochondria, biomarkers, Breast Cancer

Poster Presentation

1st International Congress of Biomarkers

PN: 1041

Approaches to isolate nano scaled exosomes as biomarkers for cancer: A systematic review

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ABSTRACT

Exosomes are Nano-sized macrovesicles that are released by many types of cells, including cancer cells. They contain miRNA, mRNA, and proteins. They can be found in serum, saliva, and semen, where they provide diagnostic value for detecting a wide range of diseases, including cancer. Thus, they could be a promising source of cancer biomarkers for liquid biopsy. Therefore, exosomes could provide a better alternative to current cancer detection methods. This article reviews different methods to isolate exosomes as biomarkers, these approaches include: electrochemical Nano sensors, Affibody Functionalized Beads, Gold Nano islands, cell ELISA based method, Nano pom-poms prepared exosomes, Microfluidic-Based Exosome Isolation and Nano-plasmatic. A search on PubMed and Google scholar databases was performed. The strategy for literature search was represented by "((cancer and exosome) or (biomarker and exosome) and (exosome and nano)" on Pubmed.gov and "nano exosome biomarkers" on Google scholar. Inclusion and exclusion criteria a year publication filter was applied for 2010–2022 interval of time. The studies selected from both databases were original articles only. Reviews and meta-analyses were excluded. Duplicated papers were also removed. Further analysis of the abstract and full text was conducted. The original articles which did not focus on our topic were excluded. Our search yielded 181 articles that were published in the years from 2010 to 2022. Forty abstracts did not meet our inclusion criteria, hence were excluded, On the whole we included 141 abstracts. Exosomes have been shown to be a promising non-invasive diagnostic component, however, effective techniques for isolating and characterization of exosomes are lacking. Hence, further research is necessary for this area.

Keywords: exosome; nano; cancer; biomarker

Poster Presentation

1st International Congress of Biomarkers

PN: 1042

Biomarkers of oropharyngeal microbiota and their relevance to COVID-19 patients

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ABSTRACT

A global COVID-19 pandemic has never been seen before, at least not by our generation. The majority of those infected with the virus will suffer from mild to moderate respiratory illness and recover without special treatment. People who are older or who suffer from underlying diseases such as cardiovascular disease, diabetes, chronic lung disease, or cancer are more likely to contract serious illnesses. At any age, anyone can contract COVID-19 and become gravely ill or die. While researchers' search for viable vaccines or medication therapies continues, nutritional strategies to boost SARS-CoV-2 immunity are being explored. Certain fermented foods and probiotics may include viable microorganisms that can boost gut immunity and lung immunity to reduce intestinal inflammation and boost mucosal immunity. We were discovered by sequencing swab specimens taken from the oropharynx of 24 patients with COVID-19, 30 patients with influenza B, and 25 healthy controls. Veillonella was shown to be the most prevalent biomarker for the COVID-19 group. The possible natural reservoir for pathogens that cause co-infections in the lungs of COVID-19 patients because a variety of species within the genus Veillonella, in particular Veillonella parvula, a substance of the typical human oral, gastrointestinal, and vaginal flora whenever separated from clinical samples. V. parvula, which is commonly considered to be prevalent in the oropharynx of our COVID-19 patients, was also overrepresented in the BALF of these patients. Besides this, we discovered that elevated systemic inflammation markers (neutrophil-lymphocyte ratio, NLR) and a rise in the percentage of Klebsiella pneumonia, Acinetobacter sp., and Serratia sp. were correlated with the severity of the disease, indicating that these changes in the microbiota of the oropharynx may have an impact on the severity of COVID-19 by influencing the inflammatory response. In the end, we found that the severity of COVID-19 was linked to changes in the oropharyngeal microbiota and functional abnormalities.

Keywords: orpharyngeal, microbiota, COVID-19, Veillonella, Klebsiella pneumonia

Poster Presentation

1st International Congress of Biomarkers

PN: 1043

Furin as a potential biomarker in SARS-CoV-2 infection in patients with Pre-existing cardiometabolic diseases

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ABSTRACT

SARS-CoV-2 entry requires cleavage of the spike glycoprotein at the S1/S2 and the S2′ cleavage sites to mediate membrane fusion. The furin cleavage site is an important determinant of SARS-CoV-2 transmission. The mean furin, presepsin, and IL-6 levels were significantly higher in the peripheral blood of SARS-CoV-2 compared to the controls. PubMed databases were screened using the following search terms: ("furin") AND (“biomarkers”). Furin is one of the biomarkers of myocarditis, destroyed lung tissue, and fatal multi-organ failure, which may be responsible for the cytokine storm caused by excessive immunological activity in some patients. In coronary artery disease SARS-CoV-2^{positive} patients, high furin plasma levels are a crucial biomarker for poor clinical prognosis. Also, the plasma levels of furin released from activated platelets are a pivotal prognostic biomarker for the progression of respiratory failure. A preexisting cardiovascular disease is linked to morbidity and mortality in patients with Covid-19, whereas Covid-19 itself can also provoke myocardial injury, arrhythmia, acute coronary syndrome, perimyocarditis, and venous thromboembolism. A study reported that humans with diabetes, hypercholesterolemia, and obesity have higher levels of furin, which is associated with an increased risk of Covid-19 complications and mortality in such diseases. According to the investigation, furin is one of the valuable biomarkers to evaluate the severity of the disease, the degree of inflammation, and the effectiveness of treatment. In summary, furin, IL-6, and presepsin are thought to play an important role in the exacerbation of SARS-CoV-2, and elevated serum furin levels in infected individuals are thought to predict poor outcomes in COVID-19 patients. Furthermore, the present study suggests that furin can be used as a predictor biomarker of disease severity in patients with Covid-19, and inhibition of furin, may be one of the potential treatment options in combating SARS-CoV-2 infection and preventing inflammation.

Keywords*:* Furin; Biomarker; Covid-19

Poster Presentation

1st International Congress of Biomarkers

PN: 1045

Understanding the Molecular Mechanisms of MiR-1236 to Identify a Novel Diagnostic Biomarker for Cancer

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ABSTRACT

MicroRNAs (miRs) are small non-coding RNAs that regulate gene expression at the post-transcriptional level. Mounting evidence suggests the involvement of miRs in tumorigenesis and the progression of cancers. Among the miRs, miR-1236 has been extensively studied in various cancers. It has been reported that miR-1236 is frequently down-regulated and functions mainly as a tumor suppressor in various human cancers. MiR-1236 has diverse target genes when it acts in tumor such as ZEB, MTA2, KLF8 (Krüppel-like transcription factor 8), p21, TPT1 (translationally controlled tumor protein), alpha-fetoprotein (AFP), and HOXB7 (homeobox B7), etc. MiR-1236 also affected abundant and complicated signal pathways, including phosphatidylinositol 3-kinase (PI3K)/AKT signal pathway and Wnt/β-catenin signaling, etc. Consistently, it has been demonstrated that miR-1236 played a key role in tumor cell proliferation, apoptosis, invasion and metastasis, as well as cancer diagnosis, and prognosis. MiR-1236 also modulates the epithelial-mesenchymal transition (EMT) process and cancer metastasis. Several reports have found that miR-1236 expression is also decreased in drug-resistant tumor cells. Additionally, miR-1236 itself is regulated by several factors. We review the biological functions of miR-1236 with the corresponding molecular mechanisms in tumorigenesis. We believe that miR-1236 may serve as a novel diagnostic biomarker and therapeutic target for cancer.

Keywords: MiR-1236, cancer biomarker, metastasis, tumorigenesis.

Poster Presentation

1st International Congress of Biomarkers

PN: 1046

Molecular mechanisms of miR-1236 in the assessment of tumor lymphangiogenesis in human ovarian cancer patients

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ABSTRACT

Tumor lymphangiogenesis is a critical component in the progression of cancers and microRNAs have been reported to be implicated in this process. Recent studies revealed the involvement of miR-1236 in the lymphangiogenic signaling by targeting vascular endothelial growth factor receptor 3 (VEGFR3). However, the importance of miR-1236 and its clinical relevance for lymphangiogenesis in ovarian cancer (OC) remains unclear. A total of 52 samples of ovarian tumors and 28 normal ovarian tissues were evaluated in this study. Expression of VEGFR3, VEGF-C, LYVE-1 and PROX1 as well as miR-1236 were assessed by Real-time PCR. VEGFR3 protein expression was investigated by immunohistochemistry. Immunohistochemistry for podoplanin marker was performed to evaluate lymphatic vessel density (LVD). We found that miR-1236 expression was decreased in ovarian tumors and correlated with clinical stage, lymph node metastasis, distant metastasis, and patient survival. Moreover, in ovarian tumors, LVD as well as gene expression of VEGFR3, VEGF-C, and LYVE-1, but not PROX1, were found to be remarkably higher compared to control tissues. We also detected a more robust positive staining for VEGFR3 in ovarian tumors than in control tissues. Furthermore, our results demonstrated an inverse association between miR-1236 with LVD, VEGFR3, LYVE-1, and PROX1 expression in ovarian tumors. Survival analysis verified a lowered overall survival rate in patients with low miR-1236 expression than in those with high expression. Our results provide evidence for translational involvement of miR-1236 in the lymphangiogenesis of OC by regulating lymphangiogenesis-related factors and support the clinical importance of miR-1236 as a new biomarker for OC.

Keywords*:* MiR-1236; lymphangiogenesis; VEGFR3;VEGF-C; ovarian cancer

Poster Presentation

1st International Congress of Biomarkers

PN: 1048

LncRNA-SAMMSON; A Novel Biomarker and Potential Therapeutic Target for cancer diseases: A Literature review

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ABSTRACT

Information over the past decade demonstrates that long non-coding RNAs (lncRNAs) are greatly expressed and have crucial functions in gene regulation. LncRNAs are a novel class of RNA transcripts with longer than 200 nucleotides. SAMMSON (Survival associated mitochondrial melanoma-specific oncogenic non-coding RNA) had been identified by Leucci et al in 2016 as a lncRNA with a critical function in melanoma cancers. Its gene is located on chromosome 3p13–3p14 and is recognized to perform as an oncogene in several malignancies. It has been first specified to be overexpressed in the vast majority (>90%) of melanomas, but not in normal adult tissues, which demonstrates SAMMSON as an attractive diagnostic biomarker for melanoma cancers. Nowadays, it has been realized that SAMMSON is overexpressed in other cancers including gastric, liver, breast, brain, and other cancers too. LncRNA SAMMSON gene is consistently co-gained with MITF (melanocyte-inducing transcription factor). Moreover, SAMMSON interacts with several other enzymes, genes, protein complexes, and signaling pathways such as mitochondrial homeostasis. The SAMMSON knockdown can significantly decrease cancer cell proliferation and metastasis. Another valuable application of SAMMSON is to distinguish cancers from similar diseases like diffuse neurosarcoidosis. In this literature review, we aim to clarify the roles of SAMMSON, its relative molecular pathways, and its functions in various cancers. We also introduce SAMMSON as a novel biomarker and potential therapeutic target in cancer therapy. However, there is still no drug targeting SAMMSON or its involved pathways but it seems hopeful to investigate.

Keywords*:* SAMMSON; LncRNA; Cancers; Metastasis

Poster Presentation

1st International Congress of Biomarkers

PN: 1049

Evaluation of the Predictive Value of Neutrophil to Lymphocyte and Platelet to Lymphocyte Ratio in Predicting Immune Thrombocytopenic Purpura (ITP)

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ABSTRACT

Immune thrombocytopenic purpura (ITP) is an autoimmune disease marked by a low platelet count and an increased risk of bleeding. Inflammation is one of ITP's aggravating elements due to inflammatory cells' function. This study aims to assess the predictive value of inflammatory and hematological indices, including neutrophil-to-lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), and hemoglobin-to-platelet ratio (Hb/Plt ratio) in predicting ITP. We retrospectively analyzed the profile of 190 patients with confirmed ITP diagnoses along with 100 healthy individuals who had no ITP-related clinical or laboratory symptoms. NLR, PLR, and Hb/Plt were calculated using the complete blood count at the time of diagnosis. The sensitivity and specificity of each parameter were assessed by the Receiver operating characteristic (ROC) curve. The results were analyzed through XLSTAT and SPSS software, and the P-Value of < 0.05 was considered statistically significant. Immune Cell count, NLR, PLR, and Hb/Plt ratio in ITP patients significantly differed from the control group. ITP patients were associated with increased NLR (P-Value: 0.002) and Hb/Plt ratio (P-Value: 0.01) indices and decreased PLR (P-Value: 0.03). Besides, the length of patients' hospitalization was significantly correlated to increased NLR (P-Value: 0.00, 95% CI: 0.81–1.12) and inversely related to PLR (P-Value: 0.01, 95% CI: 0.07-0.92). The sensitivity and specificity of NLR as the predictive marker were 69.9% and 51.3%; these two criteria for PLR were 58.8% and 57.5%, respectively. ITP patients indicated higher NLR, Hb/Plt ratio, and lower PLR at the diagnosis time than healthy individuals. The incremental course of patients' hospitalization was related to increased NLR and inversely associated with decreased PLR. Both NLR and PLR had acceptable sensitivity and specificity for predictive value in predicting ITP.

Keywords: Immune thrombocytopenic patients; Neutrophil; Lymphocyte; Platelet; Neutrophil lymphocyte ratio; Platelet lymphocyte ratio.

Poster Presentation

1st International Congress of Biomarkers

PN: 1050

Biochemical responses as early and reliable biomarkers of organophosphate and carbamate pesticides intoxication: a systematic literature review

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ABSTRACT

Inhibition of cholinesterase (ChE) activity has been long considered as the main diagnostic method of organophosphate (OP) and carbamate pesticides poisoning; however, it has been shown that ChE activity may also be altered due to exposure to other non-organophosphorus toxicants and variety of different medical conditions. Hence, to avoid misdiagnosis, we aimed to systematically review available documents to look for additional biomarkers of OP and carbamate poisoning.

The electronic databases in addition to Google scholar were searched for eligible articles on March 2022 using “organophosphate”, “carbamate”, and “biomarker” including all their similar terms. After collecting the relevant documents, the data were extracted and described qualitatively.

In total, data of 67 articles from 52 human and 15 animal studies were extracted. Findings demonstrated that enzymes such as β-glucuronidase, neuropathy target esterase, amylase, and lipase, in addition to hematological indicators such as CBC, CRP, LDH and CPK have higher sensitivity and accuracy in the diagnosis of OP poisoning.

Findings suggest that using various markers for diagnosis of OP intoxication is helpful for appropriate management, and early identifying the patients at risk of death. The suggested biomarkers also help to avoid misdiagnosis of OP poisoning with other similar conditions.

Keywords: Biochemical marker; Biomarker; Diagnosis; Organophosphate; Carbamate; Poisoning

Poster Presentation

1st International Congress of Biomarkers

PN: 1052

Diagnostic salivary biomarkers in oral cancer: A review

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ABSTRACT

Oral cancer is usually diagnosed at advanced clinical stages due to its asymptomatic nature and absence of symptoms in early phases. One of the major causes of failure in oral cancer treatment and its poor prognosis is delayed diagnosis. Salivary cytokines are noninvasive diagnostic tools, which have been studied as potential diagnostic biomarkers for early diagnosis of oral cancer and oral potentially malignant disorders. Electronic literature search was conducted in Scopus, Medline, Embase and Web of Science databases using the terms “oral cancer”, “oral leukoplakia”, “oral potentially malignant disorders”, “saliva”, “cytokine”, and “interleukin” until January 2022. The articles were screened by two independent reviewers and data were extracted. A total of 233 articles were screened and 37 articles were included in the study. Interleukin (IL) 1β, IL6, and IL8 were significantly higher among patients with oral cancer compared to healthy controls. Patients with oral potentially malignant disorders, in comparison with healthy controls, showed significantly higher salivary levels of IL-6 and TNF-α. It seems some salivary cytokines increase in patients with oral cancer and oral potentially malignant disorders. Therefore, using salivary biomarkers along with other techniques could be used as a screening tool to improve the early detection of these conditions. More clinical studies are needed to reach a standard range for salivary biomarkers.

Keywords*:* Oral cancer; Oral potentially malignant disorders; Salivary biomarkers

Poster Presentation

1st International Congress of Biomarkers

PN: 1054

Boosting the cytotoxic effects of radiation by copper sulphide nanoparticles in cancer radiation therapy

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ABSTRACT

One of the greatest challenges in radiation therapy (RT) is the side effects of high doses due to considerations of adjacent healthy tissue radiation tolerance. In addition, radio-resistance of cancer cells is a major issue in radiation therapy. Consequently, it would be significantly important to develop new approaches to enhance the treatment efficacy. Here, we examined the potential of Fe_3O_4@Cus-PEG nanoparticles as a radiosensitizer agent. nanoparticles were synthesized and characterized for hydrodynamic diameter, morphology, and X-ray diffraction. MTT assay was used to evaluate the cytotoxicity of nanoparticles on colorectal cancer cell lines. To evaluating the in vitro radio-sensitization effects of the synthesized nanoparticles, colorectal cancer cells were treated with ionizing radiation and nanoparticles. The cytotoxic effects of different treatments were assessed by the MTT assay, reactive oxygen species analysis, and quantitative real-time PCR (q-RT PCR) assay. Our in vitro assays demonstrated that the intracellular hydrogen peroxide concentration and the expression level of Bax and Caspase-3 genes significantly increased in the cells treated with the combination of nanoparticles and radiation. Whereas, the expression level of the Bcl-2 gene in the combined treatment significantly decreased compared to the radiation alone. The combination index (CI) values for the combined treatments of nanoparticles and X-ray radiation at doses of 2, 4, and 6Gy were equal to 0.88 ± 0.03, 0.73 ± 0.3, and 0.67 ± 0.02, respectively. This study suggests that Fe_3O_4@Cus-PEG nanoparticles can be used as a promising nano radio-sensitizing agent

Keywords: Colorectal cancer; Radiosensitizer; Ionizing radiation; Copper; Magnetite nanoparticles

Poster Presentation

1st International Congress of Biomarkers

PN: 1057

Selenium and Copper as Biomarker of inflammation and immune response in SARS-CoV-2-infected patients

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ABSTRACT

It is widely established that trace elements such as copper (Cu) and selenium (Se) are related to the strong immune response to diseases. Cu and Se also perform as positive and negative acute phase reactants, respectively, in infectious conditions. The purpose of this study was to investigate the relationship between Cu and Se serum levels and symptoms and the IgG immunological response to SARS-CoV-2 infection. 130 SARS-CoV-2 patients with mild to severe clinical symptoms had blood samples and nasopharyngeal swabs taken. RT-PCR and anti-SARS-CoV-2 IgG were used to validate the SARS-CoV-2 infection and immunological response to the virus. The Cu and Se serum levels were examined by using colorimetric assay and atomic absorption spectrophotometry methods, respectively. Next data analyzed and a P-value lower than 0.05 was deemed statistically significant. The results indicated that the mean Cu was higher in IgG responders (112 ± 10 μg/dL, P-value < 0.05) and individuals with severe symptoms (110 ± 12 μg/dL, P-value < 0.05). In other hand, the mean Se levels were higher in IgG non-responders (111 ± 4 μg/L, P-value < 0.05) and individuals with mild symptoms (109 ± 6 μg/L, P-value < 0.05). Our data indicate that Se and Cu serum levels could serve as biomarkers for inflammation and immune response in SARS-CoV-2-infected patients. Such that immune responder patients showed severe symptoms with high and low serum levels of Cu and Se, respectively.

Keywords: Selenium; Copper; COVID-19; IgG; SARS-CoV-2 immune response

Poster Presentation

1st International Congress of Biomarkers

PN: 1058

Impacts of Mediterranean diet on severity of disease and Total Antioxidant Capacity (TAC) of serum in patients with Parkinson's disease

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ABSTRACT

Parkinson's disease (PD) as one of the most common neurodegenerative disorders may be affected by healthy dietary patterns. The aim of this study was to investigate the effects of the Mediterranean Diet (MeD) on serum Total Antioxidant Capacity (TAC) and disease severity in PD patients.In this single-center randomized clinical trial, patients with idiopathic PD ($n = 80$) were selected randomly allocated to either MeD or control group (Iranian traditional diet); an individualized dietary plan based on the MeD was designed. Serum TAC and the motor & non-motor disease aspects using the Unified Parkinson's Disease Rating Scale (UPDRS) were evaluated in two groups. Statistical Analysis of data was performed using SPSS. 70 PD patients with a mean age of 58.96 ± 8.7 and UDPRS of 41.66 ± 20.19 were analyzed in this study. MeD significantly increased serum TAC ($P < 0.001$). UPDRS score was also lowered in MeD group ($P < 0.05$). Mediterranean diet seems to have some benefits in PD. as well, TAC levels may also be affected by MeD. However, further studies are needed to confirm the mentioned outcomes.

Keywords: Mediterranean diet; Nutrition; Parkinson's disease; Antioxidant; TAC

Poster Presentation

1st International Congress of Biomarkers

PN: 1060

A comparative study of long interspersed element-1 protein immunoreactivity in cutaneous malignancies

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ABSTRACT

Skin cancer is the most common cancer worldwide and commonly classified into malignant melanoma (MM) and Nonmelanoma skin cancers (NMSCs), which mainly include basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). The extent to which Long Interspersed Element-1 (LINE-1, L1) ORF1p is expressed in cutaneous malignancies remains to be evaluated. This study aimed to assess LINE-1 ORF1p immunoreactivity in various skin cancer subtypes. The expression level of LINE-1 ORF1p was evaluated in 95 skin cancer specimens comprising 36 (37.9%) BCC, 28 (29.5%) SCC, and 31 (32.6%) melanoma using the tissue microarray (TMA) technique. Then the association between expression of LINE-1 encoded protein and clinicopathological parameters was analyzed. We showed that LINE-1 ORF1p expression level was substantially higher in BCC and SCC patients compared with melanoma samples ($p < 0.001$). BCC cases had a higher LINE-1 histochemical score (H-score) compared with SCC cases ($p = 0.004$). In SCC samples, a lower level of LINE-1 ORF1p expression was associated with age younger than the mean ($p = 0.041$). At the same time, no significant correlation was found between LINE-1 ORF1p expression and other clinicopathological parameters (all $p > 0.05$). According to our observation, LINE-1 ORF1p immunoreactivity in various skin tumor subtypes extends previous studies of LINE-1 expression in different cancers. LINE-1ORF1p overexpression in NMSCs compared with MM can be considered with caution as a tumor-specific antigen for NMSCs.

Keywords: Skin neoplasms; Retroelements; LINE-1 ORF1p; Tissue microarray; Biomarker

Poster Presentation

1st International Congress of Biomarkers

PN: 1061

A new approach to the preeclampsia puzzle; MicroRNA-326 in CD4+ lymphocytes might be as a potential suspect

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ABSTRACT

Alongside many complications in understanding the etiology of Preeclampsia (PE), several determinants, such as the imbalanced proportion of anti-angiogenic/proangiogenic T-cell subsets, especially CD4+ (Th17/Treg), as well as alterations in the expression profile of related cytokines, miRNAs, and transcription factors might have been implicated in PE pathogenesis. After sample collection and preparation, CD4+ cells were isolated from PE and non-PE pregnant woman and were cultured. Furthermore, analysis such as flow cytometry, real-time PCR, western blotting, and ELISA were performed to assess determinants related to PE manifestation, including sFlt-1, sEng, STAT-3, RORγt, SMAD-7, Foxp3, IL-17, IL-22, Ets-1, and miRNA-326. Our results showed that the miRNA-326 expression level increased in CD4+ Cells and Th17 in PE patients which downregulated Ets-1 expression that acts as a negative control for Th17 development. Furthermore, we showed that the number and expression level of Th17 s and transcription factor RORγt escalated, respectively. While Treg and its related transcription factor (Foxp3) demonstrated a decrease. Flow cytometry analysis illustrated that the Th17/Treg ratio increased in PE. Additionally, we demonstrated that expression, concentration levels of cytokines (IL-17 and IL22), and anti-angiogenic molecules (sEng and sFlt-1) soared in isolated CD4+ cells from PE patients, which could be correlated with PE pathogenicity. In conclusion, we comprehensively evaluated immunological factors and molecules involved in PE manifestation. Interestingly, the CD4+ T-cell subset could be an extra source of antiangiogenic factors for the maintenance of this hypertension disorder.

Keywords: Preeclampsia; miRNA-326; sFlt-1; sEng

Poster Presentation

1st International Congress of Biomarkers

PN: 1062

Recent advancements in biosensor designs toward detection of intestine cancer miRNA biomarkers

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ABSTRACT

Cancer diagnosis and treatment have been of broad interest among scientists in the last decades due to the high death rate, widespread occurrence, and recurrence after treatment. The survival rate of cancer patients depends greatly on early detection and appropriate treatments. Therefore developing new technologies applicable for sensitive and specific methods toward cancer detection is an inevitable task for cancer researchers. Abnormal miRNA expression is contributed to severe diseases such as cancers and ince their expression level and type differ strictly during carcinogenesis and later metastasis and treatments, the improved detection accuracy of these miRNAs would undoubtedly lead to early diagnosis, prognosis, and targeted therapy. Considering the relation between the expression profile of specific miRNAs and the early diagnosis and treatment of cancers, the improved detection accuracy of miRNAs would lead to unprecedented progress in early treatment. However, the number of researches which mainly targets improving detection specificity remains rare. Many researchers are trying to focus on applying biosensors to tests, disease screening, and non-invasive diagnostics. Since the miRNAs have been demonstrated as potential biomarkers for cancer diagnosis, prognosis, and therapeutic targets, they are gradually outstretched as an important research area. Despite numerous achievements that have been reported for miRNA detection, some essential issues are remaining which should be addressed toward the biosensor applications in the field of cancer diagnosis and treatment. Therefore, more efforts should be paid in the future for the construction of reproducible and reliable sensing platforms and also the field of miRNA biosensors should focus on the detection of these biomarkers in body fluids especially in a circular system due to its non-invasive nature. In this review, we will provide the recent developments in biosensors to detect intestine cancer miRNA biomarkers and also discuss the challenges and outcomings of this field.

Keywords: miRNA; Intestine Cancer; Biosensors; Early detection; Nanomaterials

Poster Presentation

1st International Congress of Biomarkers

PN: 1064

Designing efficient methods to detect amyotrophic lateral sclerosis disease based on CSF and blood biomarkers

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ABSTRACT

Amyotrophic lateral sclerosis (ALS) is known as a fatal and mostly sporadic neurodegeneration disease involving upper and lower motor neurons, including cortical, bulbar, and spinal motor neurons. Due to the lack of knowledge about potential biomarkers in this disease and its rarity, today's diagnoses are based on ruling out other diseases, neurography, and electromyography examination, which takes a time-consuming procedure to finally detect. The search strategy for conducting this research was based on the PRISMA guideline with the search query of ((amyotrophic lateral sclerosis [Title/Abstract] AND biomarkers [Title/Abstract]) AND (CSF[Title/Abstract] OR blood [Title/Abstract])) implementing in Two databases including PubMed and Elsevier. The inclusion criteria were: high-impact articles, peer review journals, and relevant subjects in regard to our work. Random-effects models were used to determine the pooled effect sizes. ALS disease is classified into familial and sporadic types. In both, TAR DNA-binding protein 43 (TDP-43), phosphorylated-TDP-43 (pTDP-43), RNA-binding Protein Fused in Sarcoma (FUS), and C9ORF72 are presented. Other biomarkers mainly existed in sporadic types. Neurofilament light (Nfl) and neurofilament heavy chain (NfH) are upregulated in serum and plasma of ALS patients, and studies suggested 60-80 validity for ALS diagnoses, nevertheless, the amount of Nfl soar in multiple neurodegeneration diseases with axonal damage. Likewise, Progranulin (PGRN), as an ALS biomarker, is also detected in Frontotemporal disorders and Alzheimer's disease. Finally, Milk fat globule-EGF factor 8 (MFG-E8) and extracellular vesicles containing ALS-related proteins as novel ALS biomarkers, highlighted new methods for efficient diagnosis.Based on the results, each biomarker alone is insufficient to diagnose ALS. CNS-derived exosomes contain multiple ALS-related biomarkers (SOD1, TDP-43, pTDP-43, and FUS) that are detectable in cerebrospinal fluid (CSF), blood, and even urine. Exosome detecting kits listed as exoEasy, ExoQuick, Exo-spin, ME kit, ExoQuick Plus, and Exo-Flow, are useful to reach this purpose.

Keywords: Amyotrophic lateral sclerosis; Diagnosis; Biomarkers; extracellular vesicles; Neurodegenerative disease

Poster Presentation

1st International Congress of Biomarkers

PN: 1067

The human mitochondrial cytochrome b (MTCYB) gene as a biomarker for the tracking of human umbilical cord Mesenchymal Stem Cells in the ovaries of the cyclophosphamide-induced premature ovarian failure mice model

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ABSTRACT

Mesenchymal stem cells (MSCs) can be used to decrease degenerative changes in premature ovarian failure (POF). The tracking of MSCs homed to target tissues is a significant challenge in animal models of degenerative diseases. A variety of techniques have been employed to detect MSCs in the target tissue, most notably the use of fluorescent dyes and particularly MSC-related genes. In the current study, human mitochondrial cytochrome b (MTCYB) and CM-DiI, a florescent dye, were employed as markers indicating the presence of human umbilical cord Mesenchymal Stem Cells (hUCV-MSC) in the POF mouse ovary. Mature mice were divided into three groups (10 mice in each group), 1. The control (Ctrl) group 2. The CTX group was injected IP with cyclophosphamide (CTX). 3. The CTX-MSC group, after receiving CTX, was injected with a single dose of hUCV-MSCs labeled with CM-DiI intravenously (IV). Seven days later, after killing mice, ovaries were removed for HE staining and immunohistochemical studies using the TUNEL assay. A quantitative real-time PCR was performed to detect the hMTCYB gene in the ovarian tissues of the mice.

Our studies showed CTX caused degenerative exchanges and follicular loss in the ovary. The number of follicles in the CTX-MSC group was significantly higher compared to the CTX group. The apoptotic index was decreased in the CTX-MSC group compared to the CTX group. Moreover, the expression of the hMTCYB gene indicated the presence of hUCV-MSCs in the CTX+MSC group but not in both the Ctrl and CTX groups. CM-Dil labeled MSCs were observed in the CTX+MSC groups, indicating MSC presence in this group. Our experiment offers a strategy for using the hMTCYB gene as an appropriate biomarker for detecting human-derived MSCs administered to an animal model of degenerative diseases.

Keywords: Human umbilical cord mesenchymal stem cell; Tracking; Premature ovarian failure; Biomarker

Poster Presentation

1st International Congress of Biomarkers

PN: 1069

The role of biomarkers in brain death diagnosis, A narrative review

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ABSTRACT

Brain death donors are one of the most important sources of organ supply for transplantation. In spite of many innovations in the methods of providing organs, the need for transplanted organs has not been completely resolved and many people who are on the waiting list to receive organs die due to the lack of suitable organs. Despite many advances in imaging and examinations, it is not possible to predict brain death definitively and correctly after conditions that damage the brain such as trauma and asphyxia. As a result, if we can predict the probability of definite brain death after brain injury, we can save organs for transplantation. Because the sooner and more accurately brain death is diagnosed, the more number and quality of organs will be taken with more care to preserve the organs. To identify possible biomarkers to assess brain death, a comprehensive search strategy using PubMed, Scopus, and Google scholar was performed including brain death and biomarker as keywords. Many biomarkers and inflammatory factors rise in brain death vs nonbrain dead patients such as G-CSF, interferon-γ, IL-1ra, IL-4,6,7,8,10, IP-10, MCP-1, macrophage inflammatory protein -1β, platelet derived growth factor, T cell-related, and tumor necrosis factors and so on. To evaluate the prognosis of a brain injury some biomarkers are considered in the different biological materials as CSF (alpha 1-anti chymotrypsin, levels of nucleoside (GDP), Tau protein and so on); blood (Glial fibrillary acidic protein, NSE, GFAP, NF-H, secretagogin and Hsp70, ischemia-modified albumin, the ratio of NSE, S100B to hK6 and also PGDS); urine and saliva; (microtubule associated protein tau). Also, combined biomarkers with vital signs (Rapid spikes or drops in the total power of the heart rate variability, accompanied by a cortisol surge, as well as an alternating surge of high- and low-frequency domain variables were detected in the process of brain death) but the specific relationship of just a few biomarkers with brain death has been investigated yet such as S100B protein and Red Cell Distribution Width. Biomarkers could be used to predict brain injury trends and brain death situations. There are several promising candidate biomarkers in different biological materials, but none yet meets criteria for routine clinical use.

Keywords: Brain death; Biomarkers; Diagnosis; Organ donation

Poster Presentation

1st International Congress of Biomarkers

PN: 1071

Effects of Co-exposure to Lead and Noise on the Level of Malondialdehyde (MDA) among Printing Industry Workers (case study)

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ABSTRACT

Printing industry workers are exposed to noise of industrial printing machines and lead, as an essential material in pigment particles. Although each of these has its own effects on workers' health, their combined effects will be different. So, this study aimed to investigate the effects of simultaneous exposure to lead and noise on the level of Malondialdehyde (MDA) among printing industry workers.

In this study, we surveyed 80 employees of a printing house. Noise measurement was performed according to ISO9612:2009 method using TENMARS ELECTRONICS sound-meter. MDA level was measured using the Buege and Aust spectrophotometer Model CE1010 CECIL series 1000. Blood lead analysis was performed according to the NIOSH8003 method. Statistical data were analyzed by SPSS20.0.

Daily noise exposure in the die-cut unit was significantly higher than in the other units ($\bar{L}_{Epd}$ = 87.71 ± 1.469dB). Lead concentration of those who work in the printing unit was significantly higher than other units (0.1431 ± 0.02 ppb), and the MDA concentration in the printing unit was significantly higher than in the other units (0.9963 ± 0.238 mmol/lit). The results showed a significant correlation between different work units and serum MDA concentration (P <0.001). Also, a strong positive correlation was found between blood lead concentration and MDA concentration (P = 0.622; r <0.001). While the relationship between daily exposure to noise and MDA concentration (P = 0.857) was negligible.

Exposure to noise is known to cause oxidative stress. Exposure to lead has also led to increased levels of oxidative stress biomarkers in most studies. Our results showed a significant direct relationship between blood lead concentration and mean concentration of MDA (as a marker for oxidative stress) of printing workers. However, no significant correlation was found between MDA concentration and noise and co-exposure to noise and lead.

***Keywords**:* Lead; Noise; Malondialdehyde; Printing industry

Poster Presentation

1st International Congress of Biomarkers

PN: 1073

Fludrocortisone administration increases endometrial receptivity markers via regulation of ENaC, SGK1, HAND2, miR-200a, miR-145 and microRNA 451 in mice

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ABSTRACT

Dependent on the endometrial receptivity. This study aims to investigate whether the treatment with fludrocortisone can influence the expression of a group of genes and proteins involved in the implantation process in mice. Forty adult female BALB/c mice were randomised into four groups.Vehicle receiving group; fludrocortisones receiving group (FCA); PP242 receiving group (PP242); fludrocortisones and PP242 receiver group (FCA PP242). Mice were killed on decidualization phase after gestation confirmation. The endometrial epithelium of mouse were separated to measure mRNA expression of Serum/glucocorticoid-inducible kinase 1 (SGK1), epithelial Na channel (ENaC), Heart- and neural crest derivatives-expressed protein 2 (HAND2), miRNA 145, miRNA 200a, and miRNA 451 as well as protein expression of mammalian target of rapamycin (mTOR), and eukaryotic translation initiation factor 4E-binding protein 1 (4E-BP1) in the uterine using real-time PCR and western blot, respectively. The results revealed that the administration of fludrocortisone slightly downregulated the expression of SGK1, ENaC-α, miR-145 and miR-200a, while it slightly upregulated the expression of HAND2, miR-451, mTOR and 4E-BP1 in the epithelial endometrium of the FCA-treated group when compared with the control group. The expression of miR-145 and miR-200a was upregulated whereas the expression of p-4E-BP1, mTOR, SGK1, ENaC-α, HAND2 and miR-451 was partially downregulated in the PP242-treated group in comparison with the control group. Compared to the PP242 group, combination therapy of fludrocortisone plus PP242 resulted in slightly decreased expression of ENaC, SGK1, miR-200a, miR-145 and 4E-BP1 while it slightly upregulated the expression of miR-451, and HAND2 in the epithelial endometrium. Our findings indicated that fludrocortisone did not disturb the endometrial receptivity, while increased the endometrial receptivity possibly through the modulation of the expression of genes involved in this process. The activation of the mTOR signalling pathway was also increased during the fludrocortisone treatment .The miRNA 451,145 and HAND-2 could be plays a role as a endometrial receptivity regulation markers.

Keywords: Fludrocortisone; mTOR; miR-145; miR-451; miR-200a

Poster Presentation

1st International Congress of Biomarkers

PN: 1074

miR223-3p, HAND2, and LIF expression regulated by calcitonin in the ERK1/2-mTOR pathway during the implantation window in the endometrium of mice

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ABSTACRT

Approximately one-third of infertility cases are related to the female partner, and implantation failure is the primary reason for female infertility. The current research was established to assess the impact of calcitonin on endometrial receptivity. 64 female BALB/c mice were assigned to 2 groups as follows: mice with regular ovarian cycle and mice with stimulated ovarian cycle. The two groups were further divided into four subgroups as follows: control (Ctrl), calcitonin (CT), pp242, and CT + pp242 groups. Calcitonin and pp242 were injected on days 3, 4, and 5 of pregnancy. On day 5 of gestation, all of the animals were sacrificed, and their uterine was removed for the morphological analysis, as well as the expression assessment genes and proteins. The results demonstrated that ovarian stimulation increased the rate of phosphorylation of ERK1/2 and mTOR proteins, and resulted in the upregulation of miR-223-3p ($P < .01$). The administration of calcitonin also elevated the expression levels of LIF and HAND2 gene in both regular ovarian and ovarian-stimulated cycles ($P < .05$). In ovarian-stimulated groups, the administration of calcitonin led to a decrease in the expression of miR-223-3p ($P < .001$). Calcitonin administration also markedly increased the phosphorylation of 4EBP1 ($P = .003$) and ERK1/2 ($P < .01$) in the regular ovarian cycle. It seems that calcitonin is capable of enhancing the endometrial receptivity of the uterine, thereby the overexpression of HAND2 and LIF and downregulation of miR-223-3p through the ERK1/2-mTOR signaling pathway.

Keyword: calcitonin; ERK1/2; HAND-2; Implantation window; LIF; miR-223-3p; miR-451; mTOR

Poster Presentation

1st International Congress of Biomarkers

PN: 1076

The importance of HE4 and CA125 in overall survival and recurrence-free survival of endometrial cancer

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ABSTRACT

The objective of this study was to evaluate the correlation of serum biomarkers CA125 and HE4 levels with the overall survival and recurrence - free survival of patients with endometrial cancer. This was a cross sectional study of a single center of 99 patients (mean age 53.64) with histologically confirmed endometrial cancer that preoperative serum CA125 and HE4 levels were evaluated 1-2 weeks before operation. With standard treatment of extra facial total hysterectomy and bilateral Salpingo-oophorectomy with selective pelvic and para-aortic node dissection, according to risk for recurrence (Mayo criteria). Patients with upper third (66th) percentiles of both CA125 and HE4 were classified as high risk groups. Data analysis through SPSS software, P-value < 0.05 was reckoned to be significant. The mean(SE) of overall survival(OS) among pateints with serum CA125 $\leq 22^{ku}/_{l}$ and higher $22^{ku}/_{l}$was 47.97±(2.58) and 41.78(3.75) months(P=0.466), also mean(SE) of OS in pateints with serum HE4 level$\leq 98^{\rho mol}/_{l}$ and$>98^{\rho mol}/_{l}$ was 50.14(2.06) and 38.54(3.74) respectively. The Log-Rank test, revealed a substantial difference between low risk and high-risk groups by HE4 (X^2=4.98;P=0.025). On that point, there is no significant difference between RFS with CA125 and HE4 (p=0.264) and (P=0.114) respectively. Serum HE4 levels is a significant independent prognostic factor for OS in endometrial cancer and is useful in survival studies.

Keywords: Endometrial cancer, Cancer Antigen 125 (CA125), Human Epididymis Protein 4 (HE4), Overall Survival (OS), Recurrence-Free Survival (RFS).

Poster Presentation

1st International Congress of Biomarkers

PN: 1077

The effect of Choline supplementation in mothers with hypothyroidism on changes in marker of oxidative in pre-pubertal offspring rats

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ABSTRACT

Lack of thyroid hormones during brain development is associated with both functional and structural brain alterations such as deficit cognitive. Given the known effects of choline on cognitive functions, no studies have been conducted on its effect on oxidative markers in maternal hypothyroidism. In this study, we examined the effect of choline supplementation on oxidative markers in pre-pubertal offspring rats.

To induce hypothyroidism, 6-propyl-2-thiouracil was added to the drinking water from the 6th day of gestation to the 21st postnatal day (PND). Choline-treated was started twice a day on the first day of gestation until PND 21. On PND28 Pups were sacrificed to assess their serum. The malondialdehyde (MDA) levels of the serum samples were determined by the thiobarbituric acid (TBA) method. The reduced glutathione (GSH) levels of serum Samples were determined by the Colorimetric method. The serum level of Total Antioxidant Capacity (TAC) was estimated using commercial reagent kits in accordance with the manufacturer's instructions.

In this hypothyroid state, the obvious elevation of oxidative markers (MDA) was observed, along with decreased activities of antioxidants markers (GSH and TAC) in serum with respect to the control group. Also, Choline supplementation excessed oxidative stress and made disturbance to antioxidant defense system.

It can be suggested that the maldevelopment of offspring of hypothyroid and hyperthyroid mother rat dams may be attributed, at least in part, to the excess oxidative stress and deteriorated antioxidant defense system in such conditions. Also, due to the effects of choline on the antioxidant system in hypothyroidism, it should be used with caution.

Keywords: Maternal hypothyroidism; Choline; PTU; Oxidative stress

Poster Presentation

1st International Congress of Biomarkers

PN: 1078

The effect of exercise on age related changes in marker of oxidative

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ABSTRCT

Aging is associated with increased free radical generation. Whether or not oxidative stress is the cause of the aging process, as proposed by the oxidative stress theory of aging, remains unknown. Physical activity has many well-established health benefits, but research evidence indicates that senescent organisms are more susceptible to oxidative stress during exercise because of the age-related ultrastructural and biochemical changes that facilitate formation of reactive oxygen species.

In this study, we examined the effects of treadmill exercise on oxidative markers. The study was carried out with 18-mo-old and young adult Wistar rats. They were randomly divided into three groups: young sedentary, old-exercised, and old-sedentary. The rats in the old-exercised group ran on the treadmill for 20 min/day, for four weeks. After exercise training, the rats were sacrificed to assess their serum. The malondialdehyde (MDA) levels of the serum samples were determined by thiobarbituric acid (TBA) method. The reduced glutathione (GSH) levels of serum Samples were determined by Colorimetric method. The serum level of Total Antioxidant Capacity (TAC) was estimated using commercial reagent kits in accordance with the manufacturer's instruction. The results showed an age-related increase in TAC levels. Despite the decrease in MDA with advancing age, MDA: TAC ratio increased with increasing age ($P<0.01$). The effects of exercise on this ratio were not significant. Although we found a decrease in GSH level in the group of old rats, as compared with the younger, it was not significant. These results are suggestive of oxidative stress with advancing age. MDA: TAC ratio can be a useful indicator to monitor and optimize antioxidant therapy which may reduce morbidity and perhaps increase the healthy, useful life span of an individual.

Keywords: Aging; Antioxidant; Exercise; Oxidative stress

Poster Presentation

1st International Congress of Biomarkers

PN: 1079

Development of indigenous biosensing methodology for rapid detection of endotoxin

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ABSTRACT

Endotoxins, also referred to as pyrogens, are lipopolysaccharides (LPS) present in the outer membrane of Gram-negative bacteria and represent one of the most dangerous microbiological contaminants. Severe endotoxin infections coupled with sepsis transmit an elevated mortality rate in spite of proper treatment and intensive care. These necessities the need for a rapid, sensitive and non-invasive biosensor for detection and monitoring of endotoxin levels even in extremely small concentrations.

The proposed method of endotoxin quantification is based on the use Chromogenic substrate, which monitors color development of the Horseshoe crab amoebocyte lysate assay in response to endotoxin. Bacterial endotoxin catalyzes the activation of a proenzyme in the modified horseshoe crab amebocyte lysate. The activated proenzyme then catalyzes the splitting of p-Nitroaniline (pNA) from the colorless substrate, Ac-Ile-Glu-Ala-Arg-pNA. The activation rate is proportional to the sample endotoxin concentration. After stopping the reaction, the released pNA is photometrically measured at 405 nm.

The developed color intensity is proportional to the amount of endotoxin present in the sample and can be calculated using a standard curve microscopic investigation was carried out to observe the motility of the amebocyte cells, their attachment with the *E. coli* and their response to bacterial endotoxin by the help of phase contrast microscope. Our proposed strategy can be adapted to facilitate bacterial endotoxin detection in biological specimens with 0.05EU/ml. Microscopic investigations suggest amebocyte cells are motile prior to addition of *E. coli* but after exposure with *E. Coli* LPS the amebocyte cells initiate exocytosis resulting in clot formation. Due to its portability, suitability and low cost, the chromogenic sensor is ideally suited for wide-spread use in endotoxin detection.

Keywords: Endotoxin; Infection; Disease; Biomarkers; Detection

Poster Presentation

1st International Congress of Biomarkers

PN: 1080

Suppressing Wnt/β-catenin and mTOR signaling pathway with marine algae-derived natural compounds in senescent human skin fibroblasts

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ABSTRACT

Wnt/β-catenin and mTOR intracellular signaling pathways are generally reactivated in diabetic patient. Blocking these signaling pathways by some natural marine bioactive compounds derived from Persian Gulf seaweeds can be a useful therapeutic strategy to prevent premature aging of diabetics.

In the present study, three natural flavonoid compounds were identified, which are: Naringenin (extracted from marine green macroalgae, Ulva prolifera), Apagenin (extracted from red macroalgae, Acanthophora spp.) and Fucoxanthin (extracted from brown macroalgae, *Sargassum spp.*). These compounds were extracted and purified by thin layer chromatoplate method and the accuracy of their extraction process was confirmed by FTIR, 1HNMR and GC-MS/LC-MS tests. In order to investigate the therapeutic effects of these natural marine compounds, first normal human skin fibroblast cells (HDFs) were prepared from the embryo cell bank, cultured and passaged and aged under high concentrations of glucose (150 mM).

Further, confirmatory tests were conducted to check the validity of the induction of cell senescence based on the evaluation of cell morphology under inverted microscope and measurement of beta-galactosidase activity. After confirming cell senescence, cells were treated with concentrations (0, 50, 100, 150 and 200 μmol/L) of Naringenin, Apagenin and Fucoxanthin for 8 days. Next, quantitative changes in the expression of the main genes of both signaling pathways (p21, β-Catenin, RAGE, Collagen I, MMP-1, Wnt-1, Gsk-3β, mTOR, eIF4E) in aging fibroblast cells were measured by RT-qPCR method**.**

The gene expression results obtained in this study showed that the drug formulation was able to decreased Wnt ligand gene expression, β-catenin deactivation, decreased mTOR activity, and increased autophagy activity, which ultimately leads to decreased cellular aging in diabetic fibroblast cells. The results demonstrated that the marine drug could improve the cell functions and significantly reduce the signs of cellular aging due to the synergistic effects of bioactive compounds.

Keywords: Anti-aging; Fibroblast; Glucose; Seawee ; Signaling pathways; Marine Drugs; Persian Gulf.

Poster Presentation

1st International Congress of Biomarkers

PN: 1081

In Search of Biomarkers to Assess Oxidative Stress Caused by Occupational Exposure to Nanomaterials

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ABSTRACT

Currently, a growing population of workers are exposed to nanomaterials worldwide. On the other hand, due to many uncertainties about characteristics of these materials and exposure scenarios, their health risk assessment methods are generally qualitative and lack sufficient abilities. Therefore, it is necessary to examine the effects of occupational exposure to these materials by other methods. Biological monitoring, can provide useful information in this regard.

This systematic review examines studies that have evaluated oxidative stress, caused by occupational exposure to nanomaterials, using different biomarkers. The search was conducted on PubMed, Scopus and Web of Science databases using "biomarker, oxidative stress, occupational exposure and nanomaterials" keywords. Out of 266 studies obtained in initial search, eventually 11 were included in the study.

Currently, there is no specific biomarker for investigating oxidative stress induced by exposure to nanomaterials. So the reviewed studies have used different biomarkers (8-OHdG, GPx, MPO, SOD, MDA and so on) in different biological fluids (sputum, blood, urine, WBC, EBC) for this purpose. Also, the methods of assessing occupational exposure to nanomaterials in the investigated studies were very diverse (Qualitative, semi-quantitative, quantitative and real-time methods).

Given the approach of the investigated studies regarding biomarkers and exposure assessment methods, finding a specific biomarker for investigating exposure to nanomaterials seems unattainable. But reaching a group of biomarkers, to assess exposure to nanomaterials seems more applicable and achievable.

Keywords: Occupational Exposure; Nanomaterials; Oxidative stress; Biomarkers

Poster Presentation

1st International Congress of Biomarkers

PN: 1083

The FOXL2 gene and XIST LncRNA as a novel diagnostic biomarker panel for ovarian cancer

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ABSTRACT

Ovarian cancer is responsible for more cancer-related deaths than any other cancer of the female reproductive system. Early diagnosis of this neoplasm could play a pivotal role in increasing the survival rates of the afflicted patients, and biomarkers that enable early diagnosis have proven their significance in this regard. Accordingly, this study aimed to evaluate novel biomarkers for diagnosing ovarian cancers on the mRNA, miRNA, and lncRNA transcription levels. The 20 genes with the highest mutation frequency in ovarian cancer were downloaded from the cosmic database, and the Foxl2 gene was selected as a possible biomarker for ovarian cancer using the GEPIA2 database (Log2FC<-2, p-value <0.05). Using the Venny 2.1 tool, we got the intersection between the up-regulated miRNAs in ovarian cancer from the dbDEMC database (LogFC>+1, adjusted p-value<0.05), and the Foxl2 targeting miRNAs from the starBase v3.0 database, as well as the intersection between the miRNAs corresponding LncRNAs from the starBase v3.0 database and the down-regulated ovarian cancer LncRNAs from the Lnc2cancer database. Then, we used the Cytoscape software version 3.9.1 to visualize the LncRNA-miRNA-mRNA network and determine the hub LncRNAs and miRNAs that have key roles in regulating the Foxl2 gene. The Foxl2 gene and XIST lncRNA, hsa-miR-23b-3p, hsa-miR-23a-3p, hsa-miR-185-5p, hsa-miR-513a-5p, TTN-AS1 lncRNA, OIP5-AS1 lncRNA had high scores in the maximal clique centrality (MCC) ranking method. Given that the Foxl2 gene and XIST lncRNA received the highest scores, 15 and 13, respectively, we identified them as the main biomarkers of choice. Using a single genetic marker for the detection of this neoplasm could not have the expected accuracy and efficiency; Therefore, we have identified a biomarker panel consisting of the Foxl2 gene and the XIST lncRNA that could be used together as an accurate means for early detection of ovarian cancer.

Keywords: Foxl2, XIST, Biomarker, Ovarian cancer.

Poster Presentation

1st International Congress of Biomarkers

PN: 1084

Evaluation of miRNA223-3p expression in patient's uterus with endometriosis in the secretory phase

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ABSTRACT

Endometriosis is one of the diseases in which uterine receptivity decreases and causes infertility. studies indicate the role of miRNAs in the stage of embryo implantation. Among some of these molecules, mir-223-3p can be mentioned. This study aims to understand the regulatory mechanisms better and discover the molecules involved in implantation, which can help researchers find ways to treat infertility, prevent early pregnancy loss, and improve contraceptive methods. In this case-control study, 40 women with and without endometriosis were randomly selected from those referred to the Fertility and Infertility Health Research Center of Babul University of Medical Sciences. They Performed a Histopathological examination to confirm the endometrium's secretory stage. The quantitative RT-PCR method was used to check gene expression. determined the studied genes' relative expression level, a housekeeping gene called U6 was utilized. This study showed that increased expression of the mir-223-3p in endometriosis samples was significant compared to the control group. ($P < 0.05$). these data show that mir223-3p potentially plays an essential role in Implantation failure associated with endometriosis due to Leukemia inhibitory factor (LIF) signaling and suppressing it. LIF regulates multiple processes before and during implantation, such as uterine transformation into receptivity. It can be suggested that along with mir223-3p, other molecular factors of LIF signaling can be assessed to improve the validity of the finding about the molecular mechanism of implantation.

Keywords: Endometriosis, microRNA, infertility, implantation, LIF

Poster Presentation

1st International Congress of Biomarkers

PN: 1085

Atrophy of Hippocampal Subfields as a Biomarker in Alzheimer's Disease and Mild Cognitive Impairment (MCI) Patients

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ABSTRACT

Atrophy in hippocampal subfields analysis based on MRI is widely used as a powerful biomarker for the diagnosis and management of neurocognitive diseases. However, there is still no clear consensus on the atrophy pattern in Alzheimer's disease (AD) and mild cognitive impairment (MCI). In this cross-sectional study, hippocampal subfield atrophy in AD and MCI patients is extracted and compared with the normal group (NC). in addition, the symmetry of atrophy in the subfields (left and right) is also assessed.

MRI images used in this study were selected from Alzheimer's database (ADNI). The images of 20 AD, 20 MCI patients; and 20 Normal control (NC) in the age range of 60-65 years were selected and downloaded. The volume of subfields was extracted automatically using Freesurfer version 7.1.0 software; and then normalized to the total intracranial volume. Finally, asymmetry of subfields volumes was also assessed. Analysis of covariance was used to compare the volume of subfields between the three groups (age and gender as covariates).

The results showed that the atrophy in the total hippocampus and its subfields in AD was significantly higher than in the NC, as well as in MCI groups. In terms of asymmetry, it was observed that there is a significant difference in the atrophy of the total hippocampus, hippocampal body, fimbria, the CA3 and GC-ML-DG between the AD and NC group as well as MCI group.

Atrophy of hippocampal subfields are useful biomarker in neurocognitive diseases. In this study, it was seen that the atrophy of all subfields and its asymmetry can be used for distinguishing Alzheimer's from MCI. It was seen that the pattern of atrophy in the left hippocampal subfields is more than in the right.

Keywords: Alzheimer's disease (AD); Mild cognitive impairment (MCI); Hippocampal subfields; MRI; Brain atrophy

Poster Presentation

1st International Congress of Biomarkers

PN: 1086

Developing of inverse opal structures for sensing of biomarkers

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ABSTRACT

Inverse opal photonic crystals (IOPCs) as highly ordered and well defined nano-porous structures have the unique optical properties for application in the field of optoelectronics and photonics based biosensors. Newly, these developed IO arrays have been used as selective and sensitive biosensor for various biomolecules detection like gases, DNA, pathogens, proteins, glucose and other organic molecules.

The co-assembly of silica and PS colloidal spheres were used to develop of IO structures in this study. For this purpose, after self-assembly of polystyrene microspheres on glass templates, silica precursor, as a filling material, a mixture of hydrochloric acid, absolute ethanol and tetraethyl orthosilicate solution, was filled on template surface.

Silica inverse opal (IO) structures were fabricated by the self-assembly of silica precursors and mono-dispersed colloidal crystal template method. The morphological investigation of prepared IO films was done by SEM analyses and optical image was used for checking of all periodic microporous structure of IOs surface. For first time, in this study we introduced optical density of IO films for sensing different concentration of glucose solutions and their optical images have been used for comparison of sensing properties. The intensity of the absorbance spectrum was decreased by increasing the glucose concentration using silica IO structures as the sensing chip. The 3D microporous IO arrays show perfectly optical detecting properties. The peak intensities of absorbance spectrum are able to detect the organic solvents with different refractive indices. Silica IO structures were fabricated by the self-assembly of silica precursors and mono-dispersed colloidal crystal template method. The optical density of IO films were used for sensing different concentration of glucose as a biomarker and their optical images have been compared for sensing properties.

Keywords: Optical images; Inverse opal; Photonic crystal; Glucose biomarker

Poster Presentation

1st International Congress of Biomarkers

PN: 1087

Osteogenic differentiation of the loaded stem cells on magnetic nanofibrous scaffolds

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ABSTRACT

Nanocomposite scaffolds are one of the best scaffolds used to repair and regenerate damaged tissues. Iron nanoparticles (Fe_3o_4) are FDA-approved to use in the clinic. Magnetic stimulation can induce the growth and osteogenic differentiation of mesenchymal stem cells. Therefore, magnetic nanocomposite scaffolds (MNS) can introduce functional structures for use in bone tissue engineering. We prepared polycaprolactone-based nanocomposite scaffolds containing collagen type I and Fe_3O_4 using electrospinning in this study. Next, these scaffolds were characterized by AFM, SEM, Contact Angle meter, Stress-Strain curve, and FT-IR. MTT assay and DAPI staining were used to assess the biocompatibility of MNS. The osteogenic differentiation potential of composite scaffolds was analyzed by ARS staining and gene expression study.

The results of FE-SEM observation showed that the structure of the prepared scaffolds has nano-sized fibers (70-600nm) and is porous. FTIR graphs indicated the natural structures of MNPs, Col I, and PCL have been conserved in the structures of the MNS. Also, the results showed the magnetic nanoparticles embedded in the structure of the nanofibrous scaffolds improve MNS wettability, tensile strength, and porosity. MTT assay test indicated that the MNS not only are biocompatible but also increase the growth and proliferation rate of MSCs at 5 and 7 days. In addition, ARS staining and Real-time PCR results showed the MNS induces the osteogenic differentiation of seeded stem cells on scaffolds. Magnetic nanoparticles used in the structures of nanofibrous scaffolds improved the surface hydrophilicity, mechanical strength, and porosity of MNS. In addition, these nanoparticles cause an increase the MSCs attachment, proliferation, and differentiation. Therefore, magnetic nanofibrous scaffolds can introduce functional substitutes and create a new horizon for the treatment (repair and regeneration) of patients in need of bone grafting.

Keyword: Nanocomposite scaffolds; Stem cell; Magnetic nanoparticles; Osteogenic differentiation

Poster Presentation

1st International Congress of Biomarkers

PN: 1090

The effect of the breast cancer biomarkers on survival: a data mining approach

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ABSTRACT

The low rate of breast cancer survival is a challenging issue in the developing countries. Data mining techniques predict the survival condition of the patients with high accuracy. The key biomarkers of breast cancer such as: estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) are the most important breast cancer survival predictors. The relationship of these biomarkers and other predictors with the breast cancer survival has been analyzed by a popular data mining algorithm in the current study. The data of 900 patients from The Omid Treatment and Research Center Urmia, Iran were analyzed by the classification and regression trees (CART). The missing data of the predictors were imputed and extracted rules by CART were selected based on sensitivity. When HER2 was not existence in the patient's tests, the survival status was positive. However, the lack of PR in the patient's tests lead to death. The sensitivity of the first rules in the "not dead" and "dead" groups was 89.7% and 84.1% respectively. The model of the current study extracted useful hidden rules from the breast cancer data. The extracted rules showed properly the significant role of breast cancer biomarkers on survival.

Keywords: Breast Neoplasms; Biomarker; Data Mining; Survival

Poster Presentation

1st International Congress of Biomarkers

PN: 1091

Prognostic role of biomarkers in COVID19 infection

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ABSTRACT

During infectious diseases such as COVID-19 infection, the level of some biomarkers possibly changes which indicates a correlation between disease severity and mortality. Recent studies have revealed the association between COVID-19 severity and circulating levels of some biomarkers such as C-reactive protein (CRP), interleukin-6, ferritin, etc. But, a biomarker cannot be interpreted into clinical practice for therapeutic interventions until it is verified to have a considerable impact. Therefore, the accuracy of the level of these biomarkers as a prognosis marker has been assessed. This review article has been written using information from articles published in Pubmed since the start of the pandemic of covid19. This study gathers and merges information about changes in the various biomarkers in patients with different severity of coronavirus infection and brings a new perspective to the patient management approach. In patients with COVID-19 infection, biomarkers could take a crucial role in the determination of prognosis, monitoring, and patient follow-up. However, the clinical effectiveness of these biomarkers in COVID-19 is unproven. According to the results, a panel of biomarkers rather than a biomarker may provide more reliable information. It seems logical to use guidelines that tailor the data to a properly interpret of the results. Therefore, it is now recommended, to use several clinical factors and biomarkers together in determining clinical scores that might also categorize patients at low- and high-risk for death.

Keywords: COVID-19،biomarker

Poster Presentation

1st International Congress of Biomarkers

PN: 1092

Molecular changes of Endoplasmic Reticulum Stress signaling pathway Increased Alzheimer disease biomarker in the hippocampus of aged male rats: Rescue effect voluntary exercise

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ABSTRACT

Molecular changes of endoplasmic reticulum stress signaling pathway play a significant role in Alzheimer, s disease. The aim of this study was to evaluate the efficacy of voluntary exercise on Eendoplasmic reticulum stress signaling pathway. Eighteen Wistar rats were divided into three groups (six per each): 1- Young (3 old months) 2- Aged (18 old months) 3- Aged +Exercise. Rats in the exercise group were placed in the voluntary exercise setup for two months. After 2 months of treatment with voluntary exercise, all animals were anesthetized with Ketamine (60 mg/kg) and Xylazine (10 mg/kg), hippocampus tissues were collected and used for determination of Amyloid Beta1-42 by Elisa and endoplasmic reticulum stress signaling pathway molecules include ATF 6, P.ERK, IRE-1A, CHOP, and GRP78 by Western blot. Amyloid Beta1-42 protein levels increases in the hippocampus of aged rats compared to the young group. Also, aging significantly caused induction of ER stress in hippocampus compared to the young group based on the elevated ER stress markers. Histopathological studies determined elevated apoptosis in the aging rats compared to young rats. Results showed that voluntary exercise improves these changes. The results suggest that voluntary exercise mediates maladaptive ER stress conditions possibly by creating adaptive ER stress status and driving protein folding correctly.

Keywords: Aging, Alzheimer, Endoplasmic reticulum stress, Voluntary Exercise

Poster Presentation

1st International Congress of Biomarkers

PN: 1093

Protein drug targets in MCF-7 cell line for target therapy

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ABSTRACT

Breast cancer is one of the most common cancers worldwide. The identification of new biomarkers and therapeutic targets for the development of novel molecular therapies is critical in improving patient stratification and guiding precise treatment. Identifying glycoproteins differentially expressed during cancer progression is an excellent approach to the discovery of novel biomarkers.

Our study using gene ontology [GO] enrichment analysis categorized the detected glycoproteins via mass spectrometry that are expressed in the MCF7, a metastatic breast cancer cell line, compared with the standard cell line. Detected glycoproteins are categorized as receptor proteins, proteins involved in endocytosis and metastasis. We also highlighted a subset of glycoproteins that are overexpressed in malignant line with underexpression or zero expression in normal cells. Moreover, we used GeneCards database to enrich related drugs against introduced protein targets.

Regarding detected glycoproteins in MCF7 cell line, we enriched four receptor proteins, including CD239, CD55, CD47 and CD112, which are overexpressed in cancer cells. Two enriched upregulated proteins, including Gal-3BP and vitronectin are involved in endocytosis. Also, GO analysis based on molecular function determined Cathepsin D and dipeptidyl peptidase II as upregulated proteases which have important roles in metastasis. Ten of the glycoproteins were detected only in the malignant line, and especially apolipoprotein D was expressed at dramatically high (191-fold) levels in breast cancer. In addition, summarizes of proposed drugs released from the GeneCards database to target overexpressed genes were provided.

Our analysis of detected glycoproteins in MCF-7 breast cancer cells, highlighted and described some glycoproteins that have been less studied as drug targets for the treatment of breast cancer and can be considered as diagnostic, prognostic, or predictive biomarkers or potential therapeutic molecular targets.

Keywords: Breast cancer; MCF7; Glycoproteins; Bioinformatics; Drug targets; Biomarkers

Poster Presentation

1st International Congress of Biomarkers

PN: 1094

The H3F3A CeRNA network as a novel biomarker panel for Glioblastoma multiform cancer

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ABSTRACT

Glioblastoma Multiform (GBM) has become one of the deadliest brain tumors, with a low median survival rate in children and adults. Despite the therapeutic approaches, GBM is still considered a major challenge in cancer treatment; Therefore, we need to identify new candidates for targeted therapy as well as novel biomarkers to increase the efficiency of GBM diagnosis. Recent studies have shed light on the role of non-coding RNAs in tumorigenesis, and competing endogenous RNAs (ceRNAs) have attracted much of attention in this field. In this study, we intend to delineate a ceRNA network and search for possible biomarkers for GBM patients.

The 20 genes with the highest mutation frequency in GBM were downloaded from the cosmic database, and the H3F3A gene was selected as a possible biomarker for GBM using the GEPIA2 database ($Log_2FC>+2$, p-value <0.05). Using the Venny 2.1 tool, we got the intersection between the down-regulated miRNAs in GBM from the dbDEMC database (LogFC<-1, adjusted p-value<0.05) and the H3F3A targeting miRNAs from the starBase v3.0 database, as well as the intersection between the miRNAs corresponding LncRNAs from the starBase v3.0 database and the up-regulated GBM LncRNAs from the Lnc2cancer database. Then**,** we used the Cytoscape software version 3.9.1 to visualize the LncRNA-miRNA-mRNA network and determine the hub LncRNAs and miRNAs having key roles in regulating the H3F3A gene.

We plotted a ceRNA network consisting of lncRNA-miRNA-mRNA axes. Based on the maximal clique centrality (MCC) ranking method, the XIST lncRNA, has-mir-105-5p, has-mir-129-5p, has-mir-329-3p, has-mir-323a-3p miRNAs, and H3F3A mRNA obtained the highest scores. Our findings show an interaction between lncRNAs and miRNAs leading to *H3F3A* gene regulation. This network can be used as a novel biomarker to increase diagnosis efficiency and introduce multiple candidates for targeted therapy in GBM patients.

Keywords: Glioblastoma Multiform; H3F3A; Biomarker; CeRNA network

Poster Presentation

1st International Congress of Biomarkers

PN: 1095

Epigenetic Markers of Acute Myeloid Leukemia Affected by 6-Thioguanine

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ABSTRACT

The drug 6-thioguanine (6-TG) is one of the thiopurines successfully used in oncology, especially for acute myeloid leukemia (AML). It is proposed to act as an epigenetic drug affecting DNA methylation. The aim of this study was to clarify the effect of 6-TG on the proliferation, viability and expression of genes coding for the enzymes DNA methyltransferase 3A and DNA methyltransferase 3B (DNMTs) as well as histone deacetylase 3 (HDAC3) and histone deacetylase 7 (HDAC7) in the human promyelocytic AML cell line HL60.

In this experimental study, HL60 cells and also normal peripheral blood mononuclear cells (PBMCs) were grown in RPMI 1640 medium containing 10% fetal bovine serum. They were then treated with 6-TG at their exponential growth phase. Cell viability was monitored using the Cell Counting Kit-8 assay with an enzyme-linked immunosorbent assay (ELISA) reader. The expressions of the above mentioned 4 genes were quantified using real-time PCR.

The drug 6-TG could inhibit the proliferation of HL60 cells and decrease their viability. In HL60 cells, as compared to normal PBMCs, 6-TG significantly decreased *HDAC3* ($p = 0.0034$) as well as *DNMT3B* ($p = 0.03$) and *HDAC7* ($p = 0.0031$) gene expressions, but increased the expression of *DNMT3A* gene ($p = 0.16$) after normalization to *GAPDH* as the housekeeping gene.

These findings suggest how 6-TG could alter the expression of *DNMT3A*, *DNMT3B*, *HDAC3* and *HDAC7* genes, probably useful as a biomarker for the epigenetic modifications in AML.

Keywords: DNA methyltransferase; Gene expression; Histone deacetylase; Leukemia; Thioguanine; Thiopurine

Poster Presentation

1st International Congress of Biomarkers

PN: 1096

Gene Markers of the Effects of 6-Thioguanine on Lymphoid Cancer Cell Line Nalm6

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ABSTRACT

6-thioguanine (6-TG) is one of the thiopurine drugs with successful use in oncology, especially for acute lymphoblastic leukemia (ALL). 6-TG is proposed to act as an epigenetic drug affecting DNA methylation. The aim of this study was to clarify the effect of 6-TG on the proliferation, viability and expression of genes coding for the enzymes DNA methyltransferase 3A and DNA methyltransferase 3B (DNMTs) as well as histone deacetylase 3 (HDAC3) in the human B cell-ALL cell line Nalm6.

In this experimental study, Nalm6 cells and also normal peripheral blood mononuclear cells (PBMCs) were grown in RPMI 1640 medium containing 10% fetal bovine serum. They were then treated with 6-TG at their exponential growth phase. Cell viability was monitored using the Cell Counting Kit-8 assay with an enzyme-linked immunosorbent assay (ELISA) reader. The expressions of the abovementioned 3 genes were quantified using real-time PCR. 6-TG could inhibit the proliferation of Nalm6 cells and decrease their viability. In Nalm6 cells, as compared to normal PBMCs, 6-TG significantly decreased HDAC3 ($p = 0.008$) as well as DNMT3B ($p = 0.003$) gene expressions, but increased the expression of DNMT3A gene ($p = 0.02$) after normalization to GAPDH, as the housekeeping gene.

These findings suggested that the altered expression of DNMT3A, DNMT3B and HDAC3 genes was responsible for at least part of the antitumoral properties of 6-TG, and may serve as a biomarker for the effects of this epigenetic drug.

Keywords: DNA methyltransferase; Histone deacetylase.

PN: 1098

Association of serum miR-375, miR-155 and miR-146b levels with distinguish of papillary thyroid cancer from benign thyroid masses among Iranian Patients

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ABSTRACT

Certain serum levels of microRNAs (miRNAs) throughout the body can be helpful for cancer diagnosis and prognosis. The miRNAs can be secreted from the papillary thyroid cancer (PTC) into the circulatory system. Accordingly, this study aimed to measure the serum levels of miR-146b, miR-155 and miR-375 to evaluate their diagnostic potentials in distinguish of benign from malignant lesions.

The serum levels of miRNAs were measured by real-time quantitative RT-PCR among100 patients with benign thyroid nodules and 30 patients with PTC. Fold differences (log2-DDCt) was carried out in the expression of serum miR-146b, miR-155b and miR-375 between PTC benign and tumors (Mann–Whitney U-test). The mean miR-375 and miR-155 expression levels in the PTC group were greater when comparing with the benign group. The mean fold changes in miR-375 (-10.26± 0.040) and miR-155 (-6.08± 0.061) were higher in the PTC group compared to the benign group. The mean fold changes in miR-146b (-6.04± 0.052) were higher in the PTC group compared to the benign group, but not significant. The area under the ROC curve (AUC) was estimated at 0.81 for the miR-375 with 0.76% sensitivity and 0.80% specificity to distinguish between benign and PTC lesions. The AUC was calculated to be 0.75 for the miR-155 with 0.69% sensitivity and 0.90%specificity.

According to the results of this study, the serum levels of miR-155 and miR-375 were increased in the patients with PTC, which may be useful as alternative seromarkers for the PTC.

Keyword: circulating miRNAs; papillary thyroid cancer; seromarker.

Poster Presentation

1st International Congress of Biomarkers

PN: 1099

The Relationship between Platelet-Derived Growth Factor and Tracheal Stenosis Caused by Intubation Using Immunohistochemistry and PCR

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ABSTRACT

The tracheal stenosis as an iatrogenic complication causes many concerns for both patients and physicians. There are some differential diagnoses for this problem due to presence of dyspnea. The gold standard approach for final diagnosis is bronchoscopy which is an invasive technique. So, regarding the role of fibroblast and type I collagen in tracheal stricture region, in this study, we aimed to assess platelet-derived growth factor (PDGF) to early diagnose of tracheal stenosis.

In this study, 25 patients with the tracheal stenosis and 25 cases of brain death as control group were enrolled. Tracheal sample was taken from the stricture-trachea after resection and inserted into a falcon tube containing buffered formalin and was transported to the related laboratory for the immunohistochemistry staining. A piece of the trachea was also inserted into a micro tube containing free RNA and was sent for the PCR tests after being placed into a nitrogen tank. The same steps were performed for the control group after autopsy.

Mean age in control and tracheal stenosis group was 34 (12) and 37 (9) years old. Mean duration of intubation was 15(8) and 18 (8) days in tracheal stenosis and control group respectively, with no considerably differences. PDGF level was considerably higher in tracheal stenosis patients compared to control group. The PDGF level was 10% among the control group while it was more than 85% among the patients with the tracheal stenosis.

PDGF biomarker is efficient in proliferation of mesenchymal cells such as fibroblasts, osteoblasts, tenocytes, vascular smooth muscle cells and mesenchymal stem cells as well as chemotaxis and the directed migration of mesenchymal cells. Expression of PDGF was 8.5 folds higher among stenotic tissue compared to normal trachea. This increase indicated diagnostic value of PDGF. This growth factor could be a target for detection of tracheal stenosis patients.

Keywords: Tracheal stenosis; Immunohistochemistry; PDGF; PCR.

Poster Presentation

1st International Congress of Biomarkers

PN: 1102

Specific biomarkers to manage iatrogenic tracheal stenosis, A narrative review

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ABSTRACT

Iatrogenic Laryngotracheal Stenosis (iLTS) is the most common form of acquired airway stenosis, which occurs in 4–13% of adults and up to 11% of infants following prolonged intubation or tracheostomy. iLTS can develop into a life-threatening condition leading to progressive dyspnea and ultimately airway compromise so should be consider in differential diagnosis of dyspnea.To identify possible biomarkers to assess iatrogenic tracheal stenosis instead of bronchoscopy we gathered the expression of some biomarkers in the scar formation of strictur part of the airways.A comprehensive search strategy using PubMed, Scopus, and Google scholar was performed including iatrogenic tracheal stenosis and biomarker as keywords. In the studies conducted to evaluate biomarkers corresponded to tracheal stenosis, scar tissue isolated from the stricture part of airways have been investigated. Various biomarkers were identified that indicated over or under expression. Kevin M. Motz et al. showed that Glutaminase was overexpressed in scar tissue in iLTS scar fibroblast proliferation. Glutaminase reduced glycolytic storage but had no effect on mitochondrial oxidative phosphorylation. It decreased Col I gene expression and protein production.In other studies, they concluded that the gene expression of collagen I and III, Mucin 5AC, COL1a1, α-SMA, Integrins, Ciliary alpha-1 tubulin, proliferation rate of fibroblasts also decreased, while in other reports, some genes such as cytokine interferon g (INF-g) , transforming growth factor b (TGF-B),(InterLukin-4),InterLuhin17(IL-17), T-Helper2, T-Helper1, chemokine receptor CXCR7, COL1A2, COL3A1, FN1, and MMP9, of IL-6, aSMA, and MMP13 genes were increased. Regarding comorbidities, gene expression in scar tissue was different. Ioan et al, reported that in biopsy samples taken from tracheal scar in diabetic patients, fibroblasts express CD90 (Thy-1) gene more than non-diabetic scar tissue fibroblasts. This article also reported that there is difference in mitochondria metabolites in diabetic compared to non-diabetic scar tissue. Indeed, expression of itaconate, riboflavin, pyridoxine in diabetic patients rise and in contrast acetylcarnitine and 2-aminooctanic acid in non-diabetic patients is higher. Also, in terms of stenotic location, IFN-γ is expressed considerably in iSGS more than iLTS, which can be used as a main biomarker to differentiate these two different airway stenosis. Biomarkers are expressed in serum, airway secretion and resected scar tissue sample and can be employed as prognostic, diagnostic and therapeutic factors.

Keywords: Iatrogenic tracheal stenosis; Biomarkers; Diagnosis.

Poster Presentation

1st International Congress of Biomarkers

PN: 1103

Tracking the Relative Expression and Kinetics of OncomiR-21/Tumor Suppressor miR-34a in Blood Plasma Exosomes as a Gastric Cancer Biomarker

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ABSTRACT

Gastric cancer (GC) is one of the leading causes of death worldwide and accounts for 50% of common cancers in Iran. The highest epidemic of GC in Iran is reported in Ardabil province. GC has no clinical symptoms and is diagnosed in the final stages, which requires the identification of new diagnostic biomarkers. Exosomes as extracellular membrane vesicles have diagnostic and therapeutic purposes in cancer. As molecular regulators, miRNAs play a crucial role in the pathogenesis, drug resistance, and progression of various malignancies, including GC. Among the main up-regulated circulating miRNAs that are also used in the diagnosis of GC are miR-21 and miR-34a. This research was conducted to identify selected miRNAs in exosomes of AGS apoptotic cells under the influence of coumarin concentrations and its effect in inhibiting MKN45-resistant cancer cells in vitro.

LC50 and LC75 in the AGS category were estimated through the MTT test in studying the effect of coumarin. The same concentrations were applied as treatment in AGS, and exosomes were extracted. After standardizing the concentration of exosomes, they were used to resistant MKN45 cells and primary culture. The expression of miRNAs miR-21 and miR-34a in the exosomes of the treatments was measured by the Real-Time PCR method.

The expression level of OncomiR-21 showed a significant decrease, and tumor suppressor miR-34a showed a significant increase in expression. Our in vitro studies have shown relative changes in OncomiR/Tumor Suppressor changes in sensitive and resistant cancer cell lines and primary culture under drug treatment.

This finding was consistent with in silico studies. It seems that tracking the kinetic expression ratio of OncomiR-21/Tumor Suppressor miR-34a in blood plasma exosomes in suspected individuals can be used as a marker of gastric tumor formation with drug resistance.

Keywords: Gastric Cancer Biomarker; OncomiR/Tumor Suppressor; Exosomes.

Poster Presentation

1st International Congress of Biomarkers

PN: 1104

Emerging advances in personalized medicine using exosomes as biomarkers

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ABSTRACT

Tumor cells release extracellular vesicles (EVs) to communicate with each other and the microenvironment around them. Exosomes are becoming more popular as a biomarker for tumor detection, diagnosis, and prognosis mainly due to their accessibility and capacity to mirror their mother cells. Although they have inherent disadvantages, traditional biomarkers have been successfully and widely employed in individualized treatment. Fluorescence in situ hybridization, necessitating a biopsy sample, is the most commonly used method to discover pharmaco-genomically significant sequences. The panorama of genetic aberrations in a single tumor cannot be accurately depicted by a single biopsy, which makes it challenging for clinicians to understand the overall problem. Second, tissue biopsy is invasive, dangerous, and useless for making further diagnostics. Thirdly, the limited specificity of serum biomarkers utilized in current clinical diagnosis may contribute to a lack of diagnostic efficacy. Exosomes have great potential as cancer biomarkers in personalized treatment. Exosomes transmit bioactive substances with extraordinary selectivity, which can help identify and characterize the source cells by revealing their state. Exosomes have a variety of other roles in the development of tumors, such as promoting carcinogenesis, changing the phenotype of cancer cells, and altering the microenvironment of cancer. Additionally, these exosomes respond quickly and acutely to environmental stimuli. Carcinogenesis, tumor growth, and tumor alleviation are correlated with exosome number and molecular composition. Exosomes are released by cancer cells during cancer development to adjust the tumor's microenvironment and participate in each stage of metastasis. Exosomes are intriguing cancer biomarkers in tailored treatment due to their origin-specific profile of contents and a host of other benefits. While the isolation of exosomes is a concerning topic, exosomes have the potential to be a more sensitive and accurate liquid biopsy.

Keywords: Exosome; Biomarker; personalized medicine.

PN: 1106

Evaluation of Ki-67 analytical validity as a prognostic factor in Brest cancer

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ABSTRACT

Despite major treatment advances and earlier diagnosis, breast cancer (BC) is still an important public health issue and a high priority for biomedical research. Hence, determining the prognostic factors of breast cancer is of primary concern. The objective of this study was to estimate the prognostic importance of ki-67, as a marker of cellular proliferation, via its correlation with other tumor clinicopathologic features. In this study, immunohistochemistry (IHC) staining was performed to examine ki-67, P53 status, PR (progesterone receptor), ER (Estrogen receptor), and HER2/neu (human epidermal growth factor receptor-2) in 55 pairs of fresh BC samples and adjacent noncancerous tissue.

Our results show that the expression of ki-67 was positively correlated with the histological grade of tumor, HER2/neu, and P53 status and negatively correlated with PR and ER.

As a result, because BC patients with positive ER and PR tumors have a good prognosis and tumors with positive P53 status, HER2/neu, and higher grade of tumor have a poor prognosis, our findings support the prognostic significance of ki-67 in breast cancer and can increase ki-67's analytical validity in breast cancer.

Keywords: breast cancer; ki-67.

Poster Presentation

1st International Congress of Biomarkers

PN: 1107

The application of digital biomarkers in healthcare services

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ABSTRACT

Over the last decade, digital biomarkers within the healthcare sector are fast increasing. In fact, digital biomarkers are "consumer-generated physiological and behavioral indicators measured by digital health technologies such as portable, wearable, implantable or digestible. The data collected through digital biomarkers are used to predict health-related outcomes, and represent deep digital phenotyping. The purpose of this research is to identify the application of digital biomarkers in healthcare services.

We conducted a literature search on three databases including PubMed, Scopus, and Google Scholar which were investigated from 2005 through Jun 2022. The search was performed using a combination of the following terms; technology, biomarkers, digital biomarkers, healthcare and health outcome. To be included in the review, the intended paper must use digital biomarkers interventions and the language of English. After the full-text review, 11 papers were included in this scoping review.

The digital biomarkers could be used in healthcare services, include six main domains: diagnostic, monitoring, pharmacodynamic/response, predictive, prognostic and susceptibility/risk. The full potential of digital biomarkers can only be accessed by integrating a wide variety of data sources into an electronic repository. The digital biomarkers may provide greater insights into more timely prevention, diagnosis and treatment.

The digitization of healthcare is beginning to revolutionize the way prevent, diagnose, monitor, treat, and manage health conditions. The biomarker capabilities can provide more comprehensive, objective, and continuous pictures of human function in health and disease. The validated novel digital biomarkers can enable healthcare to move from a reactive to a preventive approach.

Key terms: digital biomarkers, healthcare, information technology, monitoring, diagnostic

Poster Presentation

1st International Congress of Biomarkers

PN: 1108

Proline–glycine–proline as a prognostic biomarker for chronic rejection in lung transplantation

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ABSTRACT

Since 2000, lung transplantation has been performed as a therapeutic option for a number of end-stage pulmonary disorders in Iran. Like other countries, due to the high incidence of chronic rejection (CR), the long-term survival of this type of transplantation is inferior compared to other solid organs. CR is morphologically characterized by obliterative bronchiolitis (OB) and clinically by an irreversible decline in forced expiratory volume in FEV_1, named Bronchiolitis Obliterans Syndrome (BOS). It remains the major barrier to long-term survival after lung transplantation that develops in about 50% of recipients after 5 years. Recently, huge amounts of studies implicated on the role of inflammatory biomarkers on the pathogenesis of BOS. Both alloimmune and nonalloimmune damages, including acute rejection (AR), anti HLA Abs, gastroesophageal reflux, primary graft dysfunction (PGD) and respiratory viral infections, are concerned as the causes of BOS. However, the key factor in this scenario is not well documented. In this regard, the role of collagen type V as a target for induction of autoimmune reaction in developing CR is considered. Indeed, proline–glycine–proline (PGP) as a collagen breakdown product in the pathogenesis of lung rejection. It has been shown that after an initial cleavage of collagen by MMP-8 and MMP-9 into smaller fragments, prolyl endopeptidase (PE) is responsible for cleaving this tri-peptide out of the collagen fragments. Due to a structural homology with interleukin-8, PGP can act as a neutrophil chemoatractant via the CXCR1 and CXCR2 resceptors. PGP and PE have been shown to be elevated in lung diseases characterized by chronic, neutrophilic, airway inflammation. Sputum from patients with chronic obstructive pulmonary disease (COPD) or cystic fibrosis (CF) contains increased amounts of PGP and generates PGP from collagen in a PE-dependent manner. Taking into account that PE activity is elevated in BAL fluid of lung transplant patients with chronic allograft rejection that could be postulated for consideration of PE/PGP as important factors in lung transplantation. Finally, this information gives a new prospective role of mediators in the pathophysiology of BOS as a major etiology of induction of CR.

Keywords: lung transplantation; proline_glycine_proline; chronic rejection; survival rate.

Poster Presentation

1st International Congress of Biomarkers

PN: 1110

Avail of biomarkers in pharmaceutical science, posology and drug development

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ABSTRACT

At this moment in time, we determinedly know that robust and validated biomarkers are of pivotal importance in the field of drug discovery, development and accelerated approval of new medicines. They also contribute to more accurate and effective pharmacokinetic& pharmacodynamic considerations in determining therapeutic index to establish a well-defined successful drug regimen and treatment pathway. All the advances and innovative approaches for tailoring disease prevention and treatment has led to us to precision medicine or namely personalized medicine. In sub-category of companion diagnostics, biomarkers; impose indispensable role as assays in classifying patients' eligibility for specific treatment, selection of the most favorable drug candidates, prediction of unwanted adverse reactions and Drug-Drug Interactions, facilitating the cost& time effective process for a drug under development. There is an increasing number of medicinal products authorized in EMA and FDA categorized by the biomarker-drug pair, the first drug is trastuzumab (Herceptin), reaching more than 50 drug in year 2022. As notable examples of aforementioned purposes we can point out, Hemoglobin A_1C for antidiabetic treatment for dose optimization, DCEMRI for the detection of changes in the permeability of tumor vasculature in neoplasia, DAT density imaging as enrichment biomarker in targeting patients with early Parkinsonian symptoms, CSF biomarker PET signal to identify patients with AD for the purposes of enriching clinical trial population and many more from qualified biomarkers to more expertise ones. Above all, the horizon of this topic is Pharmacogenetic Associations shifting the paradigm of pharmacotherapy. Furthermore, effective translation of the preclinical biomarkers into the clinic will pave the way towards effective execution of personalized therapies across complex disease areas for the benefit of patients, healthcare providers and the bio-pharmaceutical industry. In this conphrensive review we debate miscellaneous aspects of unprecedented connection of biomarkers science and drug development systematically in details.

Keywords: personalized medicine; drug development; biomarker drug pair; pharmacogenetics.

Poster Presentation

1st International Congress of Biomarkers

PN: 1111

The NRG1 gene is a novel therapeutic target and diagnostic biomarker for esophageal cancer

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ABSTRACT

Esophageal cancer is not only one of the deadliest cancers but also one of the least studied. Currently, only about 20% of esophageal cancer patients survive at least five years after their diagnosis. Therefore, identifying novel biomarkers for its early detection is of utmost necessity. Furthermore, given the high mortality, it is vital to detect genes that could potentially be used in gene therapy to give patients a higher chance of survival. Consequently, in this study, we aimed to evaluate novel biomarkers for diagnosing and treating esophageal cancers on the mRNA, miRNA, and lncRNA transcription levels.

The 20 genes with the highest mutation frequency in esophageal cancer were downloaded from the cosmic database, and the NRG1 gene was selected as a possible biomarker for esophageal cancer using the GEPIA2 database ($Log_2FC>+1$, p-value <0.05). Using the Venny 2.1 tool, we got the intersection between the down-regulated miRNAs in esophageal cancer from the dbDEMC database (LogFC<-1, adjusted p-value<0.05), and the NRG1 targeting miRNAs from the starBase v3.0 database, as well as the intersection between the miRNAs corresponding LncRNAs from the starBase v3.0 database and the up-regulated esophageal cancer LncRNAs from the Lnc2cancer database. Then, we used the Cytoscape software version 3.9.1 to visualize the LncRNA-miRNA-mRNA network and determine the hub LncRNAs and miRNAs that have key roles in regulating the NRG1 gene. The NRG1 gene and hsa-miR-128-3p had the highest score in the maximal clique centrality (MCC) ranking method.

We have identified the NRG1 gene alongside hsa-miR-128-3p as novel biomarkers for the early diagnosis of esophageal cancer. Given that the NRG1 gene plays a role in inducing the growth and differentiation of epithelial cells, it could be employed in treating this cancer using the CRISPR/Cas9 gene editing system.

Keywords: NRG1; hsa-miR-128-3p; Biomarker; Esophageal cancer.

Poster Presentation

1st International Congress of Biomarkers

PN: 1112

MicroRNAs as Novel Early Detector Biomarkers in COVID-19 via Oxeiptosis Pathway

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ABSTRACT

During viral infection and replication, reactive oxygen species (ROS) are formed, leading to oxidative stress and organs vulnerable to infection. ROS acts as a key signaling molecule in numerous cell death pathways (such as apoptosis, autophagy, and Oxeiptosis). Similar to apoptosis, oxidative stress and pathogen infection can trigger the caspase-independent cell death mechanism known as Oxeiptosis. This newly discovered cell death does not involve any of the known cell death pathways, but it is essential in reducing inflammation caused by ROS. COVID-19 virus, one of the respiratory viruses, makes it challenging for researchers to identify the molecular specifications of infection. Based on recent studies about MicroRNAs as novel early detector biomarkers and rising lethality of this new virus and the oxidative stress it induces in cells, it is urgent that effective ways of containment and treatment be identified.

We used the articles on PubMed, Scopus, web of science, and Google Scholar databases to collect information.

Oxeiptosis is an essential cell death pathway because of its role in many biological processes, including viral infections (especially COVID-19 as the future pandemic) and inflammation. KEAP1 (intracellular ROS sensors), AIFM1 (proapoptotic factor), PGAM5 (phosphatase), and NRF2 (translation factor) have been identified as the primary components in this signaling pathway, therefore microRNAs (miRNAs) affecting them play a significant role in this cell death. As biomarkers in this disease, Mir-28 which reduces an oxidative stress suppressor protein named NRF-2, or miR-626, a Keap1-targeting microRNA, that protects cells from oxidative injury, can be used as invaluable tools.

This concept reviews the important molecules and signaling pathways that have been shown to be involved in this cell death and also explains how scientists can use these molecules and microRNAs affecting them as biomarkers to monitor and treat COVID-19 patients.

Keywords: MicroRNAs (miRNAs); Oxeiptosis; COVID-19; biomarker; early detector.

Poster Presentation

1st International Congress of Biomarkers

PN: 1113

Evaluation of Radiation and Ammonium Lactate Effects on Hyaluronic Acid Expression as a Pro-cancerous Factor in Supernatant and Exosome Isolated from Supernatant of Primary Mouse Fibroblast Cell Culture

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ABSTRACT

Previous studies show that aberrant synthesis of Hyaluronan accelerates tumor growth, angiogenesis, and metastasis. The fibroblasts are probably responsible for most of the hyaluronic acid (HA) accumulation in tumor microenvironment after radiotherapy. Our goal is to investigate and compare radiation and lactate effects on HA levels in supernatant and exosome isolated from supernatant of primary mouse fibroblast cell culture.

Fibroblast cells were prepared from skin of C57BL6 mouse. These cells were divided into three groups (no treatment, cells treated with 10 mM ammonium lactate, and irradiated cells). Then supernatant was harvested from FBS-free culture media after 48 h. Exosomes were purified by differential centrifugation (300 × g for 10 min, 2000 × g for 30 min, 16500 g for 30 min) and were pelleted by ultracentrifugation (150,000 × g for 180 min). Size of exosomes was determined using a Zetasizer. HA concentration measured using a HA ELISA Kit. Data were analyzed using one-way ANOVA.

There was a significant increase in HA-coated exosomes isolated from supernatants of irradiated cells compared to untreated cell and cells treated with 10 mM ammonium lactate ($P < 0.001$). As well, there was a significant increase in the HA concentration in the supernatants of cells treated with 10 mM ammonium lactate relative to untreated cells and irradiated cells ($P < 0.05$).

It seems that routine radiation therapy leads to massive shedding of HA-coated exosomes by normal fibroblast cells and thus exosomes-HA may contribute to tumor promotion and induce of the premetastatic niche.

Keywords: Exosomes; hyaluronic acid; radiation.

Poster Presentation

1st International Congress of Biomarkers

PN: 1114

Correlation of organochlorines with HLA and CD117 levels in acute myeloid leukemia

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ABSTRACT

Acute myeloid leukemia (AML) is a malignant clonal blood disease that is associated with the accumulation of immature myeloid cells and disruption of normal hematopoiesis. Some HLA alleles, as effective immunogenetic factors, can play a role in susceptibility or resistance to leukemia. In addition, organochlorines are one of the most important environmental predisposing factors that cause AML. The aim of this study was to investigate the relationship between the expression of HLA, CD markers, and the level of organochlorines in patients with AML.

174 patients with AML from Afzalipour Hospital in Kerman were considered as the patient group and 232 healthy individuals who did not have any underlying disease were considered as the control group. The concentration of organochlorines were measured by gas chromatography (GC). PCR-SSP method was used to determine HLA-A,-B,-DRB1 alleles. CD markers were analyzed using flow cytometry.

The results showed that the expression of HLA-A*11 and HLA-DR alleles were higher in AML patients than in the control group. Also, the level of organochlorines including DDT, DDE, and HCH was significantly higher in the patient group. In addition, the results showed that individuals who have a high level of organochlorines are associated with increased expression of HLA-A*11, HLA-DR, CD33, and CD117. Therefore, according to the obtained results, it can be said that exposure to organochlorines may be associated with an increase in factors predisposing to leukemia, including CD markers 117, 33 and HLA-DR. Finally, exposure to organochlorines may increase the incidence of leukemia by 2.8-Fold (AOR=2.8, Cl%95= 1.11-5.64, p = 0.02).

Keywords: Organochlorine pesticides; HLA; CD33; CD117; AML.

Poster Presentation

1st International Congress of Biomarkers

PN: 1115

Pretreatment with Selenium alleviate inflammatory response in renal ischemia-reperfusion injury; the role of NF kB

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ABSTRACT

Inflammation plays a significant role in renal ischemia-reperfusion injury (RIRI). The aim of this study was to evaluate the efficacy of Selenium pretreatment in protecting the kidneys against ischemia-reperfusion injury. Twenty male Wistar rats (200±20 g) were divided into four groups (five per each): 1- Sham (surgery without renal pedicle clamping), 2- Sham-Se (0.5 mg/kg selenium for 7 consecutive days, *ip*), 3- RIRI (ischemia was induced by 40 minute clamping the renal pedicle) and 4- IRIR-Se (0/5 mg/kg selenium for 7 consecutive days before I/R induction). All animals were killed 24h after I/R induction. Blood and tissue sample were collected for biochemical (plasma BUN & Cr) and western blot (NF-Kb) analyses.

The results showed that selenium pretreatment significantly improved ischemia-reperfusion induced renal dysfunction ($P<0.05$) and decreased the Nf-Kb content ($P<0.05$) of the kidney tissue.

Pretreatment with selenium significantly mitigates renal ischemia-reperfusion injury, probably due to its potent anti-inflammatory effects.

Keywords: Ischemia-reperfusion injury; Selenium, NF-Kb; Anti-inflammatory; Renal.

Poster Presentation

1st International Congress of Biomarkers

PN: 1118

Biomarkers in Alzheimer's disease – review

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ABSTRACT

Alzheimer's disease (AD) is known as a chronic neurological disease characterized by the accumulation of hyperphosphorylated tau and amyloid beta plaques in the brain. The pathophysiology of Alzheimer's disease involves chronic inflammation involving innate immune cells (such as astrocytes, microglia, and other specialized cells). In 2020, about 50 million people have been diagnosed with Alzheimer's disease. Alzheimer's often occurs in people over 65 years of age, but about 10% of patients develop early-onset Alzheimer's and are diagnosed between the ages of 30 and 60. So far, there is no known way to stop or prevent AD progression, but some treatments help improve the disease's symptoms. Inflammatory mediators such as cytokines and complements are also associated with the pathogenesis of Alzheimer's disease. Some methods, such as basic science studies, neuroimaging, biomarkers, etc., provide key insights into the factors that may drive the selective vulnerability of different brain networks to understand AD. Biomarkers are molecules that include different types of molecules, such as genes, proteins, etc., which are a sign of a condition or disease and can be considered for early diagnosis of AD, such as non-invasive and accessible environmental inflammatory biomarkers. Cerebrospinal fluid (CSF) is a possible source of neurological disease biomarkers due to its direct contact with the brain, and the molecular composition of CSF can reflect biochemical changes in the brain. CSF collection is invasive and poses limitations. Plasma tau levels are a possible source of biomarkers. Plasma Aβ levels can have diagnostic value in AD. In this review, we introduce AD-related biomarkers, discuss their possible molecular mechanisms, and summarize the latest research status of biomarkers in clinical practice and molecular diagnosis. This review provides an updated and new perspective on biomarkers for early detection of AD during AD pathogenesis.

Keywords: Alzheimer's disease; biomarker; Inflammation; precision medicine.

Poster Presentation

1st International Congress of Biomarkers

PN: 1119

Biomarkers in cardiac disease- review

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ABSTRACT

Cardiovascular diseases (CVD), such as ischemic heart disease, are the leading cause of death worldwide and contribute significantly to socioeconomic health costs and the global burden of disease. For quick and efficient diagnosis and prediction and prognosis of this disease, a lot of effort has been made to obtain new tools in research. Although many advances have been made in the diagnosis of CVDs, there is an important need to design new diagnostic methods for early and more effective diagnosis. Cardiovascular disease is usually diagnosed based on signs and symptoms depending on CVD-related biomarkers or molecular imaging (MI). A biomarker is an index to measure the severity or presence of a disease. In short, biomarkers are factors that can be used to determine the disease or physiological state of an organism. In the past decades, several genetic and clinical and even observational studies have conclusively demonstrated the significant role of circulating biomarkers in the classification, diagnosis, prediction, risk, and management of CVD. For example, RPs are recognized as biomarkers for predicting adverse cardiovascular events in CVD due to their association with specific inhibitors of the P2Y12 receptor or long ncRNAs (lncRNAs) or other molecules. Also, nanomaterials such as carbon nanotubes and gold nanoparticles are new sources for cellular response in CVDs. In this review, we first introduce the types of biomarkers and then discuss the new and innovative perspectives on the use of biomarkers in CVD.

Keywords: Cardiac disease, Biomarker, Regenerative medicine, Efficient diagnosis

Poster Presentation

1st International Congress of Biomarkers

PN: 1120

Investigating the power of regional pro-adrenomedullin in determining the prognosis of patients with Covid-19: A systematic review

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ABSTRACT

Novel coronavirus disease 2019 (COVID-19), a disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, is a major threat to global health. As of August 14, 2022, the death toll from Covid-19 was 6.44 million. Adrenomedullin (AM) is a bioactive vasodilator peptide that exhibits anti-inflammatory and tissue-protective effects. ADM has been shown to play a key role in reducing vascular (hyper) permeability and promoting endothelial stability and integrity following acute infection.

This study aims to investigate the role of adrenomedullin as a biomarker in determining the prognosis of people with covid-19.

In this systematic review study, we used keywords to search: biomarker, covid-19, adrenomedullin and extracting similar words from the Mesh database, and searching in databases: Pubmed, Google scholar, Scopus, Sid until date10 Aug 2022 was performed. The entry criteria were original articles. The exclusion criterion was the lack of access to the full file of the articles.

We identified 9 studies in this systematic review. Which included 964 patients with covid-19 and hospitalized. In the studied society, there was no equality between men and women, but all people were between 54 and 76 years old. All these studies measured adrenomedullin levels every seven days and 4 times. The average ratio of adrenomedullin among the dead to the living people was approximately 1.7. The level of ADM in the living was 1.03 pg/ml on an average of 4 times, and among the dead, their average was 1.734 pg/ml. Among the other markers that are used in the diagnosis of Covid-19, adrenomedullin expresses the highest power in determining the severity of the disease and the death of people with severe symptoms.

Keywords: Adrenomedullin (ADM); Covid_19; Biomarker.

Poster Presentation

1st International Congress of Biomarkers

PN: 1121

FGF19 can be used as a new biomarker for prostate cancer diagnosis

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ABSTRACT

Prostate cancer is the most common malignant neoplasm in males and the 6th-most-prevalent cause of cancer mortality worldwide. There is broad evidence that fibroblast growth factor (FGF) are important in prostate cancer initiation and progression, But the contribution of FGFs in this disease for diagnosis is not fully understood. Therefore, this study was conducted to investigate the biomarker potential of FGF23, FGF19, FGF15.

This case-control study included 40 patients with PC and 40patients with benign prostatic hyperplasia (BPH). Blood were collected from the participants and centrifuged. Then its serum was separated and frozen at -80 until the parameters were analyzed. We evaluated serum levels of FGF23, FGF19, FGF15, prostate-specific antigen (PSA) by ELISA. Also, we used Student's t-test and receiver operating characteristic (ROC) analysis to evaluate the data.

Serum concentrations of FGF19 and PSA were significantly higher in patients with PC, compared with the BPH group (P <.05). However, serum concentrations of FGF23 and FGF15 was not significant between the two groups (P >.05). Also, the results showed that FGF19 has good specificity (60%) and sensitivity (88%) for diagnosing prostate cancer.

Based on the obtained results, FGF19 can be used as a biomarker for prostate cancer diagnosis. Although more studies are needed.

Keywords: prostate cancer; fibroblast growth factor; prostate-specific antigen; ELISA.

Poster Presentation

1st International Congress of Biomarkers

PN: 1122

Candidate miRNAs in Human Breast Cancer Biomarkers: A Systematic Review

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ABSTRACT

Breast cancer (BC) is the most prevalent cancer and the main cause of cancer deaths among females around the world. For early diagnosis of BC, there would be an immediate and essential requirement to search for sensitive biomarkers. To identify candidate miRNA biomarkers for BC, we performed a general systematic review regarding the published miRNA profiling researches comparing miRNA expression level between BC tissues and normal tissues. A miRNA ranking system was selected, which considered frequency of comparisons in direction and agreement of differential expression. We determined that two miRNAs (mir-21 and miR-210) were upregulated consistently and six miRNAs (miR-145, miR-139-5p, miR-195, miR-99a, miR-497 and miR-205) were downregulated consistently in at least three studies. MiR-21 as the most consistently reported miRNA was upregulated in six profiling studies. Although these miRNAs require being validated and further investigated, they could be potential candidates for BC miRNA biomarkers and used for early prognosis or diagnosis.

Key words: breast cancer; microRNA; biomarker; microarray.

Poster Presentation

1st International Congress of Biomarkers

PN: 1123

PD-1 and PD1-L as biomarkers for personalized medicine

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ABSRTRACT

Personalized medicine, also acknowledged as individualized therapy, basically encompasses the prescription of specific treatments and therapeutics best intended for an individual that impact response to therapy based on genetic and environmental factors.

PD-1 (Programmed cell death protein 1, or CD279) is an immune checkpoint. When PD-1 is bound to another protein called PD-L1, it helps keep T cells from killing other cells, including cancer cells by two mechanisms. First, it promotes apoptosis (programmed cell death) of antigen-specific T-cells in lymph nodes. Second, it reduces apoptosis in regulatory T cells (anti-inflammatory, suppressive T cells). Currently, anti-PD-1 or anti-PD-L1 antibodies are a class of medicines used in the treatment of different types of cancers.

The level of expression of PD1 and PD-L1 has the potential to inform the selection of patients to receive anti-PD-1 or anti-PD-L1 antibodies, and it provides some perspective on how to use these two proteins as biomarkers for the future treatment of patients with cancer.

Keyword: PD-1; PD1-L; biomarkers; personalized medicine

Poster Presentation

1st International Congress of Biomarkers

PN: 1124

Important Virological biomarkers for Serological diagnosis of viral infectious diseases

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ABSTRACT

In the chase of improved diagnostic tests for infectious diseases, some classes of molecules being widely investigated as prospective biomarkers. Biomarkers should be molecules that can be found in all fluids, tissues and most types of cells in the body. Viral biomarker test, is a blood test wherein the samples are tested for viral contagions to confirm the presence of viral infections. A viral biomarker test is basic to identify viruses that cause a range of viral infections, such as viral fever, Hepatitis B, Hepatitis C, HIV, and other viral illnesses. Conventional laboratory tests include *in vitro* culture and isolation, protein-based assays (for example the measurement of different antibodies which are produced against different parts of the virus, or assayment of released antigenic parts of the virus that play a crucial role in its pathogenesis), microscopy (histological, pathological, and morphological assays), mass spectrometry and molecular diagnostics which uses nucleic acid-based assays such as quantitative PCR ,sequencing and microRNAs (miRNAs).Many of these methods require significant time, careful sample preparation, and expert users to perform, and are affected by technical limitations. Diagnostic tests may be carried out with acceptable criteria, but produce a wrong response that cause a false positive or false negative, which can be due to low sensitivity or specificity of the method or failure to correctly follow the criteria for collecting the sample from the patient. Selection of correct viral biomarker and laboratory method will lead to the successful treatment of infectious diseases.

Keywords: Virological biomarkers; Serological diagnosis; Viral infectious diseases

Poster Presentation

1st International Congress of Biomarkers

PN: 1127

Role of CD24 in COVID-19: Potential marker of Immune System Balancing

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ABSTRACT

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) results in systemic inflammation by directly lysing infected epithelial cells in the lung, releasing damage-associated molecular patterns, and triggering a pro-inflammatory cytokine milieu. The phrase "cytokine storm" refers to a group of immune system illnesses characterized by systemic inflammation and organ dysfunction. For the alleviating hyper-activated immune response and inflammation due to SARS-CoV2, several efforts have been performed. Nevertheless, anti-viral and anti-inflammatory medicines have had poor therapeutic effectiveness. Thus, there are urgent need to novel anti-inflammatory agent for treatment of several inflammatory diseases. Several previous studies have found a correlation between inflammation and damage, through damage-associated molecular patterns (DAMPs) which play an important role in the pathology of severe COVID-19. On the other hand, it has been revealed that CD24 has been linked to a number of DAMPs, including high mobility group box protein 1, nucleolins, and heat shock proteins. Therefore, CD24 has been linked to inflammation and cytokine storms, and it can suppress inflammation by several mechanisms. Moreover, CD24 has a role in T cell homeostatic proliferation and several autoimmune diseases. In the present study, we review the potential anti-inflammatory role of CD24 in inflammatory conditions and autoinflammatory diseases.

Keywords: COVID-19; Cytokine Strom; CD24; Severe Acute Respiratory Syndrome Coronavirus 2

Poster Presentation

1st International Congress of Biomarkers

PN: 1128

The effects transforming growth factor beta on remyelination improvement in multiple sclerosis model

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ABSTRACT

Multiple sclerosis (MS) is a demyelinating autoimmune disease of the central nervous system with symptoms such as neuroinflammation, demyelination and axonal degeneration. Mesenchymal stem cell condition medium (MSC-CM) contain trophic factors such as transforming growth factor beta (TGF-β) have immunomodulation and neuroprotection properties. The goal of this study is to investigate the impact of MSCs supernatant injection on remyelination processes in the corpus callosum of the cuprizone demyelination mice as a model of multiple sclerosis.

In this study, 15 mice were divided to three groups include control (without any treatment), cuprizone and MSC-CM treatment. For the induction of a chronic demyelination model, C57BL6 mice were fed with chow containing 0.2% cuprizone for 12 weeks. For MSC-CM preparation, after the third passage, when MSCs reached 60-70% density, the cells were trypsinized and washed three times with PBS to completely removed FBS and centrifuged. Then the cells were poured into the flask and culture medium free of FBS. After 24 hours, the mesenchymal stem cells supernatant was collected and then, the cell soup was filtered using a 0.22 micrometer filter and about 2 microliters of it was injected into the right lateral ventricle of the cuprizon mice by a stereotaxic device. After 2 weeks, the mice were killed. Remyelination was evaluated by Luxol fast blue (LFB) staining and transmission electron microscope (TEM). The specific genes of MSC-CN include TGF-β were evaluated by a quantitative real-time polymerase chain reaction (RT-PCR). According to the results of molecular analysis, MSC-CM was contain trophic factors such as TGF-β compared to other groups. The oligodendrocytes population increased significantly in MSC-CM group in comparison with the cuprizone mice. MSC-CM injection increased levels of remyelination compared with the cuprizone group, as confirmed by LFB staining and TEM analysis.

These results revealed that transplanted MSC-CM contain trophic factors such as TGF-β increased the oligodendrocytes population by enhancing remyelination in the corpus callosum of the cuprizone demyelination model of MS.

Keywords: TGF-β; Mesenchymal stem cells; Multiple sclerosis; Supernatant.

Poster Presentation

1st International Congress of Biomarkers

PN: 1129

Recombinant Subunit of Spike Protein as a Vaccine candidate, induces humoral and cellular immune responses against SARS CoV-2

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ABSTRACT

Due to the spread of the corona virus all over the world, vaccines were developed to prevent this virus. If a vaccine can stimulate cellular and humoral immunity, it can be said that the vaccine is successful in combating and preventing infection. To evaluate the stimulation of the immune response, biomarkers were monitored. These biomarkers are including IgG (humoral immune system) and CD4 & CD8 markers (cellular immune system). In this study, our aim is to stimulate the immune response by the recombinant protein synthesized as a vaccine candidate and evaluate the biomarkers for the effectiveness of the produced vaccine.

Both bioinformatics and in vitro methods were used. In silico tools were used to design spike-based subunit recombinant proteins (rRBD). Molecular docking of rRBD-ACE2 was performed by Auto Dock. These protein was synthetized and purified. Then approval test including: SDS-PAGE electrophoresis, Western Blot, LAL test, Circular dichroism (CD) spectroscopy and ELISA was performed. Checked for their ability to be identified by the anti-SARS CoV-2 antibodies by exposing them to COVID-19 serum and vaccinated samples as a biomarker for COVID-19 detection. The protein was also injected into mice, rabbits and Guinea pig. Stimulation of the humoral and cellular immune system were assessed by ELISA (antibody) and IHC (CD4 & CD8 marker). The antibody titer was measured to assess their neutralization efficiency (VNT). Histological studies were performed to rule out complications of rRBD injection.

The anti-spike antibody titer were increased in the animals injected with recombinant protein. In evaluation of humoral immune system, Antibody *titer* rapidly increased and remained for a long time. The VNT results revealed that the produced antibodies (IgG) could neutralize the cultured live virus. Also, the cellular immune system (CD4 & CD8 marker) was significantly stimulated. The antibody was detected in 50 patients and 70 vaccinated sample using ELISA method.

Subunit vaccines could also be considered as robust tools for effective vaccination against COVID-19. Using a combination of in silico, in vitro and in vivo experiments, it was shown that the injection of spike-based recombinant proteins could stimulate humoral and cellular immunological responses against SARS CoV-2. Furthermore, the recombinant protein also could be used as a biomarker for accurate detection of antibodies in the serum of COVID patients.

Keywords: SARS CoV-2; Spike Protein; Vaccine; Humoral Immunity; Cellular Immunity; COVID Biomarker.

Poster Presentation

1st International Congress of Biomarkers

PN: 1132

Antitumor effects of chitosan -*Campylobacter jejuni* supernatant nanoparticles on colorectal cancer: Preparation and characterization

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ABSTRACT

Colorectal cancer (CRC) is one of the most common malignant cancer and the second leading cause of cancer-related death worldwide. Considering all facts about CRC this study evaluates a chitosan based nanoparticle consisting of supernatant of *Campylobacter jejuni* on the expression of *bcl2*, as a key pro-survival gene of the apoptosis pathway and *gli2* gene, as a main activator of hedgehog signaling pathway, which is involved in the self-renewal of colon cancer stem cells (CCSCs) on Caco2 cell line.

Chitosan NPs were synthesis by ionic gelation method. *C.jejuni* culture supernatant were prepared and loaded on CS NPs, and then characterized by dynamic light scattering (DLS), Scanning electron microscope (SEM) and Zeta potential. Chitosan -*Campylobacter jejuni* supernatant nanoparticles toxicity and apoptosis were detected by MTT assay as well as the expression of *bcl2 and gli2* genes by real-time PCR method.

In current study we observed Cs-*Cj* sup NPs with an average size of 159.7 nm and a zeta potential of -11.6 mv and suitable SEM morphology with an Entrapment efficiency of 59% at a concentration of 15 µg/ml significantly increased apoptosis of cancer cells via decreasing expression level of *gli2* and *bcl2* genes as compared to the control group.

These results open a new window for colorectal cancer treatment with the concept of anti-cancer therapy by chitosan -*Campylobacter jejuni* supernatant nanoparticles.

Keywords: Colorectal cancer; *Campylobacter jejuni*; Nanoparticles.

Poster Presentation

1st International Congress of Biomarkers

PN: 1133

Biomarkers in dental diseases – review

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ABSTRACT

Most of the world's population is affected by dental caries as a very common multifactorial infectious disease. Pathological diagnosis in the early stages can significantly affect the patient's discomfort, prognosis, therapeutic intervention, survival rate, and recurrence. A biomarker is a biological indicator of natural or pathogenic processes, and the identification of biomarkers is useful for the prevention, diagnosis, and prognosis of diseases, as well as for monitoring the progress of pathological disorders. Some molecules found in biological fluids and oral environments, such as RNA, lipids, proteins, metabolites, and even microbes, can act as biomarkers. Pathological diagnosis in the early stages can significantly affect the patient's discomfort, prognosis, therapeutic intervention, survival rate, and recurrence. Saliva has many biomarkers that can be used in the early diagnosis of tooth decay. For example, IL-2-RA, IL-13, IL-4, and eotaxin/CCL11 were identified as potential salivary biomarkers for non-invasive caries detection. In this study, we perform a systematic review on the introduction of biomarkers and their potential use in dental caries.

Keywords: Dental; Biomarker; Dental disease; Salvia.

Poster Presentation

1st International Congress of Biomarkers

PN: 1135

Comparison of IgG Serum Levels in Oral Lichenoid Lesions Before and After Treatment with Corticosteroids

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ABSTRACT

Lichen planus, is considered as a premalignant condition with an unknown etiology. The present study aimed to determine the IgG serum levels in different oral lichenoid lesions before and after treatment with topical corticosteroids.

Two groups of 23 individuals, including oral ulcerative lichenoid lesions patients (OULP) and healthy ones were evaluated. Biopsy was carried out while VAS (Visual Analog Scale) was used for an evaluation of symptoms. By applying local corticosteroids, IgG serum levels were determined before, three weeks after, and at the end of the study (9 weeks) with ELISA and turbidimetry methods respectively.

While IgG serum level was significantly higher before the intervention (p=0.01), it was decreased significantly in the case group after treatment (p=0.02). In addition, pain intensity was reduced significantly in the case group (p=0.05).

The level of serum IgG in patients with OULP is higher than in the control group, IgG serum level and pain severity were effectively decreased among the treated with topical corticosteroids. If these results are confirmed by further studies, it can be used to identify the etiology of lichen planus, which is a premalignant lesion, and with further research on other treatments that can reduce this biomarker, it can also be used to treat lichen planus.

Keywords: IgG; Topical steroids; Oral lichenoid lesions; Visual analog scale.

Poster Presentation

1st International Congress of Biomarkers

PN: 1136

Evaluation of the effect of Chitosan nanosystems carrying the culture supernatant of probiotic bacteria *Lactobacillus acidophilus* and *Bifidobacterium bifidum* on the expression *β-catenin* involved in colorectal cancer

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ABSTRACT

Colorectal cancer (CRC) is one of the common gastrointestinal cancer worldwide. Probiotics, as non-pathogenic and useful microorganisms in the digestive system, have shown good anti-cancer effects in treatment. This study aimed to evaluate the anti-proliferative effects of chitosan nanoparticles (CS NPs) carrying the culture supernatant of probiotic bacteria *Lactobacillus acidophillus* and *Bifidobacterium bifidum* on the expression of *β-catenin* gene of Wnt signaling pathway of colorectal Cancer.

The supernatant of *L.acidophillus* and *B.bifidum* were prepared and encapsulated in chitosan nanoparticles (Ch-NPs). Characterization of nanostructure was carried with dynamic light scattering (DLS), scanning electron microscope (SEM) and Zeta potential. The effects of *L.acidophillus* and *B.bifidum* supernatant and CS NPs on the viability and proliferation of cancer cells were evaluated via MTT assay following with real time PCR method. Analysis showed that the average particle size of CS NPs- *L.acidophillus* and *B.bifidum* supernatant were 478.6 nm and 566.9 nm respectively, Zeta potential of *L.acidophillus* was -8.9 mV and *B.bifidum* was -5.3 mV with suitable SEM morphology. *L.acidophillus* and *B.bifidum* led to decrease β-*catenin* expression of Wnt signaling pathway. The use of probiotics bacteria supernatant with nanoparticles as an effective drug prevents the development of colorectal cancer and also the growth of cancer cells, therefore the survival of colon cancer patients increases significantly.

Keywords: Colorectal cancer; *Lactobacillus acidophilus; Bifidobacterium bifidum;* Probiotic; Chitosan nanoparticles.

Poster Presentation

1st International Congress of Biomarkers

PN: 1137

Comparison of serum and salivary folate levels in patients with oral squamous cell carcinoma

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ABSTRACT

Oral cancer is the sixth most common cancer in males and the fifteenth in females. Folate is essential for maintaining normal function of nucleotide synthesis and DNA methylation. Disruption of folate metabolism can lead to abnormal cell activity and proliferation .The aim of this study was to compare the serum and salivary levels of folate in patients with oral squamous cell carcinoma (SCC) with healthy subjects. In this cross-sectioned study, 30 patients with oral SCC referred to oral and maxillofacial department and 30 healthy individuals were studied. Two cc saliva and 5cc venous blood were taken from participants and were evaluated with Human Folate ELISIA Kit. Independent T test and Pearson correlation coefficient was used and statistical analysis was done using SPSS 17. The result was considered to be significant if the P-value was less than 0.05. Serum folate levels in patients with oral squamous cell carcinoma (8.18 ± 4.37 ng/mL) were significantly lower than healthy subjects (10.61±5.79 ng/mL) (P=0.005). It was also found that folate levels in saliva were significantly lower in patients with squamous cell carcinoma (1.13 ± 1.32 ng/mL) than healthy subjects (2.84 ± 4.40 ng mL) (p= 0.029). Serum folate levels in patients with oral SCC (r_p=0/135, P = 0/006) and healthy controls (r_p=0/133, P = 0/003) were correlated with salivary folate levels. Since the levels of serum and salivary folate in patients with oral squamous cell carcinoma were significantly lower than that of healthy individuals, low folate levels are likely to be associated with oral SCC. Also, it might be possible to use salivary samples instead of a serum to check the folate level as a non-invasive method.

Keywords: Biomarkers; Folic acid; Saliva; Squamous Cell Carcinoma of Head and Neck.

Poster Presentation

1st International Congress of Biomarkers

PN: 1138

Non-coding RNAs as a therapeutic option in lupus erythematosus

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ABSTRACT

Autoimmune diseases are a type of chronic disorder in which the immune system destroys cells in the body as a result of a loss of tolerance to self-antigens. One of the most well-known examples of these diseases is systemic lupus erythematosus (SLE), which is distinguished by the production of autoantibodies in various body parts. Although the cause of SLE is unknown, genetic and environmental factors may influence disease progression. While twin studies provide sufficient evidence for genetic involvement in SLE, other phenomena such as metallization, histone modifications, and changes in the expression of non-coding RNAs (ncRNAs) also suggest the involvement of epigenetic factors in this disease. Among all epigenetic changes, ncRNAs appear to play the most important role in the pathogenesis of SLE. The ncRNAs are classified into two types based on their length and size: microRNA and long non-coding RNA (lncRNA). SLE pathology is associated with dysregulations in microRNAs such as miR-181, miR-146, miR98, and mir155, as well as lncRNAs such as GAS5, NEAT1, TUG1, and lnc-DC. Overall, understanding the role of these two groups of ncRNAs in SLE pathophysiology provides a better understanding of the disease. It also opens up new avenues for the development of targeted therapies for this disease.

Keywords: Auto-immune disease; Autoimmunity; systemic lupus erythematosus; non-coding RNA; Micro RNA; Lnc-RNA

Poster Presentation

1st International Congress of Biomarkers

PN: 1139

The impact of COVID-19 on diagnostic biomarkers in neuropsychiatric and neuroimmunological diseases: A review study

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ABSTRACT

Coronavirus disease 2019 (COVID-19) is an infectious respiratory disease, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Evidence-based emerging reports of neurological manifestations show that SARS-CoV-2 can attack the nervous system. However, little is known about the biomarkers in disease in neuropsychiatric and neuroimmunological disorders. One of the vital keys in management of COVID-19 is the accurate diagnosis for effective treatment, and subsequent prevention. Traditionally, biomarkers provide valuable information in the early detection of disease etiology, diagnosis, further treatment and prognosis. Moreover, ongoing investigations on hematologic, biochemical and immunologic biomarkers in non-severe, severe or fatal forms of COVID-19 patients provide an urgent need for identification of clinical and laboratory predictors. In addition, several cytokines acting through mechanisms to emerge immune response against SARS-CoV-2 infection are known to play a major role in neuroinflammation. Considering the neuroinvasive potential of SARS-CoV-2 via direct and indirect pathway, which can be capable of triggering a cytokine storm, in this review the current evidence on existence of close interactions between SARS-CoV-2 infection and possible impairment in the immune, nervous, and endocrine systems, results in alternations in psycho-neuroendocrine-immune (PNI) circuits are discussed. We also highlight the hematologic (such as NLR, PLR, and CRP), biochemical and immunologic biomarkers (such as IL-6 and IL-8) in COVID-19 diagnosis. We will also address insights into COVID-19 prognostic biomarkers in patients with in neuropsychiatric and neuroimmunological diseases. The valuable information obtained from biomarkers represents further treatment and prognosis of development of COVID-19 among neurological disorders.

Keywords: COVID-19; SARS-CoV-2; Neuropsychiatric; Neuroimmunological diseases; Biomarkers.

Poster Presentation

1st International Congress of Biomarkers

PN: 1140

Combined hydroalcoholic extract of *A. Vera* and copper oxide nanoparticles possess more cytotoxic effect against K562 cell line

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ABSTRACT

In recent studies, anticancer effects of *Aloe vera*and copper oxidenanoparticles (CuO NPs) have been documented.Here, we tested whether combining of the hydroalcoholic extract of *A. vera* and CuO NPs could provide synergistic cytotoxicity against K562 cell lines and peripheral blood mononuclear cells (PBMC).The K562 cells or PBMCs (1×10^5 cells/100 µl/well) were incubated for 24 h with serial dilution of Aloe vera extract (0, 20, 40, 60, 80, 160 and 320 mg/ml) or serial dilution of CuO NPs (0, 50,100,200 and 400 µM) .At end time of incubation, the survivability present of cells was determined by MTT methods.In another experiments, The K562 or PBMC cells were treated with combination of Aloe vera extract and CuO NPs at minimal cytotoxic concentrations and the inhibitory present was calculate.The hydroalcoholic extract of *A. vera*and CuO NPs had cytotoxic effects against K562 cell line in a dose dependent manners. Unlike *A.vera,*the marginal safety of CuO NPs is low because the IC_{50} value of the CuO NPs against K562 cell linehad not significant difference compared to theIC_{50} value of the CuO NPs against PBMCs.Moreover, combined treatment with minimal cytotoxic dosesprovided synergistic benefits and lead to more cytotoxic effect against K562 cell line than their individually treatment of K562 without any additive cytotoxic effect against PBMCS.As a result, this combination provide more favorable cytotoxicity against K562cell line without any additive cytotoxicity against PBMCs.

Keywords: K562; Copper oxide nano particle; *Aleo Vera.*

Poster Presentation

1st International Congress of Biomarkers

PN: 1141

Downregulation of BCL-2 gene expression in MCF-7 cells after treatment with resveratrol and carboplatin

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ABSTRACT

Breast cancer (BC) is one of the major prevalent cancer among women. Various treatment options are available for BC. But, successful treatment is not fully obtained. Accordingly, study the new treatment options effects of resveratrol and carboplatin in BC cells (In-vitro). The MTT assay were utilized for evaluating the single and double treatments of carboplatin and resveratrol after 48 h treatment time. The BCL-2 gene expression level was evaluated by real time PCR method. The growth inhibitory effects were observed in double combinations versus single therapies ($P<0.05$). BCL-2 were downregulated in double combinations in compared to single therapies and uninduced cells ($P<0.05$). These results showed that, the combinations of carboplatin and resveratrol induced significant anti-proliferative effects in BC.

Key words: Resveratrol, Carboplatin, Breast cancer

Poster Presentation

1st International Congress of Biomarkers

PN: 1142

Boosting the Anti-cancer Effect of HSP-90 inhibitor by combination with Thymoquinone in HT-29 cancer cells

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ABSTRACT

The resistance to various chemotherapeutic drugs considered as major obstacle in colorectal cancer therapy. In this regard new therapeutic options should be studied. So, in this study, the effects of Thymoquinone (TQ) in combination with NVP-AUY922 as HSP90 inhibitor in colorectal cancer cell (HT-29 cells) was evaluated. HT-29 cells were cultured and treat with Thymoquinone and NVP-AUY922 in various doses for 24 hours. Then, cell viability assay was performed. Furthermore, in combinations, various concentrations of both agents examined using cellular viability analysis.

The TQ significantly decreased cellular viability in combination to NVP-AUY922 in colorectal cancer cell line. Treatment with TQ could enhance the cytotoxicity of NVP-AUY922 in HT-29 as compared to NVP-AUY922 alone ($p<0.05$).

Our results proposed the anti-proliferative effects of TQ and NVP-AUY922 by cytotoxic pathway and cell death induction.

Keywords: Thymoquinone; Colorectal cancer; HSP-90 inhibitor.

Poster Presentation

1st International Congress of Biomarkers

PN: 1143

Hematological Parameters as Predicting Factors for Severity of COVID-19

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ABSTRACT

Coronavirus disease 2019(COVID-19), which is the pandemic of 21st century, is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Prognostic factors play an essential role in predicting the patients who need more care. Therefore, the current study aimed to investigate the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) ratio as discriminated indexes in prognosis of patients with COVID-19. Age, NLR, PLR, white blood cell (WBC), neutrophil count, lymphocyte count and platelet from 1007 hospitalized patients with COVID-19, who were admitted to two referring hospitals in Ardabil, North Western Iran. All confirmed cases divided into non-severe and severe groups.

534 (53.4%) males and 473 (47.3 %) females with mean age of 52 years were enrolled in this study. Patients with severe COVID-19 have lower counts of lymphocyte, but have higher NLR, comparing to non-severe patients (P = 0.001). Also, there was no significant difference in PLR between two groups (P = 0.84). Patients who categorized in severe group had lower lymphocyte mean count, higher mean neutrophil count (P = 0.001). Patients who categorized in severe group had lower lymphocyte mean count (P = 0.001). Elevated NLR can be assumed as an independent biomarker, which could provide a crucial indicator in the monitoring patients with COVID-19 on admission. Increased NLR was correlated with the severity of COVID-19. Assessment of NLR could be proposed to identify high risk individuals with COVID-19.

Keywords: COVID-19; Hematological parameters; Prognosis; Severity.

Poster Presentation

1st International Congress of Biomarkers

PN: 1144

Novel biomarkers for cancer immunotherapy

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ABSTRACT

Cancer is considered to one of the most life-threatening disorders globally. This disease is more lethal because it gets relapsed even after the treatment and is also associated with common side effects like hair loss, memory impairment, appetite loss, etc. For the past few years, immunotherapy for treatment of cancer has always been conversed among scientists as it employs patient's immune system for treatment .It plans to amplify the immunological response of the body and manipulates the mechanism between oncogenic and immunogenic cells within the micro-environment. The utilization of immunological responses of patients' bodies to treat cancer has revolutionized the medical field, but some patients do not respond as this treatment is predicted to. Immunotherapy's immunological response has a wide spectrum and is not specific to cancerous cells and in some patients, it has been reported for side effects. To overcome this limitation, biomarkers are employed for cancer immunotherapy. According to NIH, biomarkers are molecules that are associated with cells and are used for the diagnosis of a particular disease. By employing these biological molecules for cancer immunotherapy, we can specifically treat our cancerous cells. In this paper, we will be conversing about the invention and the historical overview of biomarkers in cancer immunotherapy, which constitutes immune checkpoints, T cell therapy, etc. In addition to this, we will also discuss various biomarkers used for cancer immunotherapy, strategies (like whole genome sequencing, gene expression technology, flow cytometry, etc) employed for biomarker identification in detail, and their advantages, limitations, current research, and prospects associated with each method.

Key words: Biomarker‹Cancer‹Immunotherapy

Poster Presentation

1st International Congress of Biomarkers

PN: 1146

Role of melatonin in helping to detect multiple sclerosis

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ABSTRACT

Multiple sclerosis (MS) is a chronic and inflammatory disease of the central nervous system (CNS) that is common in people between the ages of 20 and 40. This disease has increased significantly in recent decades in different geographical areas. In order to control and reduce the disease prevalence, early identification of at-risk people and patients in the early stages of the disease is important. Melatonin is one of the biomarkers that can be used for early diagnosis of the disease. Melatonin is a hormone that is released from the pineal gland in response to darkness, and it has several functions like regulating the formation and function of immune cells and anti-inflammatory actions on nerve cells.

We reviewed 200 articles about multiple sclerosis, melatonin, and the relationship between them from January 1, 2016, to July 31, 2022, and finally used information in 10 of them to write this article.

Depending on the stage of inflammation, this hormone can have both pre-inflammatory and anti-inflammatory properties. Elevated levels of this hormone cause the production of anti-inflammatory cytokines such as interleukin 4 (IL-4) and IL-10, in contrast, reduces inflammatory cytokines such as tumor necrosis factor alpha (TNF-α). Therefore, low levels of melatonin have been linked to neurological problems such as MS. Therefore, measuring melatonin can be helpful in early diagnosis and control of this disease, especially in less advantaged cities and countries.

Keywords: Multiple sclerosis; Melatonin; MS

Poster Presentation

1st International Congress of Biomarkers

PN: 1148

Heart fatty acid binding protein, FGF21, troponin I and CK-MB in patients with heart coronary diseases in Ilam, Iran.

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ABSTRACT

Coronary artery disease (CAD), is one of the leading causes of death in developed countries. The aim of this study was to evaluate the novel biomarkers hFABP and FGF21 for early detection and evaluation of the severity of CAD. This study was conducted in the specialized heart hospital of Ilam city. A total of 70 patients referred to the cardiac intensive care unit underwent initial clinical examinations and patient characteristics and required demographic information (such as age, Sex, history of diabetes mellitus, dyslipidemia and smoking) were recorded. Patients based on the number of involved coronary vessels and the severity of the disease were divided into three groups, 0ne, two and three vessels disease. HFABP, FGF21, troponin I concentration and CK-MB enzyme activity were measured.

The results of this study revealed that H-FABP increased significantly in all patients. The highest increase in FGF-21 was related to the group of coronary heart patients with two and three constricted vessels. The levels of troponin I and CK-MB showed the highest significant increase in the group of patients with 3 vessels disease. ROC curve results showed that the sensitivity and specificity for early diagnosis of coronary artery disease the HFABP (100%, 100%), FGF21 (100%, 98%), CTnI (85%, 83%) and CK-MB (80%, 72%) respectively. The results of the present study showed that HFABP and FGF-21 have the highest sensitivity and specificity for the early detection of CAD in comparison with routine tests, and their use not only helps in the early detection of heart diseases, but also helps in the rapid recovery of the disease before the cardiomyopathy occurs. In this way, the death of heart patients can be prevented due to early diagnosis and rapid initiation of treatment approaches.

Keywords: HFABP; FGF21; CTnI; CK-MB; Coronary heart disease; Ilam

Poster Presentation

1st International Congress of Biomarkers

PN: 1150

Effect of PLX3397 as CSF1R inhibitor on microglial population and remyelination in the cuprizone model

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ABSTRACT

Multiple sclerosis (MS) is a kind of autoimmune and demyelinating disease with pathological symptoms such as inflammation, myelin loss, astrocytosis, and microgliosis. The colony stimulating factor 1 receptor (CSF1R) is an essential factor for the microglial viability and function, and PLX3397 is its specific inhibitor of CSF1R. In this study, we assessed the effects of microglial ablation on remyelination process.

The fifteen male C57BL/6 mice (8 weeks old) were divided into 3 groups include control, cuprizone and PLX3397. In order to demyelination model induction, the animals were fed with 0.2% cuprizone diet for 6 weeks. For microglial ablation, PLX3397 (290 mg/kg) was added to the animal food for 14 days. The microglial population was measured using immunohistochemistry. The rate of remyelination was evaluated using Luxol Fast Blue staining and electron microscopy. The expression levels of CSF1R gene were assessed by qRT-PCR method. Data were analyzed using GraphPad Prism and SPSS software.

Gene results showed that PLX3397 treatment reduced CSF1R expression. The results showed that the administration of PLX3397 (290 mg/kg for 7 days) significantly ($p \leq .001$) reduced microglial cells more than 80% so microglia viability is depend to CSF1R marker. PLX3397 administration also significantly increased remyelination compared to the cuprizone mice, which was confirmed with the results of LFB and TEM. According to the results, the administration of PLX3397 for 14 days enhanced remyelination in acute demyelination model. These positive effects was related to the reduction of microglia after PLX3397 administration.

The results of present study revealed that PLX3397 reduced microgliosis through CSF1R inhibitor. It also enhancing remyelination in the corpus callosum of the cuprizone model mice. Therefore PLX3397 administration with microglial reduction can be appropriate approach for treatment neurodegenerative diseases such as MS.

Keywords: Microglia; PLX3397; Multiple sclerosis; Remyelination.

Poster Presentation

1st International Congress of Biomarkers

PN: 1152

Development of ultrasensitive miRNA-based genosensor using perovskite nanocomposite and AuNPs for determination of miRNA-21 as a significant biomarker for rapid and highly-sensitive diagnosis of gastric cancer

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ABSTRACT

MiRNAs are very important as regulators of gene expression due to their interference with intracellular messenger RNA (mRNA). MiRNAs can be used as diagnostic biomarkers in diseases, especially cancer diagnosis. The most important diagnostic clinical techniques are microarrays and qRT-PCR, which have limited linear quantitative range, incomplete sensitivity for long sequence homogeneity, and the inability to detect new miRNAs and the need for a large sample volume, its high cost, and the need for computing infrastructure for analysis and interpret data. Today, electrochemical biosensors are considered as fast, sensitive, selective and low-cost analytical tools that provide the possibility of evaluating very low sample levels with minimum sampling volume and have the capability of multiple detection.

In this study, an electrochemical oligonucleotide genosensor was developed to detect and measure miRNA-21. To achieve this goal, multilayer nanocomposites of perovskite and graphene oxide and AuNPs were produced. The obtained nanocomposite was fixed on the working electrode surface. Then the single-stranded RNA probe was immobilized on the modified electrode. The interaction of the RNA probe with the target miRNA by changing the intensity of the electrochemical signal enables the identification and detection of miRNA in the sample.

Using this technology, we were able to detect miRNA-21 sensitively with a low detection limit, with a linear range of 1 fM to 1 nM and limit of detection 0.13 fM. The results were also confirmed by examining real samples of gastric cancer cell lines. In addition, the designed biosensor had a special selectivity against the mismatches.

The results showed that the prepared genosensor has favorable biocompatibility, high sensitivity and specificity for target sequence detection. This biosensor was evaluated to check the ability to detect the target biomarker in polymerase chain reaction samples as well as real samples of different types of gastric cancer cell lines. These advantages can introduce the proposed genosensor as a new and effective sample of biosensors.

Keywords: Cancer; Biomarker; miRNA-21; Genosensor; Electrochemical.

Poster Presentation

1st International Congress of Biomarkers

PN: 1153

Expression Analysis of Circulating miR-217 as Promising Biomarker of Acute Lymphoblastic Leukemia

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ABSTRACT

The role of serum-based biomarkers such as microRNAs in cancer diagnosis has been extensively established. This study aimed to determine the expression levels of bioinformatically selected miRNAs and whether they can be used as biomarkers or a new therapeutic target in patients with Acute Lymphoblastic Leukemia (ALL).

In the present study, the genes and signaling pathways involved in ALL pathogenesis were surveyed based on literature and database. Then according to these paths, the most critical miRNA was selected for further analyses using predictive databases. The expression levels of bioinformatically selected miR-217 in the serum of 21 ALL patients and 21 healthy controls were measured using quantitative real-time PCR. The receiver operating characteristic (ROC) curve and the associated area under the curve (AUC) was used to assess candidate miRNA diagnostic value as a biomarker.

The results showed that the expression level of miR-217 was markedly decreased and down-regulated in the newly diagnosed ALL group compared to the controls. Furthermore, ROC analysis showed that serum miR-217 could differentiate ALL patients from healthy individuals with an AUC of 0.81, a sensitivity of 95%, and a specificity of 61% (P=0, 95% CI: 0.69–0.94). There was no significant difference in the relative expression level of miR-217 between men and women, children and adults, and the ALL subtypes. Moreover, no statistically significant correlation was observed between the expression of miR-217 with age, platelets count, white and red blood cell count, and hemoglobin.

The results suggested that miR-217 may have a potential role in the pathogenesis of ALL and could be considered as a possible diagnostic biomarker and therapeutic goal in this disease due to its appropriate sensitivity and specificity and higher Yuden index in newly diagnosed ALL patients.

Keywords: MicroRNA; Biomarker; Acute Lymphoblastic Leukemia; ALL; miR-217.

Poster Presentation

1st International Congress of Biomarkers

PN: 1154

Carvacrol exerts anti-inflammatory, anti-oxidative stress and hepatoprotective effects against diclofenac-induced liver injury in male rats

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ABSTRACT

Diclofenac (DIC) is an NSAID that can cause toxic effects in animals and humans and carvacrol (CAR) is a monoterpene compound that displays effective pharmacological and biological actions. The purpose of this work was to assess the influences of CAR on DIC-induced liver injury and oxidative stress in male rats . The male Wistar rats were segregated into four groups. Group 1, control group; Group 2 received DIC-only (10 mg/kg bw, p.o.); Groups 3, received CAR-only (10 mg/kg bw, p.o.) and group 4 received DIC plus CAR . The results of this work indicated that the amounts of the serum protein carbonyl, AST, ALT, ALT, total bilirubin, nitrite content, MDA, serum TNF-α, and liver TNF-α gene expression were remarkably increased and the levels of the GPx, GSH, CAT, and SOD were significantly reduced in DIC-only treated animals compared to the control group. On the other hand, treatment with CAR after exposure to DIC led to significant improvements in abnormalities of DIC-induced liver injury and serum biochemical factors . The findings of this study indicated that the administration of CAR could alleviate the noxious effects of DIC on the antioxidant defense system and liver tissue.

Keyword: Carvacrol, anti-inflammatory, anti-oxidative stress, hepatoprotective, diclofenac-induced liver injury

Poster Presentation

1st International Congress of Biomarkers

PN: 1155

The nephroprotective effect of ellagic acid against diclofenac-induced renal injury in male rats: Role of Nrf2/HO-1 and NF-κB/TNF-α Pathways

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ABSTRACT

Despite the promising effect of the nonsteroidal anti-inflammatory drug (NSAIDs) on controlling the chronic symptoms of different diseases, their toxicity has restricted the long-term administration of these agents. The lack of suitable substitution provides opportunities for innovation of combined-modality strategies that could reduce the toxic side effects of these drugs. In the present study, we aimed to evaluate the protective effect of ellagic acid, a phenolic compound found in plants, on diclofenac-induced nephrotoxicity.

The results of the treatment of 32 Wistar rats with diclofenac (50 mg/Kg) and/or ellagic acid (10 mg/Kg) for seven days showed that, unlike diclofenac that shifted the ratio of the redox system in favor of oxidative stress, ellagic acid reduced the tissue levels of malondialdehyde (MDA), protein carbonyl (PC) and diminished serum nitrite content. Moreover, through upregulating nuclear factor-erythroid factor 2-related factor 2 (Nrf2) and heme oxygenase-1 (HO-1), ellagic acid might increase the activity and the tissue levels of several antioxidant enzymes such as catalase (CAT), superoxidase dismutase (SOD), glutathione peroxidase (Gpx), and glutathione (GSH) in diclofenac-treated rats. This phenolic agent also prevented diclofenac-mediated inflammatory responses by suppressing the expression of nuclear factor (NF)-κB/tumor necrosis factor (TNF)-α and reducing the number of infiltrated lymphocytes in the kidney tissue. Taken together, our study demonstrated that ellagic acid may produce a protective effect against diclofenac-induced renal failure by exerting both antioxidant and anti-inflammatory properties. This finding indicates that this agent might be a valuable candidate to be used alongside NSAIDs such as diclofenac to alleviate their side effects.

Keywords: Diclofenac; Ellagic acid; Nephrotoxicity.

Poster Presentation

1st International Congress of Biomarkers

PN: 1157

Rutin exerts anti-inflammatory effect against paraquat-induced liver injury in male rats

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ABSTRACT

Paraquat is one of the most essential bipyridinium herbicides that can lead to liver toxicity. Rutin is a bioflavonoid with antioxidant properties. The study purposed the examination of paraquat on liver function and gene expression of IL-1β in rats with paraquat-induced hepatootoxicity.

48 Wistar male rats were divided into 6 groups. The first group was the negative control group and the second one was the experiment group without treatment, the rats received 50 mg/kg of their weight edible paraquat daily and distilled water one hour later. Rats in the third group received 50 mg/ kg of their weight paraquat as gavage every day and one hour later received 50 mg/ kg of their weight edible silymarin. In all fourth, fifth, and sixth groups, 50 mg/ kg of rats' weight (soluble in distilled water) was gavage and then the fourth group was rutin gavage for 14 days with 25 mg, the fifth group was rutin gavage for 14 days with 50 mg and the sixth group was rutin gavage for 14 days with 100 mg. 14 days later of gene expression IL-1β investigate.

Rutin decreased gene expression of IL-1β in liver tissue.Unlike the paraquat administrated rats, which showed a remarkable increase in the expression levels of proinflammatory cytokines, including IL-1β as compared to the control rats, those rats which were exposed to increasing concentrations of rutin (25, 50, and 100 mg/kg) after exposing to paraquat showed to have lower expression of cytokines.

The paraquat induces liver toxicity by affecting gene expression. Rutin may be a promising drug for the treatment of hepatotoxicity by reversing the effects of paraquat.

Keywords: Rutin; Hepatotoxicity; Paraquat; Silymarin.

Poster Presentation

1st International Congress of Biomarkers

PN: 1158

Application of MicroRNAs in Personalized Medicine in Acute Myeloid Leukemia

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ABSTRACT

Acute myeloid leukemia (AML) is a highly heterogeneous disease in cytogenetic and molecular biology, but it mostly treated with a (one size fits all) approach consisting of highly toxic chemotherapy. Drug resistance is a major therapeutic challenge in the treatment of AML and the standard care including the 7+3 regimen unchanged for the past decades. So, what measures lead to better AML management?

MicroRNAs affect many cellular processes and plays a role in different step of tumorogenesis such as initiation, progression, metastasis, and resistance to chemotherapy.

Information is collected from articles published in Scholar and Pubmed databases.

As microRNAs have a role in different steps of AML, these biomarkers can be used as tumor specific signatures for diagnosis, prognosis, and therapeutic purpose and can be used as a biomarker for personalized medicine. Because AML is a heterogeneous disease, it seems that patients benefit from personalized medicine. The miRNAs are associated with resistance and sensitization to cancer drugs and modulating their activities may provide opportunities for cancer therapy. The following technological approach could be used to target miRNAs:

- Downregulate or block the function of oncogenic miR (miR antagonist)
- Upregulate the expression of miR that have tumor suppressive function (miR mimics)
- miRNAs can also involve in enhancing the efficacy of an anticancer drug and increase drug response.

miRNA-based personalized medicine for AML will also reduce the emergence of chemoresistance by selecting the most appropriate therapeutic approach for each patient and help to achieve a cure in the majority of patients. It will save time and improve patient quality of life by limiting the adverse effect of unsuitable treatment.

Keywords: AML; miRNA; Personalized medicine.

Poster Presentation

1st International Congress of Biomarkers

PN: 1161

A brief overview of biomarker in cancer

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ABSTRACT

Cancer is one of the most prevalent life threatening diseases which is spreading because of the lifestyle we are living. Cancer is due to uncontrolled growth of cells which can be cured if diagnosed in early stage of life. There are three major treatment of cancer namely: Surgery, Chemotherapy & Radiotherapy. In the Nanakali Hospital for Oncology & Hematology Diseases which located in Erbil & Zhyanawa Center for Radiotherapy treatment which located in Sulaymaniyah, we researched about two cases, 42 Y male, 40 Y Female, with nasopharyngeal cancer, differentiated type, not poorly differentiated type, & the second case with Breast cancer. We realized that PET scan is more useful for determining the stage of cancer than CT scan. Treatment of cancer depends on the various internal and external factors. Cancer is screened by different screening test and a number of treatments are now available these days such as immunotherapy, chemotherapy, surgery, radiation therapy. For a diagnosis and treatment program to be effective, researchers & Scientists must be continuing their academic & scientific research.

When more resources become available, the program can be extended to include rare cancers as well as cancers for which survival is poor as of now. Comprehensive cancer center with all diagnostic, therapeutic and research facility is the need of the hour.

Keywords: Cancer, Nasopharyngeal cancer, Chemotherapy, radiation therapy

Poster Presentation

1st International Congress of Biomarkers

PN: 1163

Discovery of new candidate genes as biomarkers oflung carcinoma by analysis of co-expressed genes in the network of overexpressed genes in lung cancer; anintegrated bioinformatics analysis

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ABSTRACT

Lung cancer (LC) is a frequently diagnosed malignancy that in the advanced stages with metastasis still have poor prognosis. Therefore, the molecular mechanisms of progression and new diagnostic biomarkers for different types of cancer have been studied extensively.

In the present study, a systems biology approach was used to find novel biomarkers. In order to identify the main biomarkers of lung tumor tissues, the EST (Expressed Sequence Tags) libraries of various types of LC were compared with the normal tissue libraries using the Digital Differential Display (DDD) tool in the Unigene section of the NCBI database. Here, we identified 16 genes whose expression in lung cancer tissues were more than 1000 times that of normal tissues. Then, the key up-regulated genes were used for drawing gene network by COXPRESdb which allows relative expression analysis of thousands of genes simultaneously.

According to the drawn network, generally 48 genes were related to main upregulated 16 genes of LC, so it can be predicted that they will also be involved in the process of carcinogenesis. Gene Ontology (GO) tool was used to predict the function of co-expressed genes. The main functions of co-expressed genes in the network were apoptosis, MAPK signaling, cancer pathways, cell cycle, regulation of transcription and cell proliferation, etc. By examining these co-expressed genes, the involvement of 39 genes in LC has been previouslyreported. But nine genes were discovered that their involvement in LC has not reported until now, including EIF1B, PPP2R2B, BTK, ATXN1, GABARAPL2, MAP1LC3A, RANBP9, SNCA, LOC344887.

This study employs computational biology to find the new candidate genes that could be involved in LCprogression, opening a new window in this field. More studies with in vitro validation are needed to be undertaken in future studies.

Key words: Lung carcinoma; Cancer biomarkers; Gene network; Gene discovery; Bioinformatics tools.

PN: 1164

Investigating the effects of palmitate and chicoricacid on sphingosine 1-phosphate receptor 1 (S1PR1) levels in PBMCs

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ABSTRACT

Sphingosine 1 phosphate (S1P) has a key role in many cellular processes such as inflammation. Binding of S1P to sphingosine 1-phosphate receptor 1 (S1PR1) activates S1P signaling pathway. Targeting S1P signaling pathway could be considered as potential therapeutic target for type 2 diabetes (T2D). Chicoricacid (CA), a phenolic compound, has beneficial effects on T2D. Although, the exact molecular mechanism is still unclear. So, we aimed to investigate the effects of palmitate and CA on S1PR1 in peripheral blood mononuclear cells (PBMCs) from newly diagnosed patients with T2D. Twenty newly diagnosed patients with T2D were enrolled in our study. The protocol of present study approved by Ethics Committee of Shahrekord University of Medical Sciences (code: IR.SKUMS.REC.1399.115). After isolation of PBMCs, these cells were treated as follows: control groups (untreated, treated with BSA 1 % for 12 h), CA groups (treated with 50 μM CA for 6 h), palmitate groups (treated with 500 μM palmitate for 12 h), palmitate + CA groups (treated with 500 μM palmitate for 12 h and then treated with 50 μM CA for 6 h). At the end, concentrations of S1PR1 in the PBMCs were quantified using ELISA. S1PR1 protein levels significantly increased in response to palmitate as compared to untreated cells in patients with diabetes ($p< 0.001$). However, CA dramatically decreased S1PR1 protein levels ($p< 0.001$). Also, CA ameliorates palmitate-increased S1PR1 levels in these cells, however it wasn't significant. Our finding showed that CA could be considered as a novel S1P inhibitor. So, it could be a useful in diabetes therapy.

Keywords: Type 2 diabetes (T2D); Palmitate; Chicoricacid (CA); Sphingosine kinase 1 (SPHK1); Sphingosine 1-phosphate receptor 1 (S1PR1).

Poster Presentation

1st International Congress of Biomarkers

PN: 1165

Evaluation of epidemiological, histopathological and frequency distribution of Tumor markers in patients with urinary tract cancers referred to Alla Cancer Control and Prevention Center (MACSA) - Isfahan, 2012-2020

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ABSTRACT

Cancers today put a huge burden on the health system of countries. Due to population growth, aging, lifestyle changes and development of sedentary lifestyle and unhealthy eating habits and more exposure to carcinogens, the prevalence of this deadly disease in society is increasing day by day. One of the relatively common cancers that is closely related to lifestyle is urinary tract malignancies. Since there is not much information about the epidemiological and histopathological features of this type of cancer in the country and in order to design better interventions for the prevention and control of these diseases, the present study was designed and conducted. In this cross-sectional study, the files of patients referred to the Iranian Cancer Prevention and Control Charity Institute (MACSA), a unique center for providing supportive and palliative care to cancer patients in Isfahan, have been reviewed. After reviewing the electronic database of the center and identifying patients diagnosed with Urinary tract cancers, while obtaining informed consent from patients or their families, the required information was completed through interviews and then analyzed using SPSS software. A total of 199 cases of Bladder Cancer and 97 cases of Kidney and Urinary tract Cancer were studied. Among Bladder Cancer cases, 169 cases were male (84.92%) and 30 cases female (15.08%). The mean age of diagnosis was 65 years Among them, 107 cases had a negative Family History (equivalent to 53.73%) and 92 cases had a positive Family History (equivalent to 46.23%). In total, 55.8% of patients had underlying disease. The most common underlying diseases were Hypertension (20.1%), Diabetes (19.1%), Coronary artery disease (14.7%) and Hyperlipidemia (10.55%), respectively. The most common pathology was Urothelial Carcinoma (91%), the most common Grade was Grade 3 (72.5%) and the most common Stage was Stage III (81.2%). Among Kidney Cancer cases, 66 cases were male (68.04%) and 31 cases were female (31.96%). The mean age of diagnosis was 85.98 years Among them, 40 had a negative Family History (equivalent to 41.2%) and 57 had a positive Family History (equivalent to 58.8%). The most common pathology was ccRCC (76.1%), the most common Grade was Grade X (44.3%), and the most common Stage was Stage III (54.2%). According to this study, most of the patients with urinary tract malignancies that referred to MACSA, were in the upper stages of these cancers and used the palliative care services of this center. According to our study, tumor markers do not examine in these patients, although there is not any FDA approve tumor marker for Kidney cancer, but Bladder Tumor Antigen (BTA), Chromosomes 3, 7, 17 and 9p21, FGFR2 and FGFR3 gene mutations and fibrin/fibrinogen are routinely cheeked in the USA laboratory for Bladder cancer (1). It seems that reducing smoking, effective use of tumor markers as well as timely screening can play an important role in reducing the mortality rate of patients with these cancers.

Keywords: Bladder, Kidney, Epidemiology, Histopathology, Tumor Marker, Molecular Marker, Iran, Isfahan

Poster Presentation

1st International Congress of Biomarkers

PN: 1166

Chemical characterization and anti-breast cancer effects of copper nanoparticles using Artemisia Dracunculus ethanolic extract on 7,12-Dimethylbenz[a] anthracene-induced mammary gland carcinogenesis in Sprague Dawley male rats

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ABSTRACT

The aim of the recent research was to investigate the anti-breast cancer effects of copper nanoparticles using Artemisia Dracunculus seed ethanolic extract (CuNPs).

We studied functional groups of *A.Dracunculus* extract in the reduction and capping process of CuNPs by FT-IR, crystallinity and FCC planes by X-ray diffraction (XRD) pattern and surface morphology, shapes, and size of CuNPs by scanning electron microscopy (SEM) and transmission electron microscopy (TEM). *In vivo* design, induction of breast cancer was done by 7,12-Dimethylbenz[a] anthracene (DMBA) in 50 animals. After 10 days, the animals were randomly divided into six subgroups, including healthy control, untreated control, two groups receiving the *A.Dracunculus* at 2 and 6 mg/kg and two groups receiving the CuNPs at 2 and 6 mg/kg concentrations.

Both doses of *A. Dracunculus* and CuNPs (especially CuNPs6) significantly ($p \leq 0.05$) reduced the weight and volume of liver, mammary gland, kidney, spleen, ALP, AST, ALT, GGT, cholesterol, LDL, triglyceride, total and conjugated bilirubin, urea, creatinine, glucose, ferrous, ferritin, erythropoietin, GR, IL1, IL6, IL12, IL18, IFNY, and TNFα and increased HDL, total protein, albumin, WBC, lymphocyte, neutrophils, platelet, RBC, Hb, PCV, MCV, MCH, MCHC, SOD, CAT, GPx, IL4, IL5, IL10, IL13, and IFNα compared to the untreated group.

A. Dracunculus and CuNPs (especially CuNPs6) significantly ($p \leq 0.05$) treated breast cancer with reduction of organs free of metastasis compared to the untreated group. Seemingly, the Cu NPs can be used for the treatment of breast cancer.

KEYWORDS: Chemical characterization; Anti-breast cancer; Copper nanoparticles using Artemisia Dracunculus.

Poster Presentation

1st International Congress of Biomarkers

PN: 1167

Anti-human ovarian cancer, cytotoxicity, and antioxidant effects of Matricaria chamomilla green-formulated cu nanoparticles: Describing a new chemotherapeutic supplement

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ABSTRACT

The recent research showed that the copper nanoparticles (cuNPs) formulated with Matricaria chamomilla aqueous extract having potent antioxidant and anti-human ovarian cancer activities in vitro condition.

For evaluating anti-ovarian cancer and cytotoxicity effects of cuNPs and Matricaria chamomilla aqueous extract, we used MTT assay. For determinate the properties of the cuNPs that were produced from the reaction between copper chloride solution with aqueous Matricaria chamomilla extract, we used UV–Visible Spectroscopy (UV-Vis), Field Emission Scanning Electron Microscopy (FE-SEM), Fourier Transformed Infrared Spectroscopy (FT-IR), and Transmission Electron Microscopy (TEM).

For evaluating the antioxidant features of cuNPs, and Matricaria chamomilla aqueous extract, we used the DPPH test, in this test butylated hydroxytoluene was a positive control, the results of this test showed that the cuNPs have an effective antioxidant feature. In the antioxidant test, the IC50 of cuNPs and BHT were 144 and 201 µg/mL, respectively. The result of this test showed that cuNPs have no cytotoxicity on normal cell line (HUVEC) and have potent anti-ovarian cancer features dose-dependently against PA-1, SK-OV-3, and SW-626 cell lines. The IC50 of GNPs were 249, 361, and 433 µg/mL against PA-1, SW-626, and SK-OV-3 cell lines, respectively.

Probably, potent anti-human ovarian cancer activities of cuNPs formulated with Matricaria chamomilla aqueous seed extract because of antioxidant properties. After evaluating the effectiveness of this formulation in clinical trial researches, it can be a good alternative to chemotherapy drugs.

Key words: Matricaria chamomilla green-formulated cu nanoparticles; Anti-human ovarian cancer; Cytotoxicity;antioxidant.

Poster Presentation

1st International Congress of Biomarkers

PN: 1168

The importance of tracking fate and origin of circulating tumor DNA in precision oncology era

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ABSTRACT

In precision medicine, circulating cell-free DNA from tumours in blood (ctDNA) provides real-time information on genetic and epigenetic changes during tumor developmen. Clinical applications of ctDNA are developing in oncology such as tumor genotyping, monitoring tumor burden, early detection, therapeutic responses and treatment resistance. Despite the applications, the origin of ctDNA in circulation and its fate remain ambiguous.

The release of ctDNA can come from several sources, including apoptosis, necrosis, and active release of tumor cells (CTC), or micrometastases. There are also neutrophil extracellular DNA traps (NETS), eosinophil extracellular DNA traps (EETS), and particulate structures (exosomes and cell-surface-bound exosomes) or macromolecular structures (virtosomes). Based on some features such as tumor type and size, number of tumors, and tumor differentiation and stage could potentially provide an explanation for the different concentrations of ctDNA in different conditions of tumor.

Several different fates have been considered for ctDNA, among which the most possible fate was degraded by nucleases and macrophages available in the blood, which are quickly metabolized/eliminated by the liver and kidneys. A part of ctDNA in the blood is observed in the shape of cell-surface-bound ctDNA (csb-ctDNA), which is bonded to the surface of erythrocytes and leukocytes. Further, linking ctDNA to serum proteins is considered as the next probable scenario. Then, ctDNA is able to interact with immune cell at the next level while ctDNA is a potential regulator of the immune function in response to disorders.

It is essential to identify and characterize possible ctDNAorigins, as well as to understand how ctDNA fate is regulated, in order to strengthen clinical applications, especially in precision oncology. The full understanding of these processes helps to make some progress toward the discovery approaches to tumor early detection, and finding new molecular targets and developing novel therapeutic strategies.

Keywords: Circulating cell-free DNA; Precision Medicine; Exosomes; Virtosomes.

Poster Presentation

1st International Congress of Biomarkers

PN: 1169

The significance of long noncoding RNAs as potential cancer biomarkers

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ABSTRACT

Cancer is caused by a collection of abnormalities in DNA that eventually cause division to go uncontrolled. Early detection of a disease that may be treated immediately can be crucial in reducing the risk of cancer. Non-coding RNAs, which are approximately 200 nucleotides in length and do not code for proteins, are emerging as useful biomarkers in the field of cancer detection and treatment. Some of this RNA's roles include interfering with cytoplasmic RNA stability; influencing epigenetic alterations; facilitating transcription via remodeling complexes; splicing hnRNA; interacting with specific transcription factors; binding to mRNAs; and degrading them. Gene expression is influenced by long non-coding RNAs via cis and trans promoter regions. They can act as a guide, scaffold, or intermediary molecule for protein-protein or protein-RNA interactions. Additionally, LncRNAs have been shown to modify gene expression through influencing chromatin structure. The third most common cancer in both men and women is found in the large intestine. The availability of multiple types of colonoscopies has led to the earlier and more frequent detection of colon cancer in its advanced stages. There is evidence that lncRNA expression or dysfunction is associated with cancer development and progression. These non-coding transcripts are known to inhibit cell proliferation, migration, and invasion, all of which are hallmarks of malignancy. LncRNAstherapy in cancer patients opens the door to non-invasively assessing gene expression. Because of this, these transcripts can serve as biomarkers in the detection of cancer.

Keywords: Cancer; Long non-coding RNA; Transcripcion factor; Protein; Gene expression.

Poster Presentation

1st International Congress of Biomarkers

PN: 1170

Evaluation of the Efficacy of the Cu -Thiosemicarbazones Complexes onExpression Changes of CPEB2 gene in Acute lymphoblastic leukemia

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ABSTRACT

The pathophysiology of ALL involves the abnormal proliferation and differentiation of a clonal population of lymphoid cells. The prognosis for all patients is bleak; just 10% of adults and 30% of pediatric ALL patients survive. Increased CPEB2 levels promote the migration and growth of these cancer cells in cancer tissues. The aim of this study was to evaluate the effect of Cu-thiosemicarbazone complexes on the expression of the CPEB2 gene in acute lymphoblastic leukemia.

For the current work, Cu-thiosemicarbazone complexes were generated in two concentrations: 15.5 and 17 µM after 72 hours. The JurkatE6.1 cell line, which was purchased from the Pasteur Institute, was given a prepared dose of Cu- Thiosemicarbazones 24 hours after cell passage. Real-Time PCR was utilized to analyze the differences in CPEB2 and GAPDH expression after RNA extraction and cDNA synthesis. Finally, Rest 2002 Software was used to analyze the data while Excel was utilized to make the diagrams.

The results of our research showed that following a 24hour treatment with Cu- Thiosemicarbazones at concentrations of 15.5 and 17 µM, the expression of CPEB2 reduced in comparison to the GAPDH housekeeping gene. According to the findings, changes in CPEB2 gene expression decreased after 24h at a concentration of 15.5 µM and 17 µM decrease were statistically significant These changes included 15.5 µM (0.423) and 17 µM (0.621) at 24h, respectively. ($P < 0.001$)

CPEB2 expression was shown to change after receiving Cu- Thiosemicarbazones at two different concentrations, according to the results of the current investigation. Cu-thiosemicarbazones positive potential and efficacy were demonstrated by the fact that it was able to decrease gene expression in two kinds of different concentrations within 24 hours.

Keywords: CPEB2; Acute lymphoblastic leukemia; GAPDH; Cu- thiosemicarbazones complexes.

Poster Presentation

1st International Congress of Biomarkers

PN: 1171

Investigating the Effect of Complex1 (Methotrexate+ Cyclophosphamide), Complex2 (Cyclophosphamide+ Cytarabine), Complex3 (Cytarabine+ Mercaptopurine) on Expression Changes of CPEB2 in Acute Lymphoblastic Leukemia

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ABSTRACT

Acute lymphoblastic leukemia (ALL) affects lymphoid progenitor cells in the bone marrow and blood often in children. Several genetic alterations are associated with the outcome in children with ALL. CPEB2 is a sequence-specific RNA-binding protein that belongs to the cytoplasmic polyadenylation element-binding protein (CPEB) family. The aim of this study effect of the Investigate the Effect of Complex1 (Methotrexate+ Cyclophosphamide), Complex2 (Cyclophosphamide+ Cytarabine), Complex3 (Cytarabine+ Mercaptopurine) on Expression Changes of CPEB2 in Acute Lymphoblastic Leukemia. In this study, appropriate concentrations of the Complex1 (1μM Methotrexate+ 20μM Cyclophosphamide), Complex2 (20μM Cyclophosphamide+ 1μM Cytarabine), Complex3 (1μM Cytarabine+ 5μM Mercaptopurine) were prepared according to the IC50 of the drug. The Jurkat E6.1 cell line was treated with prepared Complexes 24h after cell passage. The expression changes of CPEB2 and GAPDH were investigated using Real-Time PCR after RNA extraction and cDNA synthesis. The Results of the research showed that after 24h of treatment with Complex1 (1 μM Methotrexate+20 μM Cyclophosphamide), Complex2 (20μM Cyclophosphamide+ 1μM Cytarabine), Complex3 (1μM Cytarabine+ 5μM Mercaptopurine) the expression of CPEB2 decreased significantly as compared to the control group. According to the findings, Complex1 (Methotrexate+ Cyclophosphamide), Complex2 (Cyclophosphamide+ Cytarabine), Complex3 (Cytarabine+ Mercaptopurine) over 24h were the optimal concentrations and time for this drug's effect. The expressions of CPEB2 were 2.326, 0.562, and 0.282 at the specified concentrations and times. (p-value 0.001). As a Conclusion expression changes in CPEB2 as an oncogene gene after treatment with Complexes, two concentrations of the drug successfully decreased CPEB2 expression. Overall, Complex2 (20μM Cyclophosphamide+ 1μM Cytarabine), Complex3 (1μM Cytarabine+ 5μM Mercaptopurine) had a positive effect on expressions CPEB2 at 24h, and this decrease in expressions was statistically significant (p-value 0.001).

Keywords: cDNA, GAPDH, CPEB2, Oncogene

Poster Presentation

1st International Congress of Biomarkers

PN: 1172

Evaluation the Effect of Cytarabine on Expression of LncRNA TUG1 in Acute Lymphoblastic Leukemia

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ABSTRACT

Genetic defects accumulate throughout a number of stages and interfere with the normal regulation of cell growth, differentiation, proliferation, and survival, leading to T-cell acute lymphoblastic leukemia. The most used antineoplastic drug and alkylating ingredient is cytarabine. The current study set out to assess Cytarabine's impact on TUG1 expression variations in acute lymphoblastic leukemia Jurkat E6.1 cell line at two different doses after 48hours. The IC50 values for cytarabine, which were 1 and 5 M, were used to prepare doses in the study. The Jurkat E6.1 cell line was donated by the Pasteur Institute, and cytarabine was administered 48 hours after cell passage. Real-Time PCR was used to examine the expression changes of the housekeeping genes TUG1 and GAPDH after RNA extraction and cDNA synthesis.

The Results of the research demonstrated that after 48h of treatment with drug of cytarabine of 5µM, the expression of TUG1 decreased significantly as compared to the control group. According to the findings, doses of 1µM of cytarabine at 48h are the optimal concentrations and time for this drug's effect. ($P < 0.001$) At the specified concentrations and times, the expressions change of TUG1 were 1.05 and 0.642.

The study's conclusions indicate that after Cytarabine administration, 1 mM of the drug was successful in increasing TUG1 expression. Overall, cytarabine had a favorable impact on the TUG1 expression rise at 48 hours, which was statistically significant. It has been better at raising the expression of the examined gene as a result of the suppressor role of the TUG1 gene in acute lymphoblastic leukemia and in accordance with the outcomes of the drug at a low concentration of 1µM.

Keywords: TUG1; Jurkat E6.1 Cell Line; Housekeeping Gene.

Poster Presentation

1st International Congress of Biomarkers

PN: 1173

The effects of hydroalcoholic extract of *Helichrysum oocephalum* Boiss on human cervical cancer cell (Hela) apoptosis

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ABSTRACT

Cervical cancer is the most common cancer in women. A vast majority of cervical cancer is caused by the human papilloma virus (HPV). Nowadays, due to the fact that chemical drugs may link to serious side effects, using of medicinal plants is considered as an effective approach in direction of making adjuvant drugs for treatment of various types of cancers such as cancer of cervix. The genus Helichrysum is a member of the Asteraceae family. *Helichrysum oocephalum* Boiss which is also known as Immortal Flower, is native to Iran and grows in limited areas of northeastern parts of the country. Various specious of Helichrysum have been identified that possess the ability to inhibit the proliferation of cancer cells by effecting on different molecular pathways, lead to cell cycle arrest and apoptosis induction in cancer cells. Apoptosis is a programmed cell death that induces cells to commit suicide and causes morphological changes. The main component of apoptosis is a protein lysing system called caspase. Caspases are a group of enzymes called cysteine proteases. Apoptosis in nucleated cells occurs through two pathways: 1-Death receptor-dependent pathway (external) 2-mitochondrial pathway (internal). In this study, we investigated the effect of *H. oocephalum* hydroalcoholic extract on the expression of BCL2, BAX, Caspase3, and Caspase8 genes through the induction of apoptosis in a cervical cancer cell line (Hela). Our findings demonstrated that hydro-alcoholic extract of *H. oocephalum* caused toxicity in Hela cells in a dose- and time-dependent manner and induced apoptosis on Hela cells via the intrinsic and extrinsic apoptosis pathways.

Keywords: Cervical cancer, Hela cell, Apoptosis pathways, Helichrysum, Oocephalum

Poster Presentation

1st International Congress of Biomarkers

PN: 1174

miRNA-222 may act as a biomarker in Polycystic Ovary Syndrome

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ABSTRACT

Polycystic ovarian syndrome (PCOS) is a complex and multifactorial endocrine abnormality. miRNAs are small and non-coding RNAs that are considered as non-invasive prognostic biomarkers in various diseases such as cancer. Upregulation of miRNA-222 in PCOS may consider as a potential biomarker in the pathogenesis of PCOS. *Astragalushamosus* is a traditional herb that offers a wide range of pharmacological effects. This study aimed to evaluate the expression of miRNA-222 as a potential biomarker in PCOS. Wistar female rats were divided into five groups. PCOS was induced using Estradiol Valerate. Chitosan/alginate hydrogel-loaded *A. hamosus* extract was usedto treat the PCOS rats for four weeks. Ovarian morphology and hormonal titration including progesterone, estrogen, insulin, and testosterone were evaluated. The expression of miRNA-222 and *IRS1* was evaluated by real time-PCR. PCOS rats showed an increase in the number of corpuses luteum but a decrease in the number of ovarian follicles after treatment. Moreover, treatment with the extract led to a significant upregulation of *IRS1* and downregulation of miRNA-222. Decreased levels of insulin, testosterone, and estrogen along with the increased level of progesterone werealso observed.

This study introduced miRNA-222 as a potential biomarker for the diagnosis of PCOS due to a decreased expression at the post-treatment stages.

Keywords: Polycystic ovary syndrome; miRNA222; IRS1; Chitosan/alginate; *Astragalus hamosus.*

Poster Presentation

1st International Congress of Biomarkers

PN: 1175

G protein-coupled receptor 75 (GPR75) as a novel molecule for targeted therapy of Colon cancer

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ABSTRACT

G protein-coupled receptors (GPCRs) are a large family of transmembrane proteins expressed in many organs that activate internal signal transduction cascades through binding to different ligands including neurotransmitters, peptides, and lipids. G protein-coupled receptor 75 (GPR75) is a novel member of the GPCR family which has an important role in many diseases such as obesity, cancer, and metabolic syndrome. Until now three ligands have been detected for GPR75 including 20-HETE, CCL5, and RANTES. Recent studies suggest that 20-HETE through GPR75 triggers signaling pathways including PI3k/Akt and RAS/MAPK leading to a more aggressive phenotype in prostate cancer cells. Additionally, PI3k/Akt and RAS/MAPK signaling pathways activate NF-KB, which is substantial in various pathways of cancer development such as proliferation, migration, and apoptosis.

The findings indicate that inhibiting GPR75 in humans leads to less energy intake and body fat stores while increasing glucose tolerance and insulin sensitivity. According to these discoveries, GPR75 could be a potential drug target for treating diseases such as obesity, metabolic syndrome, and cancer.

Keywords: G protein-coupled receptors 75; Molecular Targeted Therapy; Colon Cancer.

Poster Presentation

1st International Congress of Biomarkers

PN: 1176

Potentiation of Folate-Functionalized PLGA-PEG Nanoparticles Loaded with Metformin for the Treatment of Breast Cancer: Possible Clinical Application

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ABSTRACT

Folate receptor expression increase up to 30 percent in breast cancer cells and could be used as a possible ligand to couple to folate-functionalized nanoparticles. Metformin is an anti-hyperglycemic agent whose anti-cancer properties have been formerly reported. Consequently, in the current study, we aimed to synthesize and characterize folate--functionalized PLGA-PEG NPs loaded with Met and evaluate the anti-cancer effect against the MDA-MB-231 human breast cancer cell line.

FA-PLGA-PEG NPs were synthesized by employing the W1/O/W2 technique and their physicochemical features were evaluated by FE-SEM, TEM, FTIR, and DLS methods. The cytotoxic effects of free and Nano-encapsulated drugs were analyzed by the MTT technique. Furthermore, RT-PCR technique was employed to assess the expression levels of apoptotic and anti-apoptotic genes, including Bax, Caspase7, Caspase3, p53, Bcl-2, and hTERT.

Assessment of MTT result indicated that Met loaded FA-PLGA-PEG NPs exhibited cytotoxic effect in a dose-dependently manner and had more cytotoxic effects relative to the free Met and Met loaded PLGA-PEG NPs. The remarkable up-regulation of Caspase7, Caspase3, Bax, and p53 gene expression were shown in treated MDA-MB-231 cells with Met laded FA-PLGA-PEG NPs than treated cells by Met loaded PLGA-PEG NPs and free Met forms. Furthermore, a significant down-regulation of hTERT and Bcl-2 gene expression was revealed in Met loaded FA-PLGA-PEG NPS compared to free Met and Met loaded PLGA-PEG NPs. Folate-Functionalized PLGA-PEG Nanoparticles are suggested as an appropriate approach to elevate the anticancer properties of Met for improving the treatment effectiveness of breast cancer cells.

Keywords: Metformin; Folate Functionalized-PLGA-PEG; Nano-carrier; Breast cancer.

Poster Presentation

1st International Congress of Biomarkers

PN: 1177

Fabricating a Robust POSS-PCL Nanofiber Scaffold for Nesting of Mesenchymal Stem Cells: Potential Application in Bone Tissue Regeneration

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ABSTRACT

According to recent studies, electrospun Poly (Ɛ-caprolactone) (PCL) is an absorbing candidate for the formulation of biocompatible scaffolds used in tissue engineering. Tissue engineering is a set of techniques for producing or reconstructing tissue, whose primary purpose is to restore or improve the function of tissues in the human body. Tissue engineering combines the principles of materials and cell transplantation to develop alternative tissues or promote endogenous regeneration. However, this electrospunscaffold, consisting of PCL, has disadvantages such as low cell adhesion, inactivity of the surface, osteoinduction, and acidic destruction of the scaffold that causes inflammation at the implant site, often making it unsuitable implant. This study aimed to improve PCL base cellular scaffolds with the formulation of polyhedral oligomeric silsesquioxane – Polycaprolactone (POSS-PCL) nanofiber scaffolds. The present research focuses on the synthesis of nanofibers for their cell interaction features, and application in bone tissue engineering and regeneration.

POSS/ PCL Nanocomposites with 2, 5, and 10 wt. % of POSS were synthesized in the Trichloromethane, then POSS – PCL Nanofibers were prepared by the electrospinning technique .

In this study, the structures of nanohybrids and nanofibers have been evaluated by FTIR, HNMR, XRD, SEM, EDX, and DSC. The biocompatibility of formulated POSS-PCL scaffolds was detected using mesenchymal stem cells (MSCs). Then several parameters were examined, involving DCFH ROS detection system, gene expression (cell viability/apoptosis, osteogenesis potentiality, and redox molecular homeostasis. Based on our results, POSS-PCL nano-scaffolds in comparison with PCL have shown a robust potentiality in homing, growth, and differentiation of stem cells.

Keywords: Electrospinning; Mesenchymal stem cell; Nanocomposite; Polyhedral oligomeric silsesquioxane; POSS-PCL; Tissue engineering.

Poster Presentation

1st International Congress of Biomarkers

PN: 1178

Efficacy of Gene Silencing in Head and Neck Squamous Cell Carcinoma Treatment: A Systematic Review

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ABSTRACT

Head and neck squamous cell carcinoma (HNSCC) is one of the most prevalent health problems in the world. Despite developments in chemotherapy and radiotherapy treatments, there does not seem to be significant success in the patient's survival rate. Assessment of genetic patterns and tumor-specific markers significantly impacts the development of low-complication treatments for cancers. Different genetic markers with various effects on different cancers have been studied and represented various results. The aim of this study is to report genetic markers with therapeutic effects in head and neck cancer .Data were obtained using PubMed, Embase, Scopus, ProQuest, Web of Science websites; A systematic review was performed based on data from 34 selected studies, including 1517 squamous cell carcinoma of the head and neck, 118 animal specimens ,13 apoptosis-related genes, 22 proliferation-related genes and 12 animal studies- related genes .These studies demonstrated the effect of gene silencing such as FAP, CRT, TRAF, RAC1 on reducing proliferation using MTT. Despite all other reported genes, KLF4 siRNA increased proliferation. Apoptosis-related articles studied by flow cytometry, demonstrated that silencing of genes such as UCA1, CRR9, H19 is effective in increasing early and late apoptosis. Among the genes influencing the rate of late apoptosis, TNF α - had the highest effect with a 29.4% increase in late apoptosis, followed by Myosin6 with a 27.55% increase in late apoptosis and HDAC8 gene with a 21.4% increase in late apoptosis. Among animal studies that examined tumor weight after gene silencing, jagged 1 gene had the highest effect on tumor weight reduction.TNF-α can be introduced as the most effective gene in increasing apoptosis. Furthermore, Jagged1 had the highest effect on tumor weight reduction.

Keywords: Gene silencing, head and neck squamous cell cancer, apoptosis, proliferation

Poster Presentation

1st International Congress of Biomarkers

PN: 1179

Discovering Biomarkers for Non-alcoholic fatty liver

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ABSTRACT

Non-alcoholic fatty liver disease (NAFLD) has become a major cause of chronic liver disease. It is considered a growing public health concern worldwide, with a prevalence of more than 30% in the general population. Early diagnosis of NAFLD can help to treat it. Evidence has shown that S100 proteins serve key roles in the occurrence and development of liver disease and can be used as potential therapeutic targets or diagnosis markers. Therefore, this study was conducted to investigate the biomarker potential of S100A9, S100A8, and S100A4.This case-control study included 50 healthy subjects and 50 patients with NAFLD. Blood were collected from the participants and centrifuged. Then its serum was separated and frozen at -80 until the parameters were analyzed. We evaluated serum levels of S100A9, S100A8, and S100A4 by ELISA. Also, we used Student's t-test and receiver operating characteristic (ROC) analysis to evaluate the data. Serum concentrations of S100A9, S100A8, and S100A4 were significantly higher in patients with NAFLD, compared with the healthy subjects (P <.05). Also, the results showed that S100A9, S100A8, and S100A4 has good specificity and sensitivity for diagnosing NAFLD. Based on the obtained results, S100A9, S100A8, and S100A4 can be used as a biomarker for NAFLD diagnosis. Although more studies are needed.

Keywords: NAFLD‹S100 proteins‹ELISA

Poster Presentation

1st International Congress of Biomarkers

PN: 1181

Can host genetic diversities act as prognostic biomarkers in COVID-19?

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ABSTRACT

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), responsible for the coronavirus disease 2019 (COVID-19) outbreak, has shown a vast range of clinical manifestations from asymptomatic to life-threatening symptoms. Previous studies demonstrated that some variations in host genetic mayaccount for wide spectrum manifestations. In the present review,we categorized these variations into several groups. As the virus entry-related genes, ACE2 variants such as E23K and K26R,higher expression of TMPRSS2, missense variants for the FURIN gene, down-regulation of DPP-4, APOE ε4/ε4 allele, and missense mutations of Bsg are associated with higher affinity to spike antigen and, therefore, severe disease. As the most important immune-related genes alterations, HLA variants such as HLA-A*11:01 and HLA-B*51:01, down-regulation in the expression of IFNs, variations in chemokine receptors gene, deletion of TICAM2, chromosome 3 cluster rs11385942 variant, high expression of perforin, NKG2C, and Ksp37 in NK cells, as well as rs7041 variant of vitamin D-binding protein are correlated with poor prognosis. Interestingly, while some host epigenetics modifications such as absence of EZH2 and H3K27me3 downregulation could increase the expression of ACE2, some others such as H3K4me3 and H3K9me2 can induce the expression of inflammatory pathways like IFNs, leading to a good prognosis. In conclusion, current review discusses different genetic variations which potentially can be used either as predictive or prognostic biomarkers in COVID-19.

Keywords: SARS-CoV-2; COVID-19; ACE2; Genetic diversity; Mutation; Vaccine.

Poster Presentation

1st International Congress of Biomarkers

PN: 1182

Tannic acid downregulates miR-29b-3p in K562-CML cell line

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ABSTRACT

MicroRNAs (miRNAs) are non-coding, single-stranded RNAs with 18-25 nucleotides that have recently been implicated in the regulation of many biological processes such as development, differentiation, apoptosis, proliferation, and hematopoiesis. miRNAs exert their function by promoting degradation of the mRNA or repressing its translation. In addition, miRNAs have been demonstrated in the development of human cancers, either as tumor suppressors or as oncogenes. Aberrant miRNA expression has been described for a variety of solid tumors and hematological malignancies. The growing evidence shows that alteration of miR-29b has been correlated with cell proliferation, tumor initiation, metastasis, and resistance to chemotherapy. Moreover, studies show that depending on cellular contexts, miR-29b can function as an oncogene or a tumor suppressor. Tannic acid (TA), a phytochemical agent with anti-bacterial andanti-tumor activity, inhibits cell growth in various types of cancer, including leukemia. In this study, we are aimed to survey the miR-29 expression pattern in TA-treated K562 cells. K562 cells were treated with TA for 12 and 48 hours and then proliferation and apoptosis were assayed with trypan blue and acridine orange/ethidium bromide staining, respectively. Moreover, the expression of miR-29-3p was evaluated by stem-loop real-time PCR.

Treatment with TA decreased cell proliferation in a concentration-dependent manner and, 50% inhibition of cell viability was obtained at 10μM. In addition, the enhancement ofapoptosis rate was associated with down-regulation of miR-29b-3p expression level in treated cells compared to control cells. Overall, considering the alteration of miR-29b-3p along with inhibition of cell proliferation, miR-29b-3p could be suggestedas a biomarker to predict response to the therapeutic agents.

Keywords: CML; microRNA; Tannic acid.

Poster Presentation

1st International Congress of Biomarkers

PN: 1183

In vitro study on the synergic effect of arsenic trioxide and deferoxamine on the viability of AML-M3 cell line

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ABSTRACT

Determination of the synergistic effect of arsenic trioxide and deferoxamine on viability in AML-M3 cells in vitro. First, arsenic trioxide and deferoxamine were prepared and an APL-related cancer cell line called NB4 was used for cell culture. To determine the EC_{50} of arsenic trioxide and deferoxamine over three days, different concentrations of each drug separately and their combined treatment for 24, 48, and 72 hours were added to cells cultured in RPMI medium and expression and the cell viability was evaluated by the test. Finally, all the results of all stages are collected using one-way ANOVA and T-test statistical methods in which a p-value <0.05 was considered significant, and the product and abstract are presented. The effect of ATO and DFO drugs on NB4 cells is sufficient for cell apoptosis and the synergistic effect of these two drugs is able to destroy leukemic cells of AML-M3 and thus reduce the effects of this leukemia in these patients and improve the condition of AML-M3 leukemic patients.

Keywords: Acute myeloid leukemia, Acute promyeloid leukemia, Deferoxamine, Arsenic trioxide, MTT

Poster Presentation

1st International Congress of Biomarkers

PN: 1184

Determining the Gut microbiota of Patients with Colorectal Cancer by Shotgun Sequencing Method and Investigating the Presence of Bacterial Cancer Biomarkers in This Group

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ABSTRACT

Colorectal cancer (CRC) is one of the most common cancers and one of the main leading causes of cancer-related deaths worldwide. Gut microbiota is part of a complex microbial ecosystem in the human body. Changes in microbiotacould lead to various diseases. Studies have shown that bacteria individually and collectively are involved in CRC progression. The change in the frequency of some of these bacteria in people's colon is very important. Therefore, these bacteria couldbe used as biomarkers for CRC diagnosis. Stool samples of 10 patients with CRC confirmed by colonoscopy (patients admitted to the colorectal department of Imam Khomeini hospital in Tehran) and 10 healthy individuals were collected in special containers. DNAs extracted from stool samples (using stool DNA isolation mini kit, Favorgen Co.) were sent for shotgun sequencing (HEPIA, Switzerland). After receiving the sequencing data in fastQ format, they were analyzed using relevant software such as OneCodex, Excel, and SPSS.

On average, about 1200 types of bacterial species with different frequencies were identified in each person's stool sample. In terms of the presence or absence of 199 bacterial species, there were significant differences between patients and healthy individuals, including *Clostridium difficile* as a biomarker for CRC diagnosis, which was more prevalent in the colon contents of patients compared to healthy individuals (80% difference) (p= .0032).

Considering that *C. difficile* has been suggested as a biomarker for CRC diagnosis, in this study, this bacterium was much more prevalent among patients compared to healthy individuals. Therefore, identifying and determining the abundance of this bacterium could be used as a preliminary screening method to diagnose CRC in the community.

Keywords: Gut microbiota; colorectal cancer; Shotgun sequencing; Biomarker; *Clostridium difficile.*

Poster Presentation

1st International Congress of Biomarkers

PN: 1185

Increased Autophagy induces kidney injury in the Renal Ischemic Reperfusion rat model: Rescue effect of Selenium by improving effect on autophagy biomarkers in the kidney

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ABSTRACT

Autophagy plays a significant role in renal ischemia-reperfusion injury (RIRI). The aim of this study was to evaluate the effect of Selenium pretreatment on kidney injury induced by ischemic reperfusion.

Twenty male Wistar rats (200±20 g) were divided into four groups (five per each): 1- Sham (surgery without renal pedicle clamping), 2- Sham-Selen (ip injection of Selenium with 0.5 mg/kg for 7 days), 3- RIRI (ischemia model was induced by 40 minute clamping the renal pedicle) and 4- RIRI-Selen (ip injection of Selenium with 0.5 mg/kg for 7 days). All animals were anesthetized 24h after I/R induction. Blood and tissue sample were collected for biochemical (plasma BUN & Cr) and western blot (p62, Lc3 II/Lc3I, Caspase 3) analyses.

The results showed that Selenium pretreatment significantly increased p62 and decreased Lc3 II/Lc3I ratio in the RIRI-Selen compared to RIRI group.Also our result demonstrated that Selenium pretreatment significantly decreased cleaved caspase3 in the RIRI-Selen compared to RIRI group.

It can be concluded that selenium, by inhibiting autophagy provides protection against kidney ischemia-reperfusion injury.

Keywords: Ischemia-reperfusion injury; Selenium; P62; Lc3 II/Lc3I; Caspase3; Autophagy; kidney.

Poster Presentation

1st International Congress of Biomarkers

PN: 1186

The effect of parathyroid hormone on TH17 cells in peripheral blood mononuclear cells in end-stage renal disease cases

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ABSTRACT

Chronic renal failure is mainly associated with elevated and low levels of parathyroid hormone (PTH) and immunological deficiencies. It is remained to be contradiction about the immunostimolator or inhibitor effect of PTH in mentioned individuals. Our aim was evaluation ofthe T helper 17 (Th17) cell effects as a prominent modulator of immunity in hemodialysis patients with impaired intact PTH (iPTH).

In the present study, blood samples were taken from ESRD patients with high (>300pg/ml), normal level (150-300pg/ml), and low (<150pg/ml) serum intactparathyroid hormone (iPTH) levels (n=30 in each group). The frequency of Th17 ($CD4^+$ $IL17^+$) cells was evaluated by flowcytometry in each group. The expression level of TH17 cell-related master transcription factors, cytokines in peripheral blood mononuclear cells (PBMC), and the level of mentioned cytokines were determined in the supernatant of PBMCs. The number of Th17 cells was significantlyaugmented in cases with high iPTH against low and normaliPTH. RORɣt and STAT3 levels were remarkely higher in high iPTH ESRD subjects than other groups in the expression of mRNA and protein levels. On the other hand, these finding confirmed with assessing IL-17, and IL-23 in the supernatant of cultured PBMCs.

Our data illustrate that elevated PTH in hemodialysis cases may impress increase the differentiation of naïve CD4+ T cells into Th17 cells in PBMC.

Keywords: Chronic kidney disease; IPTH; TH17; STAT3; RORɣt

Poster Presentation

1st International Congress of Biomarkers

PN: 1188

The effect of parathyroid hormone on inhibitory immune checkpoints in hemodialysis patients

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ABSTRACT

Parathyroid hormone (PTH) impairment, is one of the signaturecomplexities in cases receiving long-term hemodialysis, on the other hand, this variation is assumed as a potential factor in the progressing of an immune defect leading to various infections in hemodialysis cases. Thus, we aimed to investigate the impact of PTH variation on immune checkpoint inhibitors (ICs) in hemodialysis patients.

105 hemodialysis patients were categorized into three groups based on their serum intact parathyroid hormone (iPTH) values as follows: high (>300pg/ml), normal (150-300pg/ml), and low(<150pg/ml) serum iPTH levels (n=35 in each group). Then, the expression levels of ICs including cytotoxic T-lymphocyte-associated protein 4 (CTLA4), programmed cell death protein 1 (PD-1), T cell immunoglobulin-3 (TIM-3), and lymphocyte activation gene-3 (LAG-3) molecules were assessed using real-time PCR and western blot analysis in peripheral blood mononuclear cells (PBMC) of patient samples.

The group with high serum iPTH indicated a significantly augmentation in CTLA-4, PD-1, LAG-3, TIM-3 expressions in comparison to the other groups.

Our study illustrated that along with increased level of iPTH in hemodialysis patient, inhibitory immune checkpoints expressionraises in PBMC.

Keywords: Hemodialysis; Parathyroid hormone; Inhibitory checkpoint; Regulatory T cells; Hyperparathyroidism.

Poster Presentation

1st International Congress of Biomarkers

PN: 1189

Serum trace elements levels and clinical outcomes among Iranian COVID-19 patients

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[†] Yahya Yahyavi and Ozra Bagher Pour contributed equally to this work.

ABSTRACT

The relationship between immunity and trace elements levels is well known. We aimed to estimate the association of serum trace elements with severity and outcomes in the Coronavirus Disease-2019 (COVID-19) patients. In this single-centered, prospective, observationalstudy, we enrolled 114 patients admitted to severe intensive care units (ICUs) and corresponding 112 sex and aged-matched non-ICU ward patients. Demographic data, clinical characteristics, and outcomes were all collected. We analyzed serum levels of zinc (Zn), copper (Cu), selenium (Se), and manganese (Mn) in both severity groups.

The serum levels of Cu, Se, and Mn in both groups were within the normal range while Zn serum levels were lower than the normal values. Based on these findings, Zn, Cu, Se, and Mn serum levels were not associated with disease severity ($P > 0.05$). While we found Zn serum levels were strongly associated with patient outcomes ($P = 0.005$). Our results indicated lower Mn serum levels were associated with age more than 55 years ($P= 0.006$). Our results were not in favor of a causal relationship between serum trace elements levels and disease severity. We found Zn level as a strong indicator for patients' outcomes that can be considered for monitoring of patients' prognosis. Nutritional measures or supplementation can help reduce poor outcomes caused by low Zn levels in Iranian COVID-19 patients.

Keywords: COVID-19; Trace Elements; Zinc; Micronutrient; Iran.

Poster Presentation

1st International Congress of Biomarkers

PN: 1190

Cell-free DNA as a diagnostic method in patients with neuroblastoma: a systematic review

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ABSTRACT

This systematic review aims to summarize cfDNA levels and their detection methods for early detection of neuroblastoma with less invasive procedures.

After determining the search keywords, including neuroblastoma and cfDNA, these words were searched using MeSH and freely keywords in databases. Our results also showed that the diagnostic methods, isolation protocols, and sampling time were different in all studies based on extraction kits.

The qPCR method was the most used in detecting the gene segments. Samples were obtained from peripheral blood and bone marrow. MYCN amplification was the most seen genetic alteration; ALK, NSE/ (LINE-1), RET, RASSF1A, and APC mutations were often observed.

On the clinical scale, patients with higher levels of cfDNA were prone to progressed stages or recurrence of the disease in recovered patients. As some studies have shown that people with recent neuroblastoma had higher levels of cfDNA than those with long-term disease.

Keywords: Cell-Free Nucleic Acids; Neuroblastoma; Polymerase Chain Reaction; MYCN.

Poster Presentation

1st International Congress of Biomarkers

PN: 1194

Troubleshooting to help complications of detecting circulating long non-coding RNAs in pediatric acute lymphoblastic leukemia

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ABSTRACT

Acute lymphoblastic Leukemia (ALL) is the most common form of leukemia in children worldwide. The clinical diagnosis of ALL requires aspiration; the procedure which is invasive and painful, particularly for children. long non-coding RNAs (LncRNAs) have been considered as possible biomarkers for diagnosis, prognosis or monitoring of minimal residual disease (mrd) during patient chemotherapy in cancer. However, there are some complications in the identification of LncRNAs in plasma which need to be discussed. Firstly, the anticoagulant heparin in blood collection tubes has long been avoided to RNA analysis because it prevents PCR amplification. However, it has been recently shown that plasma samples produced from blood collected with heparin tubes may be appropriate for RNA expression analysis, without impacting RNA detection performance, if properly processed. In accordance with the fact that LncRNAs are highly stable in the circulation, minimal or no differences have been found between fresh and frozen specimens. Nevertheless, it is advisable to avoid any unnecessary freeze-thawing to prevent sample degradation, therefore loss of scarce amounts of included LncRNAs. Two extraction methods based on chloroform and commercial kits have been used in circulating RNA studies. However, the inconsistency of the given results awaits further standardization of these techniques. On the other hand, RNA yields are not sufficient for accurate gene expression analysis. In this case, we suggest the pre-amplification method to increase the sensitivity and reliability of results. Furthermore, using equal volume inputs are preferred to same amounts of RNA. Authors believe that the systematic approach discussed in this manuscript may help to achieve a global consensus of procedures and standardized protocol for accurate detection of circulating LncRNAs in leukemia patients and better disease management.

Keywords: Acute lymphoblastic leukemia, circulating long non-coding RNAs, Diagnostic biomarker, Prognostic biomarker, Detection

Poster Presentation

1st International Congress of Biomarkers

PN: 1195

New biomarker platform of colon cancer using quantum-based nano-biocomposite for early stage

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ABSTRACT

Because of their great sensitivity and wide analytical range, biosensors have recently become attractive analytical instruments for tiny analyses. The current study introduces a new biosensing approach based on tungsten disulfide quantum dots (WS2 QDs)-Au for swiftly and selectively detecting c-Met protein. M13 bacteriophage-based biosensors were employed as a proof of concept for the electrochemical detection of c-Met protein as a colon cancer biomarker. The M13 bacteriophage (virus) was mounted on glassy carbon electrodes modified with WS2 QDs-functionalized gold nanoparticles as the biorecognition element. SEM and square wave voltammetry (SWV) techniques were used to validate the presence of WS2 QDs, gold nanoparticles, and immobilized phage on glassy carbon electrodes. The developed biosensor was used to measure the quantity of c-Met protein in standard solutions, yielding the desired detection limit of 1 pg. Finally, as a proof of concept, the created platform was employed to assess c-Met protein levels in blood samples from colon cancer patients, and the results were compared to those of the standard Elisa kit. An intriguing aspect of this study was that several amounts of the c-Met protein in colon cancer blood samples that Elisa could not measure were simply assessed by the new bioassay technique. The designed bioassay system offers a significant deal of promise for use in biomedical laboratories.

Keywords: Biosensor; Cancer marker; Gold Nano-layer

Poster Presentation

1st International Congress of Biomarkers

PN: 1196

Investigating the Effect of Reduced Graphene and Graphene-Arginine on Sperm Fertilizing Ability

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ABSTRACT

Sperm cell maturation occurs for fertility with longevity in the female reproductive system. Inducing and maintaining the ability of in vitro fertility of sperm is an important and effective factor in the success of pregnancy techniques and in vitro fertilization (IVF). So, various strategies such as addition of calcium or creatine phosphate, can be used for enhancement of the fertilizing capacity of sperm during IVF. The change of chemical agents in sperm membrane can alter its fertility. Graphene, an allotrope of carbon, has interesting physical and chemical properties such as high electron mobility, high surface area, stiffness, strength and toughness. This nanostructure and their derivatives have been used in different fields of sciences, especially in biological and medical sciences. The aim of this study is comparison of the effect of reduced Graphene and Graphene-L-Arginine on sperm fertilizing ability. In this study, four main goals are pursued: The effect of graphene on in vitro sperm stability, Effect of graphene functionalization with arginine on increasing its solubility in polar solvents, Effect of graphene functionalization with arginine on its effect on In vitro sperm stability, determining the best concentration of Graphene and Graphene-L-Arginine to increase In vitro sperm stability. In this descriptive analysis study, we synthesized reduced and L-arginine-functionalized graphene by microwave method and characterized by TEM, SEM, FTIR and RMAN techniques. Acquired sperm samples from healthy volunteers were treated with different concentrations of reduced Graphene and Graphene-L-Arginine (1, 2, 3, 4, 5, 8, 10, 12, and 15 µg/ml). Sperm motility and morphology were assessed at 0, 0.3, 5, 10, and 15 minutes. Results showed that water solubility of Graphene-Arginine was higher than reduced Graphene. This increase in solubility facilitates the use of functionalized graphene in chemical and physiological fluids. Between reduced Graphene and Graphene- L-Arginine, Graphene- L-Arginine had more significant effects on increase of sperm fertilizing ability in same concentrations. On the other hand, reduced Graphene has more toxicity than same concentrations. In concentrations of 1, 2, 3, 4, 5, 8, and 10 µg/ml of Graphene- L-Arginine and 1, 2, 3, and 4 µg/ml of reduced Graphene, significant increase of fertilizing ability for sperm was occurred. In concentrations of 12 and 15 µg/ml of Graphene- L-Arginine and 5, 8, 10, 12, and 15 µg/ml of reduced Graphene, cell death, reduction of sperm motility and viability as well as membrane lysis was significantly observed. The reason for the higher activity and effect of L-Arginine-functionalized graphene is the synergistic effect of graphene (cholesterol extraction and enhancement of fertilizing ability) and L-Arginine (enhancement of nitric oxide synthesis and prevention of membrane lipid peroxidation) on increase sperm fertility. Based on this study, L-Arginine-functionalized graphene in low concentrations can be used in Assisted Reproductive Technology (ART) for in vitro increase of sperm fertilizing ability.

Keywords: Assisted Reproductive Technology; Sperm Fertilizing Ability; Graphene; L-Arginine; Nanostructure.

PN: 1197

Construction of Electrochemical sensor using Polydopamin-β-cyclodextrin coated on glassy carbon electrode and its application towards determination of some amino acids

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ABSTRACT

As a laboratory technique, the analysis of amino acid plays an important role in biochemical, Pharmaceutical and biomedical fields. Also amino acids exist in a free form or bound in peptides, proteins, or no peptide bonded polymers. Naturally occurring L-amino acids are required for protein synthesis and are precursors for essential molecules, such as coenzymes and nucleic acids. Electrochemical measurements were carried out in a conventional three-electrode cell (from Metrohm) powered by an electrochemical system comprising of AUTOLAB system with PGSTAT302N. The system was run on a PC using NOVA software.The ac voltage amplitude used was 10 mV and the equilibrium time was 5 s. An Ag/AgCl-Sat'd KCl and a platinum wire were used as reference and counter electrodes, respectively. The working electrode was GCE (d=2mm) and PDA-β-CD-GCE. The calibration curve for amino acids in PBS was obtained by differential pulse voltammetry (DPV).Fig. 10A shows typical DPV curves for different concentrations ofL-Cys in PBS using PDA-β-CD-GCE. The dependency between peak current and L-Cys concentration was rectilinear forL-Cys within the range of 0.06–0.2μM. The lower limits of quantitation (LLOQ) were found to be 0.06μMforpeakL-Cys. Similar results were obtained for L-Tyr, L-Gly, and L-PHe, L-Trp. For the first time, the electrooxidation and determination of amino acids was successfully performed using the GC electrode modified with polydopamine-β-cyclodextrin as a novel nono-sized biopolymer.

Key words: Dopamine, Beta – cyclodextrine, Nano biopolymer, Electrochemical nano sensor, Amino acid

Poster Presentation

1st International Congress of Biomarkers

PN: 1198

Nanoparticles encapsulation as a biomarker for the proclivity of cancer cells to metastasis

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ABSTRACT

Metastasis is the leading cause of cancer-related death, and the ability to anticipate its likelihood can have a significant impact on survival rates. The cytoskeletal processes utilized by metastatic cells for invasion are remarkably similar to the usage of the actin cytoskeleton in endocytosis. Lymph node status, tumor size, histology, and genetic testing are increasingly used to predict the development of metastasis. Identifying new prognostic indicators will be an important source for risk prediction. The adhesion and encapsulation efficiency of low-cost carboxylate-modified fluorescent nanoparticles by breast cancer cells with high (HM) and low metastatic potential (LM) were examined in the current work; benign cells were employed as controls. To determine quantifiable co-localization (Pearson's coefficients) of the nanoparticles with the observed cells, used custom-made automated image analysis techniques. Using high-content fluorescence imaging and analysis, discovered (within 1 hour) that the efficiency of nanoparticle adherence and encapsulation is significantly higher in HM cells than in LM cells, whereas benign cells are not encapsulating or adhering to the particles at all during the experiment. The procedure suggested here is simple; it does not need any special equipment, expensive materials, or intricate cell manipulations. It may be relevant to a variety of cells, including patient-derived cells. The use of patient-specific biopsy/surgery samples can conduct an easy and quantitative evaluation of metastatic possibility, which will directly impact the choice of protocols for cancer patients' treatment and, as a consequence, extend their life expectancy.

Keywords: Cancer cells; Metastasis; Biomarker; Encapsulation.

Poster Presentation

1st International Congress of Biomarkers

PN: 1200

RPLP1 is the Key Biomarker of Triple-Negative Breast Cancer in Patients with High Standardized Uptake Value in FDG-PET

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ABSTRACT

The standardized uptake value (SUV), an indicator of the degree of glucose uptake in 18F-fluorodeoxyglucose positron emission tomography (FDG-PET), is utilized for predicting tumor behavior molecularly and clinically in triple-negative breast cancer (TNBC). Numerous investigations have shown the contribution of tumor biology to increased glucose uptake in FDG-PET. They have demonstrated that the degree of glucose uptake is associated with aggressive tumor characteristics, and the SUV represented in FDG-PET has been recognized as a prognostic and predictive factor. GSE135565 and GSE162228 were downloaded using the GEOquery to obtain 60 samples of high SUV (>4) in TNBC and 24 normal breast samples, respectively. The batch effect was removed by the SVA package in R, and DEGs were determined using the following criteria: $|log2FC| > 1.5$ and adj *P*-value < 0.05. PPI network was constructed by the STRING database and analyzed by Cytoscape software. Enrichment analysis was carried out using the Enrichr database. 266 DEGs (262 up-regulated and 4 down-regulated) were identified between TNBC (high SUV) and normal breast samples. Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis is mainly enriched in Ribosome. According to Gene Ontology, SRP-dependent cotranslational protein targeting to membrane (GO:0006614), RNA binding (GO:0003723), collagen-containing extracellular matrix (GO:0062023) were enriched in biological process, molecular function and cellular component, respectively. Ribosomal protein lateral stalk subunit P1 (RPLP1), which is up-regulated in the tumor, was the only hub gene carried out from the intersection between the top 50 of the following topological algorithms: EigenVector, Eccentricity, Degree, Closeness, Centroid, Bridging, Betweenness. In summary, we identified an impactful gene for high SUV in TNBC and understood the pathways and ontologies that can lead us to understand disease progression better and provide novel biomarkers for future therapeutics.

Keywords: FDG-PET; Gene expression analysis; TNBC; Bioinformatic

Poster Presentation

1st International Congress of Biomarkers

PN: 1202

The significance of CD117 in the diagnosis of malignant and benign primary bone tumors

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ABSTRACT

Understanding the diagnostic value of CD117 to discriminate tumors with different severity is of grave importance. This study is focused on illuminating the CD117 gene and protein expression pattern, its association with tumor deterioration and its diagnostic value in different types of primary bone tumors.The local expression pattern of CD117 was detected in 180 bone tissues, including 90 tumors and 90 noncancerous tissues, utilizing real-time qRT-PCR at the mRNA level and immunohistochemistry at the protein level. The correlation of the CD117 expression level with the patient's clinical pathological characteristics and the aggressiveness of the tumor was evaluated. The diagnostic significance of CD117 and the model of association of variables and CD117 expression and their predictive values were determined. Mean mRNA expression was higher in all types of primary bone tumors than their paired non-cancerous tissues. Osteosarcoma and Ewing's sarcoma expressed higher levels of CD117 compared to benign tumors, and the CD117 expression level was significantly correlated with the size, metastasis, and recurrence of the malignant tumor. A consistent expression pattern was demonstrated for CD117 protein levels in tissues. In addition, the CD117 gene and protein levels significantly discriminate between bone tumors and normal tissue, as well as benign and malignant tumors. The data propose that CD117 may be involved in the proliferation and invasion of primary bone tumors and has the potential to monitor and treat the progression of malignant tumors.

Keywords: CD117; Bone tumors; Osteosarcoma; Ewing's sarcoma; Malignancy.

Poster Presentation

1st International Congress of Biomarkers

PN: 1205

Comparative study of the effect of vitis vinifera and Berberine on PLK3 protein using molecular docking method

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ABSTRACT

Abstract: PLK3 protein is a protein that works together with certain genetic mutations to lead to the spread of lung cancer. This protein can be a good therapeutic target for lung cancer. p53 acts as a tumor suppressor and initiates the death of cancer cells by itself, and due to the mutation known as "GOF", it becomes an oncogene and leads to the uncontrollable proliferation of cells and the spread of cancer. it leads The mutated p53 gene is amplified by a special protein called "PLK3", which transcribes the genetic code and promotes tumor cell growth through a process called "transactivation". Lung cancer caused by GOF mutation in the p53 gene, therefore activates PLK3, an amino acid called "serine 20" or "S20". Inhibition of PLK3 in p53 mutant cells reduces the function of S20 as well as the reduction of transactivation and It results in the formation of tumor cells. As a result, p53 uses PLK3 to induce the capacity of inducing auto-activison to induce carcinogenesis. In this study, two medicinal plants "Vitis vinifera" and "Berberine" were investigated to inhibit PLK3 protein using molecular docking method; to is used in the treatment of lung cancer and other diseases such as breast cancer that are caused by the same genetic mutation.

In this study, we used the Pub Chim site at pubchem.ncbi.nlm.nih.gov, Dragbank www.drugbank.com, and www.uniprot.org to examine vitis vinifera and Berberine derivatives. Also from the software ViewerLite, AutoDockTools-1.5.6, Chimera 1.15 and PyRx were also used.

Result:The plant compound "berberine" may help fight lung cancer. Researchers have also identified berberine as a potential treatment for various types of cancer, including ovarian cancer, stomach cancer, and breast cancer. It inhibits cell proliferation and migration." "Since berberine has poor biosolubility, its clinical application is limited. The main goal of this study is to improve the physicochemical parameters of berberine by formulating it into liquid crystalline nanoparticles and studying its anticancer potential in vitro against human adenocarcinoma alveolar-basal epithelial cells, A549.

These reliable source liquid crystalline nanoparticles were used to treat human lung cancer cells in vitro in an in vitro environment. According to docking studies, we found that conformation of Berberine with negative binding affinity and RMSD had a better effect on PLK3 protein to induce apoptosis and prevent cancer cell growth.

Keywords: doking, lung cancer, Berberine, Vitis Vinifera, PLK3, PyRex, chimer

Poster Presentation

1st International Congress of Biomarkers

PN: 1210

Some biological effects of galactose-specific lectins from prostate tissue with different pathologies in tumor cells model in vitro

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ABSTRACT

In cancer biology, aberrant glycosylation changes, resulting in expression of altered carbohydrate determinants on many glycoproteins and glycolipids has been known as one of the most important changes related to tumor malignancy. Some of these significant interactions related to carbohydrates are mediated through binding to specific proteins- lectins, interacting with carbohydrate determinants. Depending on their properties and distribution in tissues, lectins can play important physiological roles. Studies of physiological and biological properties of the endogenous lectins have become a very important issue in the recent years. Mammalian lectins have already been shown to exhibit different biological activities and effects, such as mitogenic and antiproliferative activities on cell lines of human cancer, action as promoting agents in cell aggregation, immunomodulatory activities. Our attention has been drawn to the role of mammalian beta-galactose-specific lectins (galectins) because galectins are also involved in endogenous regulation of different intracellular pathways with high impact on controlling cellular behavior. Tumor cells characterizes by increases expression of galectins. In prostate cancer galectins have been implicated in many cellular processes (proliferation, apoptosis, migration, invasion) and are considered as potential prognostic markers and potential therapeutic targets for this type of pathology.

In our previous study, we have shown that affinity purified cytosolic galactose-specific lectins fractions from normal and pathological prostate tissue samples are characterized with different protein composition and expressed different effects on cell viability and apoptosis of healthy blood lymphocytes in vitro.

The present study is focused on the biological effects (cell viability, and apoptosis) of cytoplasmic galactose-specific lectins fraction purified from prostatic tissues with different grades of pathologies in the pathological tumor cell lines cells (MEC1 cell line lymphocytes and Human prostate cancer PC3 cell line).

Methods: Human prostate tissue samples were obtained from patients undergoing open trans-abdominal prostatectomies for benign prostate hyperplasia and transurethral resection of the prostate (TURP). The numbers of testified tissues were: 1. Unaffected (N, normal) tissue isolated after cytoprostatectomies, n=7 (age 47-68 years); 2. benign prostatic hyperplasia (BPH) with –low-grade intraepithelial neoplasia, LGPIN diagnosis, n=35 (age 55-70 years); 3. with high-grade intraepithelial neoplasia, HGPIN diagnosis n=17 (age 50-68 years), tumor precursor; 4. atypical adenomatous hyperplasia, AAH diagnosis n=22 (age 50-75 years) and 5. prostate adenocarcinoma, PC diagnosis n=11 (age 54-67 years). All patients were otherwise healthy. Cytosolic galactose-specific lectin fractions from prostate tissue were isolated and purified by affinity chromatography. MEC1 cell line was established from EBV-seropositive patient's Chronic Lymphocytic Leukemia cells and iswidely used as a model for CLL pathogenesis. The lectin effects were studied on cell viability by MTT reduction method using the WST1-reagent(4-[3-(4-Iodophenyl)-2-(4-nitro-phenyl)-2H-5-tetrazolio]-1,3-benzenesulfonate). The concentration of cytosolic galectins comprised 5 µg/10x106 lymphocytes/well (200 µl incubation area) and 10x105 PC3 cells/well. Apoptotic cell cycle analysis studied on lymphocytes by flow cytometry method. Lectin concentration (fractions from HGPIN and PC diagnosis tissues) comprised 5 µg/10x106cells (200 µl incubation area), the incubation time was 1 h, and cells were washed with PBS. Cell cycle analysis was carried out at 0 sec, 24 h, 48 h, 72 h. The data of cell viability

experiments were analyzed by one-way analysis of variances (ANOVA) with factor – lectin source (BPH, HGPIN, AAH and PC). The data of apoptosis were analyzed by two-way ANOVA with factors: time of incubation and lectin source (HGPIN, and PC). Planned comparisons were carried out with student t-test. All tests were two-tailed unless otherwise stated, and P value less than or equal to 0.05 was taken as significant. All significant results are reported.

Results: Thus, the cytosolic galactose-binding lectin fractions from prostatic tissues with different pathologies have different effects on cell viability depending on the lectin's fractions source (prostatic tissues diagnoses). All testified lectin fractions, except from AAH tissue, markedly reduced also the cell viability in MEC1. In general, all lectins decreased the PC-3 cell viability. The strongest effect is observed for lectins isolated from BPH tissue. Based on previous studied were able to study the role of cytosolic galactose-specific lectins fraction on apoptosis from PC and HGPIN tissue lectins. The effect of lectins fraction on the cell cycle was studied in vitro in MEC1 line lymphocytes. Lectin fraction from prostatic tissue with HPGIN diagnosis significantly decreases the apoptosis of leukemic MEC-1 line lymphocytes at 48h, followed by sharp increase at 72 h. Incubation of leukemia MEC1-line lymphocytes with cytosolic galactose binding lectins from prostatic tissue with PC diagnosis leads to gradual increase of apoptosis and starting from 24h The highest rate of apoptosis is observed at 72h significantly.

Conclusion: There was studied the biological properties of cytosolic galactose-specific lectins, isolated from unaffected (norm) tissue (after cytoprostatectomies) and diseased prostate tissue with different diagnoses (BPH/LGPIN, HGPIN, AAH and PC) in vitro system.

We conclude that the effect of cytosolic galactose-specific lectins fractions 1) depends on the form of glandular tissue disease and also on the type of cell (lymphocytes, PC3, used in the research), 2) is likely to depend significantly on the cell surface glycoconjugate's nature and structure and 3) the effect of cytosolic galactose-specific lectins fractions isolated from HGPIN and PC tissues can have defensive and anti-tumor properties in tumors cell – MEC1 line lymphocytes and prostate PC3 cell line.

Keywords: Apoptosis; Cells survival viability; Gland diseases; Prostate galactose-specific lectins

Poster Presentation

1st International Congress of Biomarkers

PN: 1211

miRNA-target gene interactions in inflammation-specific sub-network of COVID-19 and neurological diseases

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ABSTRACT

SARS-CoV-2 infection can trigger neuroinflammatory responses. Inflammatory diseases of the central nervous system have been identified as potential risk factors for COVID-19. The neurotropic characteristics of coronaviruses can render neuronal tissue vulnerable to infection in older people or in patients with neurological comorbidities. In our study, a disease-inflammatory sub-network was built through human protein-protein interactions to decipher common interactions among COVID-19 and neurological diseases. miRNA-target gene regulatory interactions were retrieved for overlapping neurological genes with the inflammatory-associated sub-network. Protein-protein interactions of the COVID-19–related genes were acquired from the STRING database with a high confidence interaction (score>0.7). The resulting network was visualized using Cytoscape. To construct an inflammation-specific sub-network associated with SARS-CoV-2 infection, inflammatory hub-bottlenecks with their first interacting protein neighbors were considered. Topological characteristics of the resulting sub-network were extracted by the Network Analyzer plug-in of the Cytoscape software. Then, the possibility of cross-talk among the inflammatory sub-network and neurological disease in the COVID-19 response were studied. Towards this end, proteins involved in the inflammatory sub-network were mapped into the DAVID database to extract the significant overlapping genes among the inflammatory sub-network and neurological disease using the GAD_DISEASE_CLASS category (q-value<0.05). Key regulators of overlapping neurological genes with the inflammatory-associated sub-network were retrieved from the miRTarBase database based on the functional miRNA-target interaction support type. The inflammatory sub-network of COVID-19 was constructed by 15 inflammatory hub-bottlenecks (IL6, TNF, INS, CXCL8, STAT3, EGFR, CXCL10, TLR4, KNG1, JUN, GNB1, AGT, HLA-DRB1, IL17A, and JAK2) and their interacting proteins in the whole protein interaction network. The resulting inflammatory sub-network included a total of 297 nodes and 838 edges. Disease interaction analysis of the inflammatory sub-network showed 126 significant overlapping proteins for neurological diseases. Next, miRNA-target gene interactions were mined for the 126 candidates. The results revealed 510 miRNA-target interactions with 253 miRNAs and 67 target genes. miR-29b-3p, miR-29a-3p, miR-146a-5p, miR-29c-3p, miR-124-3p, miR-143-3p, miR-145-5p, miR-199a-5p, miR-200b-3p, miR-24-3p, miR-26a-5p target the most of these common genes. Understanding of inflammation-related molecular mechanisms through COVID-19-disease interactions analysis can be useful in monitoring treatment responsiveness for controlling the inflammatory responses.

Keywords: SARS-CoV-2 infection; COVID-19; Inflammatory response; Neuroinflammation; MicroRNA

Poster Presentation

1st International Congress of Biomarkers

PN: 1213

Evaluation of covid-19 biomarkers in newborns

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ABSTRACT

The ongoing pandemic of coronavirus disease 2019 (COVID-19) poses several challenges to clinicians. Timely diagnosis, treatment, selection of appropriate therapies and monitoring are essential to save the maximum number of lives. An important question is whether pregnant mothers transmit the virus to their fetuses or not. There are limited data available regarding COVID-19 during pregnancy. Vertical transmission of the COVID-19, has been reported in several case reports and several case series, while the data regarding its transmission is still not enough. It is well known that an infected mother can transmit the COVID-19 virus through respiratory droplets during breastfeeding. Due to the rapid spread and increasing number of COVID-19 cases, it is crucial to detect disease rapidly as well as correctly, to control the sources of infection and help patients to prevent the illness progression. Clinical signs and symptoms by itself may cannot be helpful to make the diagnosis of COVID-19. The gold standard for diagnosis is the detection of viral genome targets by real-time polymerase chain reaction (RT-PCR) in respiratory tract materials during the first week of symptoms. The real-time RT-PCR test has high false negative rate and in many COVID-19 cases it might not be positive while clinical sign and symptoms in these patients confirm COVID-19. An interesting topic that has been mentioned in the studies is that among the patients in whom the symptoms of COVID-19 have been confirmed, the positive result of the RT-PCR test in children is reported significantly less than in adults. The overall sensitivity of the RT-PCR test is reportedly between 45–60% in nasopharyngeal aspirate and swab samples. RT-PCR might not be available in an emergency setting also.Therefor RT-PCR alone, cannot be helpful screening test COVID-19 patients. Computed Tomography (CT) is a widely used diagnostic tool that is based on X-ray techniques with a help of a computer. CT scan can be used for diagnosis symptomatic patients in the diagnosis of RT-PCR-negative patients with COVID-19 symptoms who require emergency or urgent surgery. CT imaging can demonstrate typical patterns of imaging manifestations that could be used to diagnose COVID-19. It is a readily available tool in nearly all healthcare facilities in the world, and the results are immediately reported. Studies show CT scan can find the infected patients, with the sensitivity of 94.5%, however the average specificity is quite low, being around 84%. This could due to the fact that CT-scan is more sensitive than RT-PCR. The lowest specificity among the discussed papers is 25%. Biomarkers will play a crucial role in early diagnosis of COVID-19. They can be used as a complemantry tests for diagnosing also. Among known biomarkers such as D-Dimer, Lactate dehydrogenase(LDH), C-reactive protein (CRP) , erythrocyte sedimentation rate (ESR) , cardiac troponin I (cTnI), leukopenia, lymphopenia and lymphocyte subsets (CD4+,CD8+), these biomarkers have become more prominent in children. We evaluated the gathered data from last three year and reviewed biomarkers to propose some useful biomarkers to diagnose COVID-19, and based on evidence, We will present these helpful diagnostic biomarkers.

Key words: COVID-19 , Diagnostic biomarkers , newborn

Poster Presentation

1st International Congress of Biomarkers

PN: 1214

Potential role of Cancer Stem Cell Biomarkers in Rectal Cancer Diagnosis

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ABSTRACT

Colorectal cancer (CRC), also known as bowel cancer, colon cancer, or rectal cancer, is the growth of cancer from the colon or rectum (parts of the large intestine). Signs and symptoms may include blood in the stool, changes in bowel motility, weight loss, and fatigue. Most colorectal cancers are due to aging and lifestyle factors, with only a small number of cases due to underlying genetic disorders. Risk factors include diet, obesity, smoking, and lack of physical activity. Several genetic diseases are also associated with high rates of colorectal cancer. The most common is hereditary colorectal cancer (HNPCC or Lynch disease), which is present in about 3% of people with colorectal cancer. The most common polyposis affecting the colon is serrated polyposis, which is associated with a 25-40% risk of CRC. Mutations in pairs of genes (POLE and POLD1) are associated with familial colon cancer due to colon cancer being associated with metastatic disease. A gene thought to contribute to the likelihood of metastatic disease, metastasis-associated in colon cancer 1 (MACC1), has been isolated. Colorectal cancer the disease originates in the epithelial cells of the colon or rectum of the gastrointestinal tract, most commonly as a result of mutations in the WNT signaling pathway that increase signaling activity. Mutations can be inherited or acquired, and most likely occur in the intestinal crypt stem cell. The most commonly mutated gene in all colorectal cancers is the APC gene, which produces the APC protein. APC protein prevents the accumulation of β-catenin protein. Without APC, β-catenin accumulates to high levels and translocate (mobilizes) to the nucleus, binds to DNA, and activates the transcription of proto-oncogenes. These genes are normally important for stem cell renewal and differentiation, but when inappropriately expressed at high levels, they cause cancer. While APC is mutated in most colon cancers, some cancers have increased β-catenin due to mutations in β-catenin (CTNNB1) preventing its degradation, or there are mutations in other genes with APC-like functions such as AXIN1, AXIN2, TCF7L2 or NKD1. Other proteins responsible for programmed cell death that is commonly inactivated in colorectal cancers include TGF-β and DCC (deleted in colorectal cancer). TGF-β has an inactivating mutation in at least half of colorectal cancers. Sometimes TGF-β is not inactivated, but a downstream protein called SMAD is. DCC generally has a chromosomal deletion in colorectal cancer. Approximately 70% of all human genes are expressed in colorectal cancer, with just over 1% of their expression increased in colorectal cancer compared to other cancer types. Some genes are oncogenes: they are overexpressed in colorectal cancer. The chronological order of changes is sometimes important. If a previous APC mutation occurs, an early KRAS mutation often progresses to cancer rather than a hyperplastic or restrictive self-limiting lesion. Epigenetic changes are much more common in colon cancer than genetic (mutation) mutations.

Keywords: Cancer Stem Cell; Biomarker; Rectal Cancer Diagnosis

Poster Presentation

1st International Congress of Biomarkers

PN: 1216

microRNA-146b in papillary thyroid cancer

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ABSTRACT

About 75_80% of human genome is transcribed into RNA but about 3% of this RNAs encode proteins. Non-coding RNAs have many different roles in molecular pathways related to various biological processes. Recently, many researchers recognize non_coding RNAs as regulator in different molecular pathways related to diseases like different types of cancer. miRNA-146b is one of them. It is a short non_coding RNA that affect regulatory RNAs that suppress protein synthesis at post_transcriptional phase. So, this miRNA be able to have different roles in physiologic and pathophysiological processes. We searced in PUBMED database through January 2018 between papers that explain different regulatory impacts of miRNA_146b in molecular pathways which leads to papillary thyroid cancer. We found that miRNA_146b increases in papillary thyroid cancer and affect pathways on main molecules of pathway (direct) or regulatory molecules of pathway(indirect) or the molecules that have various rate in cancerous cells than normal cells. This impacts increases proliferation, migration and invasion of papillary thyroid carcinoma. miRNA-146b is the most important molecule in papillary thyroid cancer and can be an important diagnostic factor and therapeutic target.

Keywords: Papillary thyroid cancer; miRNA_146b; Molecular pathway; Regulatory molecule

Poster Presentation

1st International Congress of Biomarkers

PN: 1217

Exosomes: A Novel Biomarker for Prognosis and Diagnosis of COVID-19

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ABSTRACT

Extracellular vesicles generated by different types of cells contribute to intercellular communication by transporting biomolecules such as nucleic acids, proteins, and lipids to recipient cells. Exosomes are extracellular vesicles that circulate and have a diameter of 40 to 150 nm. They are important in a variety of processes, including cancer growth, intercellular signaling, drug resistance mechanisms, and cell-to-cell communication by fusing onto the cell membrane of recipient cells. These vesicles contain endogenous proteins as well as non-coding and coding RNAs (microRNAs and messenger RNAs), which can be transferred to diverse cell types. Exosomes can also be found in body fluids such as plasma, cerebrospinal fluid, and urine. So, they could be used as a new way to deliver therapeutic nucleic acid drugs in cancer treatment. Exosomes are found in cells infected with a virus. Because they carry viral parts like miRNAs and proteins, these exosomes are linked to infections. Exosomes also contain virus receptors, which make recipient cells susceptible to viral entry. Extracellular vesicles work as molecular patterns related to pathogens. They contain inflammatory markers and cause a strong inflammatory response. Exosomes containing dUTPase are released by cells infected with EBV. These exosomes activate nuclear factor-kappa B (NF-κB) signal transduction and stimulate macrophage cytokine production. Exosomes containing the SARS coronavirus spike S protein were found to be effective in inducing neutralizing antibody titers. Exosomes produced by SARSCoV2-infected cells have the potential to stimulate the immune system. Exosomes could also be loaded with medications or biological modulators that inhibit viral reproduction and dissemination in host cells. Exosomes have potential properties that make them preferable to other conventional nano-delivery technologies. Virus-infected cells have been found to be involved in virus transmission as well as immune system modulation by secreting exosomes containing protein particles, viral genomes, and inflammatory factors. Exosomal therapy can be developed to target respiratory viral infections such as SARS-CoV-2.

Keywords: Exosome, COVID-19, Extracellular vesicles, microRNA, Cell communication

Poster Presentation

1st International Congress of Biomarkers

PN: 1218

Curcumin sensitizes CD44$^+$ prostate cancer cells to paclitaxel via modulating miR-148a/MSK1/IRS1 axis

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ABSTRACT

Prostate cancer (PC) is the most frequent cancer and second most common cause of cancer-related death in men. PC is commonly treated with radiotherapy, chemotherapy, and hormone therapy. Paclitaxel inhibits cancer cell proliferation in PC cells. Paclitaxel can also stop the cell cycle from progressing to the G2/M phase and prevent microtubular depolymerization by binding to free tubulin. However, paclitaxel resistance is a major challenge in advanced PC. Curcumin, a natural antioxidant, has been demonstrated to have cytotoxic effects on cancer stem cells (CSCs). Curcumin also upregulates of tumor suppressor miRNAs such as miR-205, miR-143, and miR-208 while silencing oncomirs such as miR-21, miR-14, and miR-183. The goal of this study is to explore if curcumin can help lower chemoresistance to paclitaxel through the regulation of miR-148a-mediated apoptosis in prostate CSCs. Drugs and reagents were bought from Sigma-Aldrich (St. Louis, MO, USA). Paclitaxel and curcumin were suspended in RPMI and kept at -20º C. We used mini-MACS to enrich CD44+ CSCs from the PC3 cell line, which was verified by immunocytochemistry. The MTT assay and DAPi labeling were used to determine cell survival. The expression of P-glycoprotein protein (P-gp) and CD44 proteins was determined by immunohistochemistry. Real-time PCR was used to evaluate the regulatory effects of curcumin and paclitaxel on miR-148a and its target genes. Pre-treatment of CD44$^+$cells with curcumin significantly reduced the IC_{50} value and increased apoptosis rate in CD44$^+$cells compared to paclitaxel alone. In addition, our results found that the co-treatment of carcumin and paclitaxel attenuated the expression of CD44 and P-gp compared to paclitaxel alone. On other hand, Curcumin and paclitaxel combination also enhaced miR-148a levels and down-regulated the levels of its target genes MSK1 and IRS1. Curcumin improves the paclitaxel sensitivity in CD44$^+$ prostate cancer cells by raising miR-148a expression and inhibiting MSK1 and IRS1.

Keywords: Prostate cancer; Cancer stem cells; Curcumin; Paclitaxel; miR-148a

Poster Presentation

1st International Congress of Biomarkers

PN: 1219

New Insight into the Autophagy Mechanism

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ABSTRACT

It is well known that autophagy is a crucial mechanism in cells involved in biological evolution, the immune system, and cell death and is associated with fatal disorders such as cancer, autoimmune diseases, and nervous system degeneration. Autophagy serves two purposes. It improves cell viability while promoting cell death. Numerous studies have demonstrated that autophagy is crucial for both cell survival and cell death. However, autophagy promotes cancer progression in several cancer types. Many studies have demonstrated that autophagy supplies enough nutrients to support the growth of cancer cells. Autophagy, a process of recycling cells, helps to keep cellular homeostasis by giving cells the nutrients they need and getting rid of old, damaged organelles, proteins, and other macromolecules. Inducing autophagy may be a key strategy for cancer prevention since it contributes to tumor suppression. Inhibiting mTOR signaling can cause autophagy, and PI3K-AKT-mTOR signaling is frequently disrupted in human malignancies. Metformin-induced mTOR signaling inhibition may also reduce carcinogenesis. Understanding apoptosis and the mechanisms that control cell growth is crucial for understanding cancer cells. A vital kinase involved in the control of various cellular functions, PI3K-Akt-mTOR is activated by a variety of cellular stimuli. Alteration in the PI3K-Akt-mTOR signaling pathway, which is necessary for healthy human physiology, can lead to human cancers. A key regulator of cellular survival under stress is the PI3K-Akt pathway. The PI3K-Akt pathway, which is associated with autophagy and apoptosis, is required for cell survival and proliferation. Starvation, growth hormones, and cell stressors all control mTOR, a critical regulator of autophagic activities. mTOR activity is controlled by the survival PI3K/AKT pathway, which is similarly impacted by autophagy.

Keywords: Autophagy; PI3K-Akt-mTOR pathway; Apoptosis; Cell growth

Poster Presentation

1st International Congress of Biomarkers

PN: 1220

Allicin sensitizes gastric cancer cells to 5-flourouracil via down-regulating *WNT5A*, *DKK1*, and *MDR1* mRNA expression

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ABSTRACT

Gastric cancer (GC) is the fifth most common cancer and its mortality rate is high worldwide. In advanced stages, it usually metastasizes to the lung, liver, peritoneum, and bone marrow. 5-fluorouracil (5-FU) is approved for the treatment of GC, but chemo-resistance limits the application of it for GC. Allicin is the major component of garlic that has antibacterial, antiviral, and anticancer properties. Thus, the combination of 5-FU with adjuvants such as allicin may overcome multidrug resistance (MDR). Drugs were purchased from Sigma-Aldrich. The human 5-FU resistant gastric cancer cell line MKN-45 was previously established by Pouremamali et al. The GC cells were grown in RPMI1640 (Gibco, UK) medium supplemented with 10% fetal bovine serum (FBS, Gibco, UK), and 1% antibiotics. The anticancer effects of allicin, 5-FU, and allicin/5-FU on the 5-FU resistant MKN-45 cells were evaluated by MTT assay and DAPi staining. immunocytochemistry assay was used to determine the expression of P-glycoprotein (P-gp) and CD44 proteins. Finally, we quantified the expression levels of *WNT5A, Dickkopf-1* (*DKK1*), and *MDR1*mRNA in the GC cells. The results of this study indicated that the combination of allicin with 5-FU significantly increased apoptosis compared to 5-FU alone (P<0.05). Real-time PCR results illustrated that *WNT5A, MDR1,* and *DKK1* mRNA expression levels were down-regulated in the allicin- and allicin/5-FU-treated cells. Indeed, the combination of allicin and 5-FU significantly decreased the expression of the P-gp and CD44 proteins (P<0.05). Altogether, our findings confirmed that the combination of allicin with 5-FU could reverse multidrug resistance in the GC cells by reducing the expression of *WNT5A, DKK1*, *MDR1*, P-gp, and CD44 GC biomarkers.

Keywords: Allicin; Gastric cancer; Cancer biomarkers; CD44; P-gp

PN: 1222

Salivary CA-125: A Tumor Marker for Oral Squamous Cell Carcinoma

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ABSTRACT

In Sudan, oral cancer is the second most common cancer, and OSCC represent the majority of the cases. Up to date and despite the fact that; saliva can be collected simply and non-invasively, there is no approved salivary tumor marker for OSCC. The purpose of this study is to investigate the reliability of salivary CA-125 as a tumor marker for OSCC by measuring and comparing its level in patients with OSCC and healthy controls as well as to compare its level among different histopathological grades of OSCC. 100 subjects were enrolled; 50 of them were patients with OSCC, while the other 50 were matched healthy controls. Non-stimulated whole saliva was collected before administration of definitive treatment. The concentration of salivary CA-125 was quantified by automated immunoassay analyzer, which utilizes one-step sandwich fluorescent enzyme immunoassay (FEIA). The level of salivary CA-125 was 342.65 U/ml in cases of OSCC which was significantly increased compared with 203.65 U/ml in the healthy controls, (P 0.017). Statistically significant differences in the level of salivary CA-125 among different histopathological grades were observed, (P 0.014). The sensitivity, specificity, accuracy, positive and negative predictive values were; 48%, 78%, 63%, 68.6% and 60%, respectively. This study is considered to be the first of its type in Sudan and it showed that; Salivary CA-125 can be a potential tumor marker for OSCC. However, its use in clinical practice needs further validation.

Keywords: Tumor marker; OSCC; CA-125; Saliva

Poster Presentation

1st International Congress of Biomarkers

PN: 1224

The Function of miR-146 in Covid-19

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ABSTRACT

After the pandemic was made public in March 2020, the diagnosis of Covid-19 became extremely important. MicroRNA, known as small non-coding single-strand RNA molecules, by regulating gene expression post-transcriptionally, can control diverse range of biological pathways. MicroRNAs would be prospective diagnostic markers for Covid-19 because they have been investigated as biomarkers in a number of viral diseases such as HBV, HCV, Varicella and Influenza. In this study we reviewed the function of miR-146, one of the earliest cases of miRs triggered by an immunological response, in contracting Corona virus. This review described a number of recent articles to investigate the function of mirR-146 family as clinical biomarkers for Covid-19 patients from Google scholar and PubMed data bases. To assess the potential of miR-146 members as an innovative biomarker in severe and mild Covid-19, significant expression of miR146b was observed when compared to healthy individuals. MiR-146b levels were found to be 2.3 times higher in mild Covid-19 patients and 1.9 times higher in severe Covid-19 patients when compared to healthy subjects. Recent survey has focused on the role of miR-146a-5p as a negative modulator of immune system via tumor receptor factor-associated factor 6 (TRAF6) and IL-1 receptor activated kinase 1 (IRAK1), regulates the pro-inflammatory cytokines (IL-8, IL-6) and production of cytokine-response genes, under the name of promising markers for severe Covid-19. The study of individuals with various degrees of Covid-19 severity revealed that the relative expression of anti-neuro-inflammatory miR-146a was reduced while the expression of its target, TRAF6 mRNA, increased. Given the role of miR-146 members in the pathogenesis of Covid-19 patients, it appears that members of this family are promising biomarkers in the diagnosis of Covid-19.

Keywords: MicroRNAs; miR-146; Covid-19.

PN: 1226

The role of Doppler middle cerebral artery peak systolic velocity in the diagnosis of anemia in premature neonates in Urmia Shahid Motahari hospital's NICU

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ABSTRACT

All infants physiologically experience a decrease in hemoglobin levels in the first 2 to 3 months of life. Transcranial Doppler ultrasonography has been introduced as a non-invasive method for monitoring blood flow in cerebral arteries. This study aimed to investigate the role of doppler parameter of peak systolic velocity (PSA) of middle cerebral artery (MCA) in diagnosing anemia in premature neonates admitted to the neonatal intensive care unit of Urmia Shahid Motahari Hospital. Preterm infants with a history of color doppler brain ultrasonography in the first two days after birth in 2019 were enrolled in this study. All neonates with physical abnormalities, intrauterine growth restriction, and infection were excluded and finally, a total of 109 premature neonates went under evaluation. Anemia is defined as hemoglobin (Hb) <13.5g/dL and hematocrit (HCT) <45%. The doppler effect of MCA PSA was calculated by using a Volsun 730 device in a silent room. The mean PSV of MCA in the anemic and non-anemic neonates was 33.56 and 25.81, respectively, which was significantly higher in the anemic neonates ($p<0.001$). Pearson's correlation coefficient showed a significant inverse relationship between PVS and anemia indices including Hb and HCT ($r = -0.39$ and $r = -0.32$, respectively, $p<0.001$). According to the results obtained from the ROC curve, the PSV of the MCA had a cutoff point of 21.99, 98% sensitivity, and 95% specificity for neonatal anemia detection. Based on the results of this study, PSV of MCA can be considered a reliable predictor of anemia in the premature neonates admitted to NICU.

Keywords: Transcranial Doppler Parameter, Peak Systolic Velocity, Middle Cerebral Artery, Anemia, Premature Neonate

Poster Presentation

1st International Congress of Biomarkers

PN: 1229

Effects of physical activity and zinc supplementation on prenatal stress-induced depressive-like behaviors in adolescent female rat: challenges and opportunities of oxidative stress biomarkers

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ABSTRACT

Many studies have shown the deleterious influence of prenatal stress (PS) on neurological and behavioral manifestation in offspring, however, little is known about how to minimize these negative effects. The present study examined the effects of prenatal intervention of physical activity and zinc on PS-induced anxiety and neuro-inflammatory biomarkers in adolescent female rat offspring.

Pregnant rats were divided into 5 groups: control, stress, stress + exercise, stress + zinc, and stress + exercise + zinc. The stress groups were exposed to the restrain stress for 5 consecutive days (G15-19). Rats in the exercise and zinc groups were subjected to either forced treadmill exercise (30 min/daily), or zinc sulfate (30 mg/kg/orally), or both throughout the pregnancy and similarly exposed to the stress. At postnatal day 25-27 anxiety-like behaviors of offspring were recorded using elevated plus maze and the gene expression of interleukin-1β (IL-1β) and tumor necrosis factor-α (TNF-α) were measured in the prefrontal cortex.

Anxiety- like behaviors significantly increased in the stress group. Prenatal zinc, but not exercise, reversed PS-induced behavioral impairments. RT-PCR analysis showed that the TNF-α and IL-1β gene expression was significantly increased in offspring of the stress group ($p<0.05$). Prenatal zinc supplementation, but not exercise, downregulated the mRNA level of the both neuro-inflammatory biomarkers to around control levels. TNF-α and IL-1β expression did not differ in pups prenatally exposed to both exercise and zinc.

Prenatal zinc supplementation improved PS-induced behavioral impairments partly through triggering the anti-inflammatory properties. Intensive involuntary exercise was not be able to prevent PS-induced behavioral deficits and neuroinflammatory responses. It seems that strenuous exercise increases the amount of brain pro-inflammatory cytokines which may mask or conceal the direct influence of the exercise under consideration. How exercise may positively modulate PS-induced changes, further research is needed to elucidate these effects.

Keywords: Anti-inflammatory responses; Anxiety, Physical exercise; Prenatal stress; Zinc.

Poster Presentation

1st International Congress of Biomarkers

PN: 1230

Evaluating the effects of melatonin and nicotinamide mononucleotide on expression levels of inflammation cytokines (IL6, IL-1b) in the isolated heart of aged male rats with the ischemia-reperfusion injury

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ABSTRACT

Ischemic heart diseases are the major reasons for disability and mortality in elderly. In this study, the effect pretreatment of Nicotinamide mononucleotide and melatonin, alone or together, on cardiac function, the expression levels of inflammation genes (IL-6 and IL-1b) in aged rat's heart with region ischemic reperfusion (IR) injury have been investigated.

Forty aged male Wistar rats, 24 months (350-450g), were randomly allocated to five groups including sham, IR, NMN, melatonin, and NMN+ melatonin. NMN (100 mg/kg) was administered for every other day for 28 days before IR. The rat's heart are suspended in the Langendorff apparatus and, myocardial IR injury was induced by LAD coronary artery ligation (ischemia) for 30 minutes and then reopening of it (reperfusion) for 60 minutes. In the groups receiving melatonin 5 min before the start of reperfusion, 50μM melatonin was added to the Krebs solution and the hearts were reperfused with Krebs containing melatonin for 15 min then, a series of isolated hearts were frozed to assessment of gene expression of inflammation factors (IL-6, IL-1b) by PCR. Each of treatment, melatonin and NMN had cardioprotective effects in old rats, there was a significant decrease in gene expression level of inflammation factors (IL-6, IL-1b) in treated groups in comparison with IR group ($p<0.001$).

It seems combination therapy with melatonin and NMN can be a promising strategy to attenuate myocardial IR damages in aged hearts by reducing inflammation gene expression.

Keywords: Aging; IR injury; Nicotinamide mononucleotide; Melatonin; Inflammation.

Poster Presentation

1st International Congress of Biomarkers

PN: 1232

Effects of prolonged exposure to ELF-EMF on HERVs expression in human melanoma cells

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ABSTRACT

Human endogenous retroviruses (HERVs) are ancient remnants of exogenous retroviral infections. Their abnormal activation is associated with several diseases, such as cancer and autoimmunity. Epigenetic and environmental factors are probably playing essential roles in the expression of these elements. This study aimed to examine the 96-hour effects of ELF-EMF on HERV-H, K, and W expression in human melanoma cells. SK-MEL-37 cells (the human skin malignant melanoma) were continuously exposed to ELF-EMF (50 Hz) at 1.5 and 3 mT intensity for 96 hours. Following mRNA extraction, the expression level of HERV-H, K, and W was assessed by qPCR. According to our results, exposure to ELF-EMF intensities for 96 hours could significantly downregulate HERV-H, K, and W env gene expression ($P<0.001$). Our obtained data suggest that low intensity and long-term exposure to ELF-EMF may pave using this type of radiation as a novel therapeutic approach by neutralizing the HERVs upregulated expression in melanoma cells.

Keywords: Extremely low-frequency electromagnetic fields (ELF-EMFs); prolonged exposure; Human Endogenous Retrovirus; Melanoma.

Poster Presentation

1st International Congress of Biomarkers

PN: 1233

Evaluation of miR-30c expression pattern and its effect on the progression of prostate cancer by targeting PLK1-FOXO1 pathway in DU-145 cell line

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Abstract

The microRNAs (miRNAs) are small molecules that regulate gene expression post-transcriptionally. In this study, we hypothesized that miR-30c overexpression might, through diminishing the Forkhead box protein O1 (FOXO1) phosphorylation by Polo-like kinase1 (PLK1), result in the blocking of prostate cancer (PCa) progression. For this purpose, after overexpressing miR-30c, cell proliferation, apoptosis, and specific gene expression correlated with the PLK1-FOXO1 pathway were assessed.

The study "miR-30c overexpression confers prostate cancer progression by targeting the PLK1-FOXO1 pathway" (IR.TBZMED.VCR.REC.1400.496) was approved by the ethical board of the Tabriz University of Medical Sciences. DU145 cells were transiently transfected with miR-30c mimic, inhibitor, and negative control (NC), then the expression level changes of miR-30c precursors were analyzed in these cells. MTT assay and ELISA cell death assay kit assessed cell proliferation and apoptosis, respectively. Expressions level of miR-30c, apoptosis-related genes, and the PLK1-FOXO1-related proteins were assessed using RT-qPCR and Western blot assay. Overexpression of miR-30c in DU-145 cells resulted in suppressed cell viability ($P < 0.05$), migration, and invasion ($P < 0.01$ *and* $P < 0.05$, *respectively*). In contrast, the apoptosis of cells was enhanced; in fact, the miR-30c inhibitor's transfection significantly diminished the apoptosis level in DU145 cells compared with the NC group. In contrast, the miR-30c mimic transfection enhanced the apoptosis rate in comparison to NC group. Also, the phosphorylation of FOXO1 by PLK1 in DU-145 was decreased. Furthermore, in the present study, we demonstrated the alteration of expression levels of pro-apoptotic genes Bac and Bax after transfection with miR-30c precursors to determine the enhanced apoptosis after the upregulation of FOXO1. Data revealed that these genes up-regulated after overexpression of miR-30c. We hypothesized that miR-30c overexpression through the PLK1-FOXO1 pathway might suppress PCa progression in this study. Hence, we would address whether miR-30c overexpression led to acts as tumor-suppressive effects in PCa. Our findings reflected that miR-30c overexpression impeded PCa progression, at least partly through the PLK1-FOXO1 pathway. These findings shed light on a novel strategy of a miR-30c functional role in the progression of PCa, focusing on the PLK1-FOXO1 pathway as a novel approach for healing advanced PCa.

Keywords: miR-30c, Prostate cancer, PLK1, FOXO1.

Poster Presentation

1st International Congress of Biomarkers

PN: 1234

Correlation between Placental growth factor as a biomarker and pregnancy-related complications during the pregnancy

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ABSTRACT

Placental growth factor (PlGF) is a multi-tasking cytokine and can stimulate endothelial cell (EC) growth, migration, and survival. PlGF binds to vascular endothelial growth factor receptor 1 (VEGFR-1) and acts as the antagonist of VEGF on Flt-1 receptors. It is an angiogenic growth factor, which is produced by placenta. PlGF rises during pregnancy and inconsonance in the level of it causes complications, therefore it may be used as a biomarker to predict, diagnose and treat the pregnancy-related complications. In this review article, we want to find a correlation between PlGF as a biomarker and pregnancy-related complications.

Keywords: Placental growth factor; biomarker; pregnancy; cytokine; angiogenic

Poster Presentation

1st International Congress of Biomarkers

PN: 1235

The Role of Interleukin-6 in Determining the Prognosis and Initiation of COVID-19 Treatment

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ABSTRACT

COVID-19 was reported in December 2019 in China and was proclaimed such a pandemic as 11-March 2020. As of 4 September 2022, over 600 million confirmed cases and over 6.4 million deaths have been reported globally, this shows that it is still a major health problem. Interleukin-6 is a biomarker for the development of coronavirus 2 pneumonia with fatal acute respiratory syndrome (Normal: 0-17). Circulating IL-6 levels appear to be an independent prognostic biomarker in COVID-19, with high IL-6 levels associated with more complicated COVID.

In this study, we investigated optimal effect Tocilizumab (TCZ) as FDA approved anti-IL-6 receptor monoclonal antibody that should be administered as soon as possible once a patient is diagnosed with severe or critical COVID-19. This can be done with check of IL-6. One hundred files (Mean age:52.25) were reviewed from 1926 Patients that were visited by one internist in independent hospital from September 2020 to September 2021 retrospectively, and IL-6 was sent for them were selected with high inflammatory indices more than two signs, e.g. fever, pulmonary involvement and needs of oxygen demand. Forty patients (19F, 21M) were checked IL-6 and received TCZ, but the remaining 60 patients neither received TCZ nor IL-6 because they were not available in time. The Code of ethics: IR.UMSU.REC.1401.223

We found a significant negative correlation between IL-6 levels and ambient oxygen saturation (SpO2) and positive correlation between IL-6 and CRP. However, that evaluation of predictive value of these two markers, IL-6 behaved as a better predictor of disease progression.

In patient with Covid-19, IL-6 levels are significantly elevated and associated with adverse clinical outcome. While on time inhibition of IL-6 with Tocilizumab appears to be efficacious and safe.

Keywords: Interlukin-6, COVID-19, Tocilizumab, biomarker

Poster Presentation

1st International Congress of Biomarkers

PN: 1236

Biomarkers in diagnosis and follow up treatment in hydatid cyst

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ABSTRACT

Hydatid cyst caused by the larval stage of Echinococcus granulosis grows in various organs of the intermediate host such as heart, brain and especially the liver and lung. In humans, CE can cause clinical symptoms ranging from asymptomatic to life-threatening symptoms and eventually lead to death. The purpose of this study is to investigate the role of biomarkers in the early diagnosis or their use as a target in the treatment of hydatidosis.

This abstract was done to provide a summary of several studies on the identification of biomarkers in providing new targets for potential treatment and diagnosis of hydatid cysts. To the result of studeis, several reported functional miRNAs, such as miR-71, miR-19b and miR-222-3p have potential applications in the study of host-parasite interactions and as treatment targets in Hydatidosis. Another studies reveald that parasitic miRNAs incuding egrmiR-71 and egr-let-7 as biomarkers can be detected in human plasma and coluld be used as new method in the rapid diagnosis and monitoring of hydatidosis. Also studies showed under in vitro benzimidazole exposure, the expression of two *E. granulosus* miRNAs (let-7 and miR-61) were significantly affected in the cyst stage. By studying the regulation of gene expression by microRNAs, reveald that the expression of some miRNAs is different according to the life cycle stage of the parasite and shows different developmental expression. The use of biomarkers, especially micro RNAs, can be used as pioneering and new methods in the treatment and diagnosis of hydatid cysts, and the future is predicted to be very promising. Also understanding the processes of EC development using biomarkers may help to find new strategies to control hydatidosis.

Keywords: MicroRNA; Echinococcus granulosus; biomarker; Diagnosis.

Poster Presentation

1st International Congress of Biomarkers

PN: 1237

Finding a New Regulatory Channel during Liver Repair and Regeneration: Role of Notch Signaling Cascade

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Abstract

Regeneration is an evolutionarily conserved process; however, regenerative abilities vary by species and organ/tissue. The liver is one of the body's most important organs for robust compensatory regeneration. However, the fundamental molecular processes governing the regeneration of the liver after resection or damage are still extensively understood. About 110 years ago, the NOTCH gene was discovered, a cell signaling mechanism that primarily affects growing multicellular organisms and is highly well-conserved throughout evolution. Several liver diseases, such as hepatoblastoma (HB), cholangiocarcinoma (CCA), and hepatocellular carcinoma (HCC), progress as a result of malfunctions in this route. The Notch cascade plays a rudimentary role in cell fate during the embryonic stage's progression to the adult stage in liver tissue. Modulating the Notch pathway may be employed in many patients who surrender to cirrhosis due to chronic hepatitis by virus infection.

We performed a review of studies published in the Scopus (2000–2021), PubMed (2000-2021), Medline (2006–2021), and Google Scholar (2000–2021) databases, combined with studies found in the reference lists of the contained investigations. A comprehensive understanding of the molecular mechanisms of the signaling pathway could bring significant advancements in the developmental process of novel and innovative therapies. The Notch pathway is a significant player in developmental interactions and liver pathobiology; indeed, the usage of Notch ligands to expand and maintain stem cells for tissue renewal and replacement highlights their primary biological significance. Up till now, considerable information indicates that the Notch signaling pathway is involved in many developmental processes, which paves the way for new therapeutic strategies in complex regenerative organs like the liver.

In conclusion, the down-regulation of the Notch signaling pathway represents a potential therapeutic candidate against liver disease. Future studies deciphering the Notch signaling pathway involved in the fate of hepatocytes may let us identify novel therapeutic targets for liver regeneration. We encourage more work focused on these processes, which will hopefully help better recognize molecular signaling pathway mechanisms.

Keywords: Cholangiocarcinoma; Hepatoblastoma; Hepatocellular Carcinoma; Liver Regeneration; Notch Pathway.

Poster Presentation

1st International Congress of Biomarkers

PN: 1238

Investigation of Biomarkers in cancer diagnosis

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ABSTRACT

Biomarkers, meaning biological indicators, are molecules that indicate a normal or abnormal process in the body and may be indicative of a disease or illness. Different types of molecules, such as DNA, genes, proteins, and hormones, can act as biomarkers because they all provide a lot of information about health. The aim of this study is to identify biomarkers for detecting different types of cancer.

In this review article, data were collected from databases such as Scopus, PubMed, Web of Scie nce, and Google Scholar in the period of 1991 to2022. Also, to search for articles, the key words biomarker and cancer were used. In the final stage, only the articles more related to the topic that investigated the relationship between biomarkers and cancer diagnosis were included in the study.

Molecular changes used in cancer diagnosis at the protein level, in translational and post-translational effects, at the DNA level, which include mutations, rearrangements, gene duplications, translocations, deletions or insertions, and at the RNA level, changes in transcription and post-translational modifications. From transcription. It has been observed that recent research suggests the replacement of single biomarker analysis with multiparametric analysis of genes or proteins (54). Now, using emerging technologies including Gene-expression profiling, MS-based ‹Peptidomics, Biomaker family, secreted protein arrays, autoantibodies, MS-imaging of tissues, gene fusions/Translocations, Serum Proteomics, which have been used to discover cancer biomarkers, are described.Today, fast and accurate diagnostic tests, which are used first as research tools and then as molecular diagnostic tests, have greatly helped human societies in cancer diagnosis.In addition to these biomarkers, cancer can be diagnosed with several technologies and high throughput. And the high resolution has made it easy to detect these new biomarker abnormalities. Quantitative PCR is widely used in detecting DNA/RNA/miRNA abnormalities for early diagnosis of cancer. Which can be used in monitoring the result of cancer patient treatment, monitoring and follow-up. Which can be used to detect gene expression profile, single nucleotide polymorphism (SNP) and also viral load quantification in cancer related to infection. The limitations of gel electrophoresis include low resolution, poor accuracy, and unquantifiable results. As a result, capillary electrophoresis is used in single nucleotide polymorphism (SNP), gene rearrangement detection, and loss of heterozygosity (LOH).

Conclusion: As a result, cancer diagnosis has undergone a change that cancer is no longer diagnosed based only on morphological parameters. The diagnostic algorithm is further supported by immunohisto chemical and molecular changes in DNA, mRNAs, miRNAs and proteomic level.

Keyword: progress; cancer diagnosis; clinical-DNA; mRNAs; miRNA; biomarker; detect- molecular.

Poster Presentation

1st International Congress of Biomarkers

PN: 1239

In silico introduction of NRF3 as a potential theranostic biomarker in ovarian cancer

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ABSTRACT

Ovarian cancer affects the lives of many women. Despite continuous efforts and improvements in treatment over the past few decades, OC is still the deadliest malignancy in women. The overwhelming majority of OC is diagnosed at an advanced stage. Therefore, improving the diagnostic test for ovarian cancer is the goal of many molecular biologists. A better understanding of the transcriptional behavior of ovarian tumors facilitates the introduction of novel and targeted treatment strategies for OC. The collected evidence indicates a physiological relationship between the Nrf3 transcription factor and cancers. However, further studies are needed into the molecular regulation and biological function of Nrf3 in ovarian cancer cells. Evaluating the prognostic value of Nrf3 protein, the expression level of NRF3, and its relationship with patient survival and the following bioinformatics analysis were systematically performed. Oncomine, GEPIA2, GENT, UALCAN, cBioPortal, UCSC Xena were datamined to proximate expression levels of NRF3 by exploring The Cancer Genome Atlas (TCGA) and Clinical Proteomic Tumor Analysis Consortium (CPTAC) databases. Functional analysis of gene copy number and immune infiltration correlation, patient prognosis, and risk factors were also performed. Then, gene ontology, pathway analysis, and transcriptome data analysis were performed using the Enrichr. The PPI network of the NRF3 protein was conducted with STRING and GeneMANIA. Finally, Prognostic analysis was investigated using KM plotter. The results are based on experimentally validated OC-associated data compiled from several databases, and indicated that NRF3 was overexpressed in OC. The NRF3 showed lower expression in the advanced stage than the earlier stage, Higher NFE2L3 significantly correlated with better PPS and OS in OC patients. The greatest associated genes include MAFK, KEAP1, SOX2, and MAFG. NFE2L3 expression was associated with infiltration of CD4+ T cell, macrophage, and neutrophil cell, while it is negatively correlated with B cells. This systemic study of NRF3 unfolds that higher expression of this gene is linked to the progression of OC patients. The current study provides a novel perspective plus a new methodology on the distinct roles and prognostic potential of NRF3 in OC. Hence, it can be a road map for further practical studies.

Keywords: Ovarian Cancer; Nrf3, Theranostic biomarker; Data mining; Expression data; Bioinformatic analysis

Poster Presentation

1st International Congress of Biomarkers

PN: 1243

Comparison of E-Cadherin Marker Expression between Lichen Planus, Leukoplakia and Oral Squamous Cell Carcinoma

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ABSTRACT

E-cadherin is a membranous glycoprotein that acts as an adhesive agent in intercellular communication, this marker level decreases in dysplastic condition, the aim of the present study is to evaluate the expression level of the mentioned marker on Oral Lichen Planus (OLP), Oral Leukoplakia (OL) and Oral Squamous Cell Carcinoma (OSCC) lesions. In this in-vitro study was conducted on 60 pararhyme blocks of patients with OL, OLP, and OSCC (n = 20) using Immunohistochemically (IHC) staining diagnosis were classified as follows: Code 0: Not painted Code 1: Less than 25% staining, Code 2: 25% - 50% staining, Code 3: 50% - 75% staining, Code 4: More than 75% staining and reported as proportional score and data were compared according to gender and lesion type using SPSS 22.0 Software and significance level of $p < 0.05$). 60 blocks of 60 patients (30 males and 30 females) were included in the study. E-cadherin marker expression on IHC code I (< 25 % staining) and code II (25 % < 50 %) was the most in OSCC (25 %) and OL (30%) respectively and the least in OLP (10 and 20 % respectively). In IHC code 3 (50 % < 75%) and code IV (< 75 %) was the most in OLP (40% and 30 % respectively) and the least in OSCC (20% and 30 % respectively).. There was no significant difference in marker expression according to gender and lesion type ($p > 0.05$). The results of this study show that changes in cadherin expression in leukoplakia and lichen planus compared to squamous cell carcinoma can be considered as an important factor in the expression of dysplasia changes.

Keywords: Oral Leukoplakia, Oral Lichen Planus, Oral Squamous Cell Carcinoma, E-Cadherin, Preneoplastic lesions.

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Case_Control Association Study Of rs3746444 Polymorphism in mir-499 A/G and Breast Cancer Susceptibility

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ABSTRACT

Breast cancer is one of the more significant health problems that leads to second prevalent mortality of cancer in the world. The heterogeneity of breast cancer leads to problems in early detection of this cancer, but recently miRNAs which are a group of small non-coding, and endogenous RNAs that regulate gene expression and over 50% of them are located at cancer-related genomic regions or fragile sites, introduced as a new marker in this issue.

To investigate the relationship between miR-499 rs3746444 A > G polymorphisms and the susceptibility to breast cancer in the Azarbaijan women nationality, we recruited 200 cases and 200 controls in our study for allelic and genotypic levels via the PCR-restriction fragment length polymorphism technique. The statistical analysis showed a significant relation between AA genotype of rs3746444 (codominant, odds ratio (OR) = 0.58, p = 0.02236; recessive, OR = 2.92, p = 0.01695; over dominant, OR = 0.44, p = 0.0113) and BC susceptibility. The subgroup analysis of mentioned polymorphism declared the significant correlation ($p \leq 0.05$) of the positive abortion, regular menstruation, positive human epidermal receptor-2 and positive estrogen receptor with BC susceptibility in AA genotype.

The existence of an A-allele at miRNA rs3746444 elevates women's BC susceptibility in Azeri ethnicity in Iran.

Keywords: SNP, miRNA, Polymorphisms, Cancer, Breast

Poster Presentation

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Variation of hTERT genetic variants and breast cancer risk in West Azerbaijan population

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ABSTRACT

Breast cancer (BC) is considered to be one of the most important causes of death worldwide. Telomeres are essential nucleoprotein structures at the ends of eukaryotic chromosomes as well as that protect the chromosome end from degradation, innovation, and fusion. The rate of hTERT gene polymorphism varies in different societies. This study is aimed at identification Variation of hTERT gene variants has been identified in the population of West Azerbaijan.

A total of 200 subjects including 100 breast patients and 100 healthy women participated in the study of West Azerbaijan province in 2021. Polymerase chain reaction (PCR) was used to genotype the MNS16A variable number of tandem repeats and 177 bp ins/del polymorphisms in the hTERT gene. PCR-RFLP was used to genotype hTERT rs2736098. The association between genotypes and breast cancer was assessed by computing the odds ratio (OR) and 95% confidence intervals (95% CI) from logistic regression analyses. A p-value of <0.05 was considered statistically significant. The MNS16A genotype frequency distribution in breast cancer patients was: LL, 27%; LS, 15%; and SS, 58%, and in controls: LL, 14%; LS, 3%; and SS, 83%. The LS genotype increased the risk of breast cancer (OR = 5.706, 95% CI = 1.597-20.386, $p < 0.003$). The hTERT2736098 genotype frequency distribution in breast cancer patients was: AA, 23%; AG, 4%; and GG, 73%, and in controls: AA, 8%; AG, 4%; and GG, 84%. The AA genotype increased the risk of breast cancer (OR = 3.435, 95% CI = 1.454-8.114, $p < 0.003$). Also, the allelic and genotypic frequencies of the hTERT177 locus showed that the genotype of the samples was Insertion.

Based on the results, there is a significant relationship between breast cancer status among healthy and sick women with polymorphic homozygous groups.

Keywords: Breast cancer, Telomerase, Polymorphism

Poster Presentation

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Effect of Foeniculum essential oil on changes in interleukin-33 in rats with polycystic ovaries

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ABSTRACT

Due to the estrogenic properties of *Foeniculum vulgar* (fennel), the aim of this study was to evaluate the effect of fennel on serum interleukin-33 levels and uterine tissue changes in the polycystic ovary model in rats. The present experimental study was performed on 24 Wistar rats. Rats were divided into 4 groups. The first group received sesame oil (as a diluent of estradiol and fennel essential oil) for 14 days. In the second group, a single dose of 4 mg of estradiol valerate was subcutaneously administered. In the third group, fennel essential oil at a dose of 200 mg/ kg of body weight was administered for 14 days. In the fourth group, first estradiol and after 60 days, fennel essential oil was prescribed with the above dosage. Blood samples were taken from rats and serum interleukin-33 levels were measured with ELISA kit. The ovaries and uterus was examined for tissue changes.

Follicular cysts were counted in ovary tissue and polycystic ovary was confirmed. The amount of 33 serum interleukin increased significantly in fourth group. The number of endometrial vessels and uterine glands diameter statistically decreased and height of uterine tissue epithelium increased by estradiol valerate. However, the fennel reduced the number of uterine glands, but increased the height of the epithelium, endometrial vessels and the diameter of the uterine glands.

Foeniculum increases interleukin-33 in polycystic ovary. Fennel can correct some histopathological changes in rat's uterine with polycystic ovaries.

Keyword: *Foeniculum vulgar*; Estradiol; Interleukin-33; Rats

Poster Presentation

1st International Congress of Biomarkers

PN: 1248

Effect of fennel essential oil on hepatotoxicity induced by lead

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ABSTRACT

The lead damages tissues through free radicals and oxidative stress. Therefore, it seems necessary to investigate the effect of effective substances and drugs on the prevention and treatment of poisoning with it. In the current study, the effectiveness of fennel essential oil was investigated in protecting liver against lead acetate toxicity.This study was conducted on 5 groups of mice, including the control group, fennel, lead and the combination of fennel (2 doses) and lead for 14 days. At the end of the study, ALT, AST, ALP, total protein, albumin, total and conjugated bilirubin, malondialdehyde (MDA), catalase (CAT), glutathione peroxidase (GPX) were measured using commercial kits. The liver was fixed in formalin buffer and cut with a microtome. The slides were stained with the common method of hematoxylin-eosin staining and the pathological changes were examined by light microscopy.

There was no significant change in level of the AST, ALT, ALP, total protein and direct bilirubin. The lead statistically increased activity of CAT and GPX and decreased MDA level while fennel decreased activity of CAT and GPX. The lead caused changes such as cytoplasm degeneration, vacuolization and hyperemia along with cell swelling and increased intercellular space and shrinking of cell nuclei in liver tissue; while fennel essential oil reduced these changes, but no significant difference was observed between the dose of 20 and 40 mg of fennel. Lead decreases activity of antioxidant enzyme and caused histopathological changes in liver but fennel can protect against these changes.

Keywords: Lead; Fennel; Liver; Rats

Poster Presentation

1st International Congress of Biomarkers

PN: 1249

Exosomes as novel biomarkers for prediction of breast cancer

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ABSTRACT

Exosomes have recently attracted a great deal of attention from biomedical researchers. Exosomes, a type of extracellular vesicle, have served as long-distance communication packages in physiological circumstances, including breast cancer. Exosomes and their contents have essential roles in the progression of breast cancer, including carcinogenesis, metastasis, angiogenesis, immune escape, and treatment resistance. In addition, new research confirms that exosomes can serve as important biomarkers for cancer diagnosis, prognosis, and treatment. Several key breast cancer biomarkers, including mtDNA, CXC, RN7SL1 RNA, hTERT mRNA, and different miRs, have been introduced as breast cancer cell-derived exosome contents. In addition, specific exosome biomarkers could be used to assess the efficacy of chemotherapy and radiotherapy, as well as serve as biomarkers of apoptotic induction. This study aims to review the value of exosomes in predicting the various stages of breast cancer development and their diagnostic and conceivably therapeutic utility in patients with breast cancer. Periodic evaluation of specific breast cancer-specific exosomal miRNAs identified in literature reviews may aid in anticipating traditional diagnosis, particularly in women at high risk for developing breast cancer. Although the critical components of exosomes are not yet fully understood, it is essential to highlight the exosome components that can aid in breast cancer diagnosis. However, scientists have a long way to go before they entirely appreciate the role of exosomes in the progression and diagnosis of breast cancer.

Keywords: Exosomes, Breast Cancer Cell, Biomarker, Metastasis

Poster Presentation

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Alterations in MicroRNA expression of *oxaliplatin-resistant AGS cells*

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ABSTRACT

Although treatment of gastric cancer with oxaliplatin is widely used, it is frequently followed by a relapse. Therefore, there is an urgent need for a profound understanding of chemotherapy resistance mechanisms as well as the profiling of predictive markers for individualized treatment. In this study, we identified the changes in 181b-5p and 27a-3p miRNAs expressions in oxaliplatin-resistant AGS cell line.Oxaliplatin-resistant AGS cells were generated by continuously exposing AGC cells to increasing concentrations of oxaliplatin for 4 months. Cell viability was measured by MTT assay. Total RNAs were extracted from control cells and drug-resistant cells. The levels of miRNAs were quantified using real-time qRT-PCR expression analysis. The IC50 value for oxaliplatin was 80 µM in control AGS cells, whereas for oxaliplatin-resistant AGS cells was 400 µM. We found that the expression level of miR-27a-3p was decreased when the AGS cells became oxaliplatin-resistant. On the other hand, the miR-181b-5p was overexpressed in oxaliplatin-resistant cells. Taken together, the present study has demonstrated that miRNAs can be useful as biomarkers in chemotherapy of drug-resistant cancers, and targeting them in the future can be useful in the treatment of these patients.

Keywords: Oxaliplatin; AGS cell; chemotherapy; miRNA

Poster Presentation

1st International Congress of Biomarkers

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Reciprocal Effects between Inflammation and Blood Coagulation Markers in Stroke Patients

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ABSTRACT

Introduction: Stroke is a neurological impairment syndrome characterized by irreversible brain, spinal cord, or retinal cell death induced by vascular etiology. Stroke is a significant global health issue, with low-and middle-income countries bearing most of the burden. Around the world, fifteen million individuals experience a stroke each year. Stroke is the second leading cause of death worldwide and the most frequent cause of permanent disability worldwide. Hemorrhagic strokes (a blood vessel rupture) and ischemic strokes (a blood vessel occlusion) are two different types of strokes. Method: A total of 100 studies related to stroke and its inflammation and coagulation from 1989 to 2022 were conducted using PubMed, Google Scholar, and Scopus. Results: In this article, we review some of the most important inflammatory (IL-1β, IL-6, TNF-α, IL-8, IL-33, sST2, CRP, Albumin, CRP/Albumin, Procalcitonin, IL-10) and coagulation (D-Dimer, Fibrinogen, Protein C and S, EPCR, Thrombomodulin, Tissue Factor, VWF, ADAMTS13, Plasmin(ogen) system, α-2 Antiplasmin, PAI-1) markers in stroke patients and then investigate the reciprocal effects between inflammation and coagulation. Among these markers, albumin, ADAMTS13, protein C and S, EPCR, and plasmin decreased, but the other markers increased. Although an increase in some markers, such as IL-33 and thrombomodulin, indicates a favorable prognosis. Conclusion: In conclusion, after studying inflammation and coagulation and their reciprocal effects in stroke patients and other diseases, we suggest that inflammation and coagulation are integrated systems in stroke patients that act on each other in such a way that not only can inflammation activate coagulation, but coagulation can also activate inflammation. Also, we suggest that in the treatment of inflammatory and coagulation diseases, one system can be used for another system in such a way that we can reduce coagulation by reducing inflammation and vice versa.

Keywords: Stroke; Inflammation markers; Blood coagulation markers; Reciprocal effects

Poster Presentation

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Extracellular Vesicles; Invisible Micro Suttles as Clinical Biomarkers in Blood Transfusion

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ABSTRACT

Extracellular vesicles (EVs) has a multitasking role in pathological and physiological conditions. Owing to the recent advances, EVs have great potential as clinical biomarkers within the liquid biopsy family in the field of diagnostic, prognosis and monitoring of disease even in treatment of cancers. The aim of this study is to know the presence of extracellular vesicles in blood product bags and the consequences of their presence. The information was extracted from searching and reading articles in PubMed, google scholar and Scopus databases. During the storage of blood Products, it came out RBCs release EVs under special situation. In other hand, contagious viruses like HTLV-1 and HIV can transmit via these invisible messengers and they can play a potential role as immune-modulating agents in recipient body. On other hand, the efficacy of Mesenchymal Stem Cell along to Hematopoietic Transplantation linked to their immune suppressive and anti-inflammatory properties primarily due to the release of EVs. MSC-EVs may be useful for patient safety, such as lower tendency to provoke innate and adaptive immune responses and can prevent or treat acute-graft versus host disease (GvHD). According to the above issues, are EVs showing promise and helpful role in blood products transfusion?

RBC-derived EVs enriched in some cargo like complement receptor that can change normal function of these cells against to bind and clear complement-opsonized particles. Besides that, EVs contain miRNA that have biological signaling. Also, the role of extracellular vesicles that playing role in the transmission of infectious diseases and preventing GVHD by changing the immune status and inducing tolerance, their importance is revealed in the field of blood transfusion. However, the aim of this study is discussing about mentioned issues.

Keywords: Extracellular Vesicles; Blood transfusion; Biomarker

Poster Presentation

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Comparison of a panel of inflammatory and non-inflammatory epigenetic biomarkers predicting anastomotic leak in the extracellular matrix of Patients with colorectal cancer undergoing surgery

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ABSTRACT

Anastomotic leakage (AL) is a serious complication in colorectal surgery that can be difficult to diagnose owing to varying clinical presentations. It is often the reason for reoperation with intestinal obstruction due to peritoneal adhesions. Failure to repair the anastomosis correctly can lead to contamination of the abdomen with intestinal contents and cause peritonitis. In this bioinformatics-meta-analysis study, we investigated, identified and compared a panel of inflammatory and non-inflammatory epigenetic predictive biomarkers in the extracellular matrix (ECM) that play a role in the occurrence of AL. We collected imaging data, demographic information, and clinical information of colorectal cancer patients who developed AL; In the following, we identified and analyzed omics data obtained from valid databases. Clinically useful biomarker is one that is obtained noninvasively, is easily measured, and provides results that have high sensitivity and specificity. All these potential biomarkers can be assessed through either blood or peritoneal fluid samples. These types of biomarkers have the potential to be assessed either intra-operatively, to predict which patients are at high risk of complications, or post-operatively, to identify which patients may require additional management to prevent an AL from developing or allow for its early diagnosis. Although no AL biomarkers have yet been validated in large-scale clinical trials, there is confidence that personalized medicine, through biomarker analysis, can be applied to patients undergoing gastrointestinal surgery as well as anastomosis patients in the coming years. be realized.

Keywords : Anastomotic leakage (AL), Epigenetic Biomarkers, Extracellular Matrix (ECM),**CRC,**

Colorectal Surgery

Poster Presentation

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Monitoring of dopamine as a biomarker candidate in neurodegenerative diseases using surface plasmon resonance based on laccase enzyme

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ABSTRACT

The monitoring of dopamine as a significant neurotransmitters and a potential neurochemical biomarker is a critical issue to improve early diagnosis of neurodegenerative diseases. As the blood-brain barrier mainly hampered the detection of brain disorders' biomarker, many analytical techniques are developed to overcome this challenge. In this study, a highly sensitive, free-lable, and cost effective technique, surface plasmon resonance (SPR), is used to monitor dopamine as a favorable biomarker by immobilizing laccase enzyme on a surface chip. All chemicals were prepared from Sigma–Aldrich Chemical (USA). SPRSR7500DC instrument (XanTec bioanalytics GmbH,Gernmany)was used for SPR measurement. The immobilization protocol was performed through EDC/NHS esters. AFM Instrument (Veeco-Autoprobe-CP-research) was applied to record the topology images of the SPR-chip surface. SPR measurements were performed by injection of dopamine concentration range with flow rate of 25 µl/min at 25 ◦C in 10 min. The sensorgrams were analyzed using Scrubber program (Biologic Software Pty. Ltd., Canberra,Australia). Our results of SPR sensogram in consist with AFM images, demonstrate the success immobilization of laccase enzyme on the carboxymerhyl dextran (CMD) sensor chip by amine coupling. The activity of immobilized enzyme toward its phenolic substrate indicated the possibility of dopamine interaction with immobilized enzyme. The increasing of SPR singals in proportional to the dopamine concentration was investigated and association between the alterations of resonance signal and the concentration of dopamine was detected. The devised system exhibited a lower detection limit of 0.1 ng/ml (signal-to-noise ratio (S/N) = 3). In this study, we have represented a novel SPR strategy for detection of dopamine as a biomarker using laccase enzyme. As abnormality of dopamine concentration is associated with CNS disorders, the present strategy could provide a novel opportunity to develop a powerful and sensitive early diagnostic method for monitoring of dopamine as a biomarker.

Keywords: Dopamine, Biomarker, Laccase, Surface Plasmon Resonance, Monitoring

Poster Presentation

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Neurofilament light chain (NFL) a promising biomarker in predicting, diagnosing, and therapy of neurodegenerative movement disorders

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ABSTRACT

A neurodegenerative movement disorder (NMD) is an aging-related disorder characterized by the loss of neurons. It is often a protein aggregation that accumulates in the brain, leading to motor symptoms. Biomarkers are molecules that can predict the onset and progression of the disease and its clinical outcome. Neuronal Neurofilament light chain (NFL) is a cytoplasmic protein highly expressed in the vast myelinated neurons. In various neurological disorders, its levels increase proportionately to axonal damage in the brain's cerebrospinal fluid (CSF) and blood. Due to the development of measuring ultralow levels of biomarkers, NFL has been promoted as a valuable biomarker in neurodegenerative disease. This mini-review aims to investigate the role of the NFL in the prediction, diagnosis, and target therapy of Parkinson's, Huntington's, and multiple sclerosis (MS). Literature reviews show that the NFL is one of the earliest detectable alterations in predicting NMD in laboratory situations. However, Clinical trials would need to incorporate these measures in clinical situations. Also, the correlation between NFL level and other diagnostic features of disease progression like Brain MRI and clinical motor impairments has been proved. The influence of lifestyle factors and drug therapy that Reduce the rate of recurrence at the NFL level strengthens this theory that NFL can be used as a molecule that has the potential to be targeted in the targeted therapy of NMD.

Keywords: neurofilament light chain, neurodegenerative movement disease, CSF biomarker, Parkinson's disease, Huntington's disease

Poster Presentation

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PN: 1259

Biomarkers in diagnosis and treatment of Toxoplasmosis

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ABSTRACT

Toxoplasmosis is caused by the obligate intracellular protozoan Toxoplasma gondii and is a major zoonotic disease of global medical and veterinary importance. Diagnosis and genetic characterization of T. gondii infection are important for the supervision, control, and prevention of toxoplasmosis. Conventional approaches for diagnosing toxoplasmosis include imaging, immunological, and etiological methods. Detecting parasite-associated biomarkers, and stages of their life cycle, in patient body fluids may help recover diagnosis. Detection of these biomarkers such as microRNAs in biological samples from patients can be utilized as diagnostic candidates. The purpose of this study is to investigate the role of biomarkers in the early diagnosis or their use as a target in the treatment of toxoplasmosis.

Data for this review were obtained from a PubMed search using a combination of the following terms: toxoplasmosis diagnostics, disease biomarkers, and microRNAs.

A review of various studies has shown that miRNAs have a high diagnostic potential for parasitic diseases. For example, Establishes miR-712-3p, miR-511-5p, and miR-217-5p as a miRNA inhibitor for toxoplasmosis. Also, it was shown microRNAs miR-155-5p and miR-29c-3p are highly expressed and miR-21-5p and miR-125b-5p are down-expressed in acute ocular toxoplasmosis compared with asymptomatic individuals. Diagnostic methods based on the early detection of microRNAs may be an essential tool, especially for detecting microRNAs in peripheral blood before the emergence of IgM antibodies. In this context, microRNAs can be investigated as biological markers of infection, especially during the acute phase of the disease, enabling early treatment of acute toxoplasmosis in humans.

Key words: Toxoplasmosis, Biomarker, miRNA, Diagnosis, Treatment

Poster Presentation

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The effect of polyaromatic hydrocarbon biomarkers on cardiovascular diseases: a review study

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ABSTRACT

PAHs are part of PM, which is produced from incomplete combustion of organic matter. Based on research, PAHs are positively associated with oxidative stress, inflammation, and the development of atherosclerosis, a key risk factor for cardiovascular disease. This study aims to evaluate the impact of PAH biomarkers on CVD. In this review article, data was collected from databases such as Scopus, PubMed, Web of Scie nce, and Google Scholar in the period from 1990 to 2022. The selected keywords: polycyclic aromatic hydrocarbons, cardiovascular diseases, PAH metabolites, PAH biomarkers, CVD, serum biomarkers were used individually and in combination to search for articles. After screening, duplicate and irrelevant articles were removed. Finally, 50 articles related to the effect of polyaromatic hydrocarbon biomarkers on cardiovascular diseases were included in the study. In addition to the articles found through the search in databases, another 10 articles from the references of the selected articles were included.

During the biotransformation of PAH, a number of metabolites are made, such as phenols, diols, quinones, and epoxides. Phenolic isomers have the highest percentage and biomarkers used for their detection include 2-OHNAP used to trace naphthalene from heating processed food, 3-OHPHEN used to trace phenanthrene from diesel, 2-OHFLU used to trace fluorene and 1-OHPYR used to trace pyrene from cigarette and hookah smoke. Exposure to PAH metabolites is associated with CVD in various ways, such as increasing blood pressure and heart rate and causing atherosclerosis. The disease is characterized by an increase in serum biomarkers of C-reactive protein, homocysteine, cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides, as well as amyloid acute phase serum proteins. CVD risk is increased by exposure to PAH biomarkers from smoking, occupational exposure, incinerators, and car emissions. Therefore, strict controls should be implemented for sources of PAH production and exposure.

Keyword: Polycyclic aromatic hydrocarbons (PAHs)**,** Biomarker, Cardiovascular diseases**(**CVD**)**

Poster Presentation

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DNA hypermethylation of tumor suppressor gene RASSF6 as independent prognostic factor in pre-B acute lymphoblastic leukemia

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ABSTRACT

The DNA hypermethylation in the CpG island promoter of tumor suppressor genes are an epigenetic modification observed in acute lymphoblastic leukemia (ALL) and has been found to be correlated with poor prognosis and increased rates of relapse. Hypermethylation of Ras association domain family-6 (RASSF6) often plays a key role in malignant progression of solid tumors; however, its impact on the prognosis and survival of ALL patients remains elusive. The frequency of the promoter methylation pattern of RASSF6 was analyzed in the peripheral blood (PB) samples taken at the time of diagnosis of 22 pre-B ALL patients. The PB samples of 10 healthy individuals were used as the control. The methylation specific polymerase chain reaction (MSP) assay was used to detect the DNA methylation patterns. RASSF6 was frequently hypermethylated in 90.9% of the pre-B-ALL (20/22) patients. None of the healthy controls revealed RASSF6 promoter methylation. Moreover, hypermethylation of RASSF6 was significantly associated with a poor prognosis and shorter overall survival (OS) in patients with pre-B-ALL (log-rank test; $P = 0.041$).

Our study represents the first report of methylation of RASSF6 at a high frequency in patients with pre-B ALL. Furthermore, hypermethylation of RASSF6 was significantly associated with inferior overall survival in pre-B ALL patients. It may suggest that the frequent epigenetic inactivation of RASSF6 plays an important role in the pathogenesis and progression of pre-B-ALL. our results show that the frequent hypermethylation of RASSF6 can potentially serve as a useful predictive biomarker in pre-B-ALL patient prognosis.

Keywords: RASSF6; Acute lymphoblastic leukemia, DNA methylation, Prognostic factor

Poster Presentation

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Platelets and their compounds; a future nonspecific biomarker of Huntington's disease

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ABSTRACT

Huntington's disease (HD) is an autosomal-dominant neurodegenerative disease that causes significant psychiatric, cognitive, and motor impairments. Manifestation of Huntington's disease can begin 15 years before clinical and neuroradiological abnormalities appear in gene-positive individuals. It is observable that the abnormalities of HD affect not only the CNS but also several other body compartments. A platelet, a unicellular cell in the blood, is an essential part of the homeostatic system, including inflammation procedures. Studies show a high amount of mutant huntingtin protein (mHtt) in the platelets of patients with this disease, indicating this gene's hyperactivity in platelets. Aging-associated platelet dysfunction causes several molecular alterations, including cytoskeleton rearrangements, signal transduction, vesicular trafficking, and protein degradation. Therefore, assessing the contributions of aging to age-dependent pathologies, such as those affecting the nervous system, may require insight into the mechanisms of aging in platelets and their age-dependent dysfunctions. There are now efforts to identify miRNAs that might indicate disease progression, such as the platelet-related miR-34b, which has been proven to be a reliable and promising HD biomarker before symptoms appear. The other evidence suggesting platelets' importance in HD is the higher amount of mitochondrial-dependent apoptosis and platelet degeneration rates. However, some studies failed to reveal an association between HD and platelet compounds that were predicted to have a potential role in following the disease and staging it.

Keywords: Huntington's disease; Platelet; Biomarker; Neurodegenerative Disease

Poster Presentation

1st International Congress of Biomarkers

PN: 1265

Emerging role of HLA-related predictive biomarkers and SARS-COV-2 induced infection

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ABSTRACT

Pathogenesis of COVID-19 has interconnected with introducing the novel prognostic and diagnostic biomarkers related to host-based responses. The role of *human leukocyte antigen* (HLA) class I and II as a valuable predictive biomarker in predisposing, progressing and preventing factor in the case of COVID-19, based on novel treatment approach personalized medicine, are crucial issues in control of the disease. HLA, the multi-polymorphic system, produced by tissue compatibility complex, have key role in immune responses via antigen presenting to T lymphocytes. The most considerable feature of this molecules is their tremendous diversity among people in the population. The aim of this study was to discuss the emerging role of HLA-related predictive biomarkers in SARS-COV-2 induced infection. Methods: In this study three databases were searched (PubMed, Cochrane library, and Web of Science). Genetics polymorphisms of HLA among the population has been reported in recent studies known as the most effective factor in progression and severity of SARS-nCoV2 induced infection. Results: There are polymorphisms in HLA-B*4601, HLA A*02 ،HLA-B*0703 ،HLA-DR B1*1202 ،HLA-Cw*0801 ،HLA-DR0301 ،HLA-Cw1502 ، HLA-A*0201 and E*01:01 in the deferent population. Conclusion: In this study we were reviewed the potential role of HLA as a predictive biomarker for prognosis, diagnosis and treatment outcomes in patients with COVID-19. Lastly, we were discussed the potential strategies that may restore HLA function to implement novel therapeutic strategies in COVID-19 patients.

Keywords: Human leukocyte antigen (HLA), Biomarker, SARS-CoV-2

Poster Presentation

1st International Congress of Biomarkers

PN: 1266

Profiling biochemistry biomarkers associated with COVID-19 disease progression

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ABSTRACT

The COVID-19 coronavirus pandemic is an important issue in public health and medical science. Rapid infection and severe and unpredictable side effects and even death are the reasons for the importance of this virus in the occurrence of disease in people. Identification of biochemical biomarkers plays a very important role in the rapid diagnosis and timely treatment of the disease. Therefore, this study was conducted with the aim of investigating the biomarkers involved in this disease.

A comprehensive literature search was done on PubMed, Google Scholar to identify articles discussing biomarkers in this review and its clinical implications on COVID-19 in accordance with Preferred Reporting Items for Reviews and Meta -analysis (PRISMA) guidelines. By studying and examining biochemical biomarkers in recent studies, in severe or fatal phase patients of COVID-19, a significant increase in the amount of total bilirubin and functional liver enzymes; ALT and AST and renal function parameters (blood urea nitrogen, creatinine) were observed in non-survivors and survivors. A significant increase in the concentration of muscle damage markers in these patients was found in creatinine, CK and CK-MB, LDH, myoglobin, cardiac troponin I, N-terminal probrain natriuretic peptide and D-dimer in non-survivors compared to recovered patients. In addition to the increase in the amount of the above cases and serum ferritin, a significant decrease in the amount of serum albumin in patients with corona was observed. Considering the changes in the above biochemical parameters in people with COVID-19, these parameters are important biomarkers for the rapid diagnosis and treatment of this disease.

Keywords: COVID-19; biochemical biomarkers; biomarkers of disease progression

Poster Presentation

1st International Congress of Biomarkers

PN: 1268

The interplay between microRNAs and Nrf2 signaling in human cancers

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ABSTRACT

The incidence of human cancer is continually increasing worldwide and trends are predicting a 1.5-fold increase in cancer incidence until 2040. Currently, a deeper understanding of the molecular basis of cancer appears to be crucial as an initial step toward therapy. Nuclear factor E2-related factor 2 (NRF2) is an important component of the antioxidant defense mechanism and its upregulation is associated with chemoresistance and radioresistance in cancerous cells. miRNA-mediated regulation of the NRF2 signaling pathway has been shown to have important implications for the development of various cancers. Here, we review the roles of miRNAs as regulators of the NRF2 pathway in different human cancers.

NRF2 pathway is regulated in various cancers via different miRNAs. Dysregulation of NRF2 via miRNAs is most notably seen in breast and lung cancer. miR-200, miR-101, miR-140, miR-29b, miR-181c, miR-93, and miR-28 are critical regulators of the NRF2 pathway in breast cancer. And, in lung cancer, NRF2 is dysregulated by miR-140, miR-495, miR-365, miR-200, and miR-155. Neuroblastoma and hepatocellular carcinoma are at the second level of importance. miR-101, miR-141, miR-144, and miR-340 in hepatocellular carcinoma, and also miR-27a, miR-142, miR-144, and miR-153 in Neuroblastoma cause dysregulation of the NRF2 pathway. Also, NRF2 in Multiple Myeloma, Acute Myelocytic Leukemia, gastric cancer, pancreatic cancer, esophageal cancer, and nasopharyngeal carcinoma have been seen to be dysregulated by miRNAs. Altogether, we have seen that miRNAs by dysregulation of the NRF2 pathway in different cancers, induce cytoprotective gene expressions, which in turn inhibit Reactive Oxygen Species generation, causing survival of the cancerous cells. So, altering NRF2-related miRNA expression patterns in cancerous cells could be a practical outlook on cancer therapy in near future, especially in lung and breast cancer.

Keywords: microRNAs; Cancer - Nrf2 signaling

Poster Presentation

1st International Congress of Biomarkers

PN: 1269

Design and construction of recombinant CRISPR-Cas9 vector to target YAP1 gene in glioblastoma

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ABSTRACT

Alteration of YAP1, the main effector of Hippo signaling pathway, in glioblastoma (GBM) was investigated using CRISPR-Cas9 editing technology. Two sets of forward and reversed gRNA oligonucleotides for exon 1 of the Yap1 gene were designed using the CHOPCHOP CRISPR guide gRNA designing web software (https://chopchop.cbu.uib.no/). Double-stranded DNA molecules were made according to standard instructions in the laboratory and were ligated into the Px458 and Px459 CRISPR eukaryotic expression vectors using Fermentas DNA ligase enzyme. Recombinant plasmids were transformed into E.coliDH5a host competent cells using of heat shock method. Multiple PCR experiments and DNA sequencing blast analysis showed successful cloning of the segments of interest into CRISPR plasmids. Clear PCR bands were in agreement with expected values and DNA sequencing results showed 100% similarity. Development of CRISPR vector system may be used as a wide and powerful tool for editing and alteration of genes to investigate their role in different diseases.

Keywords: CRISPR-Cas9; gRNA, Yap1; Glioblastoma

Poster Presentation

1st International Congress of Biomarkers

PN: 1270

Bioactive compounds from functional foods on biomarkers

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ABSTRACT

Functional foods and their bioactive compounds have been extensively studied as a food group of high importance due to their rich amount in compounds such as anthocyanins, proanthocyanidins, flavan-3-ols, flavonols, phenolic acids, stilbenes, and dietary fibers, which provides a wide variety of potential biological activities. Nowadays, many *in vitro*, animal, clinical, and epidemiological studies support that consuming functional foods within a balanced diet may significantly contribute to reducing disease risks. This effect can be measured by biomarkers such as lipid profile, endothelial function, platelet activation, hemostasis, inflammation, type 2 diabetes, and glucose metabolism, among others. Also, there has been a trend to use gut microbiota as a biomarker. Furthermore, several functional bioactive compounds can significantly affect disease prevention and treatment, affecting the levels of those biomarkers beneficially. Therefore, adopting a diet rich in several functional foods, such as fruits, vegetables, whole grains, flaxseed, nuts, fishes, olive oil, beverages, and fortified foods, may play an essential role in preventing diseases affecting these biomarkers.

Keywords: Functional foods; Phenolic compounds; metabolic biomarkers; Gut microbiota

Poster Presentation

1st International Congress of Biomarkers

PN: 1272

The role of biomarkers in diagnosis severe cases of COVID-19

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ABSTRACT

Coronavirus Disease 2019 (COVID-19) caused by Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread fast from China to everywhere around the world since December 2019. SARS-CoV-2 is associated with acute respiratory distress syndrome, acute lung injury, chronic obstructive pulmonary disease (COPD) which can lead to death. The aim of this study was to identify COVID-19 biomarkers in order to diagnose and show the severity of COVID-19.An online database search (PubMed, Google Scholar, Scopus, Web of Science and Cochrane) was performed. The most relevant keywords were ″biomarkers″, ″SARS-CoV-2″, ″COVID-19″. Hematological, immune and biochemical parameters were extracted and analyzed.Significant increase in neutrophil to lymphocyte ratio (NLR), interleukin-6 (IL-6), C-reactive protein (CRP), serum amyloid A (SAA), Erythrocyte sedimentation rate (ESR),Prothrombin Time (PT), D-dimers, cardiac troponin (Tpi-I), lactate dehydrogenase (LDH), serum urea , creatinine , cystatin C (CysC), direct bilirubin (DBIL), cholinesterase (CHE), have been observed in severe COVID-19 patients compared to mild COVID-19 patient.

The results of the study showed that the above biomarkers can be used to predict the severity of infection caused by the SARS-CoV 2 virus.

Keyword: biomarkers; SARS-CoV 2; Severe COVID-19

Poster Presentation

1st International Congress of Biomarkers

PN: 1274

Overview of Biomarkers for the Diagnosis of Breast Cancer

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ABSTRACT

According to the data from International Agency for Research on Cancer (IARC), breast cancer is the most cancer in the world and the most frequent cancer diagnosed in women, and breast cancer is categorized into three major sub types. At present, the best available tool for the early detection of breast cancer is mammography. This imaging is the most effective approach for diagnosing breast cancer in women older than 50 years of age, but new approaches should be developed to improve the diagnosis of breast cancer since there are numerous limitations in this detection; therefore, there is an urgent demand for breast cancer early detection biomarkers. Biomarkers play an important role in the detection and management of patients with breast cancer. BRCA1/2 mutation testing is used for risk assessment in families with a high prevalence of breast cancer. Mandatory assays include estrogen receptors for identification of endocrine-sensitive cancers and HER2 in selecting patients for treatment with anti-HER2 therapy (e.g., trastuzumab, lapatinib, pertuzumab, and ado-trastuzumab emtansine). Hence, serum biomarkers such as CA 15-3 or CEA may be used in monitoring therapy in patients with advanced disease receiving systemic therapy. Among the molecular markers associated with breast cancer, the estrogen receptor (ER), the progesterone receptor (PR), the human epidermal growth factor receptor (HER2), and the Mib1/Ki-67 proliferation index are the most important ones and are firmly established in the standard care of all primary, recurrent, and metastatic breast cancer patients. Besides, more than nineteen percent of breast cancers are not metastatic at the time of diagnosis. HER2 is the most prominent and commonly used biomarker for breast cancer detection, as well as MMP-2 (Matrix Metallo Proteinase-2 immuno-reactive protein), absence of estrogen and progesterone receptors and high expression of Ki-67 (Mib-1) antigen, Osteopontin (OPN), urokinase-type Plasminogen Activator and its Inhibitors (PAI-1 and 2), and cathepsins (B and L) have also been indicated as prognostic biomarkers for breast cancer. There are hundreds of identified candidate biomarkers, but these must be validated to prove their specificity and clinical relevance.

Keywords: Breast Cance; Biomarker; Diagnosis

Poster Presentation

1st International Congress of Biomarkers

PN: 1275

Role of Nrf2/Keap1 signaling pathway in cancer

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ABSTRACT

In recent years, cancer has been recognized as one of the main causes of death in the world. Nrf2 is an important regulator of cellular defense mechanisms against xenobiotics and oxidative stress. The aim of this study was to investigate the dual role of Nrf2/Keap1 pathway in cancer. A search was conducted on Pubmed, Google Scholar, Scopus, and web of science databases. The most relevant keywords were ″biomarkers″,″Nrf2″, ″Cancer ″.Under conditions of oxidative stress or the presence of carcinogens, Nrf2 is separated from its negative regulator in the cytosol, Keap1, and transferred into the nucleus, causing the expression of target genes that play a protective role in cells against oxidative stress damage. Nrf2 not only protects normal cells from becoming cancer cells, but also increases the survival of tumor cells under pathological conditions. Nrf2 and its downstream genes(such as HO1, MRPs, P- glycoprotein) are overexpressed in many cancer cell lines and human cancer tissues. Nrf2 also participates in drug resistance by regulating the activity of several plasma membrane pumps (MRP1 and MRP2) and phase 2 detoxification enzymes.Since overexpression of Nrf2 in many types of cancers is associated with poor prognosis and poor response to radiotherapy or chemotherapy in cancer patients, thus inhibiting the transcription factor Nrf2 can be considered as a treatment strategy to increase the effectiveness of chemotherapy agents.

keyword: biomarkers; Nrf2; Cancer; oxidative stress

Poster Presentation

1st International Congress of Biomarkers

PN: 1276

Up-regulation of miR-125b-2-3p in imatinib-treated K-562 cells

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ABSTRACT

It has been demonstrated that significant alterations may happen in the expression of microRNAs (miRs) in cancerous cells and tissues. miRs can act both as oncomiRs and tumor suppressors. Since cells could secrete miRs as exosomes, they are present in numerous body fluids and could be a valuable biomarker for early detection, prognosis, and treatment of cancers. Recently, many studies have reported that miR-125b-2-3p could function as a tumor suppressor. Therefore, we decided to evaluate the expression of this miR in the presence of imatinib, as first-line therapy for chronic myeloid leukemia (CML), in K-562 cells.

K-562 cells were treated with an IC50 dose of imatinib in two groups; 12 and 48 hours-treated groups. The expression of miR-125b-2-3p was examined via semi-quantitative real-time polymerase chain reaction (qRT-PCR). The expression levels of miR-125b-2-3p were significantly increased in both 12 and 48 hours-treated groups compared to controls. But in 48 hours-treated groups, miR-125b-2-3p was markedly upregulated more. Mir-125b-2-3p may play a tumor-suppressing role in K-562 cells due to its up-regulation in the presence of imatinib. It was also shown that long-term exposure to imatinib could probably stimulate its expression more. According to the tumor-suppressing role of miR-125b-2-3p, its down-regulation in CML patients could be a considerable cancer biomarker.

Keywords: MicroRNA; CML; Imatinib; Chemotherapy; Biomarker

Poster Presentation

1st International Congress of Biomarkers

PN: 1278

Investigating Laboratory biomarkers in identifying and treating people with breast cancer

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ABSTRACT

Breast cancer is the most common malignancy and the second leading cause of death in women worldwide. Early diagnosis of this disease prevents acute and severe disease and prompt treatment. Therefore, the aim of this study is to investigate important biochemical biomarkers in the diagnosis and treatment of people with breast cancer. A comprehensive literature search was done on PubMed, Google Scholar to identify articles discussing biomarkers in this review and its clinical implications on breast cancer in accordance with Preferred Reporting Items for Reviews and Meta -analysis (PRISMA) guidelines.

By studying and examining biochemical biomarkers in recent studies, the levels of malondialdehyde (MDA), which indicates lipid peroxidation, and uric acid, G6PD, and NO synthase in breast cancer patients were significantly higher than the control group. The activities of thrombospondin-1, paraoxonase-1, and selenium in breast cancer were significantly lower than in the healthy group. Estrogen receptor alpha (ERa), progesterone receptor (PgR) and human epidermal growth factor receptor 2 (HER2) are well-established biomarkers that are evaluated during the diagnosis and treatment of breast cancer. Herceptin is a family of mucin glycoproteins MUC-1 (such as CA 15.3, BR 27.29, MCA, CA 549), carcinoembryonic antigen (CEA), oncoproteins (such as HER-2). /c-erbB2) and cytokeratins (for example, tissue polypeptide antigen and tissue polypeptide-specific antigen c) are other serum tumor markers in breast cancer.

An increase in MDA and uric acid, G6PD and NO synthase, MUC-1, CEA, cytokeratins, HER-2, Era, PgR and a decrease in thrombospondin-1, paraoxonase-1, selenium have been shown in breast cancer patients. The above biomarkers are the most common markers used to evaluate and monitor breast cancer patients.

Keywords: breast cancer; Laboratory biomarkers; identifying and treating

Poster Presentation

1st International Congress of Biomarkers

PN: 1279

Biomarkers in covid-19 and fungal infections

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ABSTRACT

Within the last 3 years, coronavirus-disease-2019 (COVID-19) caused by severe-acute-respiratory-syndrome-coronavirus-2 (SARS-CoV-2) spread globally. Among patients with COVID-19, opportunistic secondary fungal infections mostly caused by Aspergillus and Candida spp and rarely by Mycormycosis, Cryptococcosis neoformans, and other fungal diseases have also been documented. A biomarker is defined as a "characteristic that can be measured as an indicator of normal biological and pathological processes, or pharmacological responses to a therapeutic intervention". In this review, the keywords of biomarker, fungal infection and covid-19, Aspergillus, Candida in the title and abstract of articles in the PubMed were searched, that through existing researches, 11 articles chose for comprehensive review. COVID-19 infection has been lead to hypoxia, immunosuppression, host iron depletion, hyperglycemia secondary to diabetes mellitus which provide favorable conditions for opportunistic fungal pathogens. Interventions such as treatment with corticosteroids, monoclonal antibodies and mechanical ventilation may further predispose COVID-19 patients to acquiring fungal coinfections. The most common methods to date, include attempting to recover Aspergillus spp on culture media of bronchoalveolar fluid (BALF) and tracheal aspirate, utilizing serologic biomarker testing such as the conventional Galactomannan testing (GM) from BALF, tracheal aspirate and serum specimens.

Biomarkers in COVID-19 can be used in the several areas:

1.The possibility of disease
2.Diagnosis and classification
3.Identification of high-risk cohort
4.Treatments
5.Evaluation of response to treatment
6.Predicting results

Pathophysiology is essential for the primary identification of biomarkers, which is, an understanding of what virus does to the body and how the body reacts to it.

COVID-19 is a heterogeneous disease with manifestations varying with age and presence of underlaying disease. Biomarkers will play a significant role in early suspicion and diagnosis. The severity of opportunistic infections has been so much that it has led to new terminologies like CAC (COVID-19-associated-Candida), CAPA (COVID-19-associated-pulmonary-aspergillosis) and CAM (COVID-19-associated-mucormycosis).

Keywords: Biomarker; fungal infection; covid-19

Poster Presentation

1st International Congress of Biomarkers

PN: 1280

A Review of Surface Plasmon Resonance (SPR) Biosensors for the Detection of Breast Cancer Biomarkers

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ABSTRACT

Nowadays, breast cancer is becoming one of the leading causes of morbidity and mortality among women. The existing common diagnostic procedures for breast cancer screening are not considerably effective in diagnosing breast cancer in its early stages. Among all methods, the SPR sensors are popular due to their sensitivity which is related to differences in wavelength of visible light by varying even small changes in the value of biomarker properties. SPR biosensors have shown significant potential for early detection of breast cancer biomarkers. First, published articles on the detection of MUC1, CA15-3, CA27-29, CEA, CD44, BRCA1, MCF-7, miRNA (microRNA), HER2, H2O2, MDA-MB-231, SK-BR3, ErbB2, and exosomal biomarkers were searched and then related references were obtained. Afterward, they were reviewed by the authors to extract data for the present investigation. Among biosensing methods, SPR is a highly useful tool to offer optical and label-free detection of target analytes. This paper reviews current status of the field, and showcase a series of breast cancer biomarkers diagnosis by SPR; therefore, the result showed the broad range of application of SPR technology in this field. Furthermore, research opportunities are proposed to further advance the SPR biosensors from research proof-of-concept stage to actual clinical usage. Desirable optical confinement at visible/near-infrared wavelengths and other advantages such as being label-free, fast, accurate, and low-cost make SPR a key component in future cancer biosensors. Nevertheless, some challenges with SPR techniques should be overcome in future studies.

Keywords: Breast cancer, Biomarkers, Surface plasmon resonance (SPR), Biosensor

Poster Presentation

1st International Congress of Biomarkers

PN: 1281

Detection of circulating microRNAs in serum of infected mice for detection of Fasciola gigantica

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ABSTRACT

Fascioliasis is a helminthic zoonosis disease caused by *Fasciola hepatica* (F. hepatica) or *Fasciola gigantica* (*F. gigantica*) in animals and humans. Accurate diagnosis and treatment of this disease have remained challenging due to the lack of sensitivity of available laboratory tests and the development of drug resistance. Circulating MiRNAs can be used as a potential biomarker for the diagnosis, prognosis, and therapy of infectious diseases. 20 mice were randomly divided into two groups one group (n = 10) was infected with approximately 25 metacercariaes of *F. gigantica* per animal and the other group (n = 10) was inoculated with 0.9% NaCl solution as uninfected. Serum samples were obtained every 10 days to 100 days. The serum of all mice was collected, and frozen at −80 °C until use. Total RNA was extracted and using high-throughput sequencing and bioinformatic analysis for mouse genes and quantitative real-time PCR (qRT-PCR), detecting miRNAs were done as protocols. Consistent with the sequencing data, qRT-PCR results showed that the expression levels of bta-miR-21-5p were elevated gradually at infection time points. One *F. gigantica*-specific miRNA (fgi-miR-87), was identified in the sera of infected mice. These findings will be helpful to understand the roles of circulating miRNAs in host-parasite interaction and to potentiate serum miRNAs as diagnostic targets for *F. gigantica*. This study is ongoing in other aspects. Further investigations for detection and understanding of miRNAs role in detection are recommended.

Keywords: Fasciolia gigantica, Biomarkers, miRNA, fgi-miR-87

Poster Presentation

1st International Congress of Biomarkers

PN:1282

Anti-inflammatory effects of Gallic acid in Letrozole-induced rat model of polycystic ovary syndrome

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ABSTRACT

Polycystic ovary syndrome (PCOS) is a highly prevalent and multifaceted metabolic and endocrine disorder worldwide. This syndrome characterized by hyperandrogenism, polycystic ovaries, and insulin resistance. Besides, inflammatory markers such as IL-6 and TNF-α are higher in PCOS patients due to hyperandrogenism which result in insulin resistance. Currently, natural products have gained importance in the treatment of several diseases including PCOS. Gallic acid (GA), a powerful flavonoid, has anti-diabetic, anti-inflammation, antioxidant effects. Therefore, in this study we aimed to investigate the effects of GA on pro-inflammatory markers in Letrozole induced rat model of PCOS.

In this study eighteen female Wistar rats (42-day-old) were randomly divided into three groups: control group: rats that received carboxy methylcellulose (CMC 0.5 %), PCOS group: rats that treated with letrozole (1mg/kg) dissolved in CMC 0.5 % orally for 21 days, and GA group that received the same dose of Letrozole followed by GA (100mg/kg) dissolved in CMC 0.5% for one month. At the end of the experiment, all the rats after overnight fasting were euthanized and blood samples were obtained by cardiac puncture. Serum levels of IL-6 and TNF-α were determined using rat ELISA kit.

PCOS induction resulted in a remarkable increase in serum levels of IL-6 in comparison with the control group ($P<0.05$). After treatment with GA, IL-6 levels reduced significantly compared to the PCOS group ($P<0.05$). Moreover, we found that Letrozole administration led to increase of TNF-α ($P<0.05$). However, treatment with GA significantly attenuated Letrozole-induced rise in serum levels of TNF-α ($P<0.05$).

The current results demonstrated the therapeutic potential of GA through reduction of IL-6 and TNF-α which are considered as one of the underlying causes of insulin resistance. GA as a potent polyphenolic compound may be a better candidate as an alternative medicine in treatment of PCOS.

Keywords: PCOS; Gallic acid; IL-6;TNF-α

Poster Presentation

1st International Congress of Biomarkers

PN: 1283

Estimating the power of cardio-metabolic biomarkers to predict cardiovascular diseases over different ages in Healthy Heart Cohort of Yazd, Iran

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ABSTRACT

Cardiovascular diseases (CVD) are one of the most common causes of death in the world. Since diagnosing and control of potential risk factors of the disease can reduce the prevalence of CVD and its burden, it is necessary to identify powerful biomarkers. The present study was conducted to estimate the power of cardio-metabolic factors to predict CVD over different ages in Yazd Healthy Heart cohort.

A total of 1623 people aged 40 to 74, which were without CVD, participated in the study. A conditional time-dependent receiver operating characteristic (ROC) curve was used to estimate the predictive power of cardio-metabolic indices including abdominal volume index (AVI), body obesity index (BAI), systolic blood pressure index (SBP), and diastolic blood pressure index (DBP) adjusted by age.

101(6.2%) subjects developed CVD. A significant relationship was observed between mean age ($p<0.001$), AVI (0.004), DBP ($p<0.001$), SBP ($p<0.001$), and an individual's CVD status. BAI has considerable predictive power for people under 55 years at 60 months and for 45 to 50 years old adults at 120 months. AVI prediction is reliable at 60 months for people under 45 years, between 50 to 55, and around 65. Performance of this marker is better for people under 50 years old at 120 months. DBP performed well at 60 months for adults between 43 to 50 and higher than 70 years old people and at 120 months belonged to under 55-year-old adults. The best predictive power of SBP occurred at both ends of the age range at 60 months. The best performance of SBP was observed between 50 to 55 and around 60 at 120 months.

Since both incidence of CVD and the value of the biomarkers are age-dependent, it is necessary to adjust age in evaluating the performance of the markers to predict CVD.

Keywords: Cardiovascular Diseases; Anthropometry; ROC Curve

Poster Presentation

1st International Congress of Biomarkers

PN: 1286

NMD pathway a distinct artificial intelligence of tumor cell for tumor progression; providing new revenue for therapy decision making

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ABSTRACT

NMD as a Nonsense-Mediated RNA Decay pathway is responsible for mRNA quality control by which the sensitivity level of unfolded protein response (UPR) to therapy-mediated cellular stress can be manipulated. NMD can operate two pathways in normal and mis-spliced mRNA turn-over rate, wherein IRE1α as a normal mRNA target can be alleviated toward deducting the sensitivity level of UPR responses. The main point is the notion that what condition can dictate this switching from degradation of nonsense mRNA to normal mRNA manipulation from which the final physiological condition contributes to c-Myc functions based on its expression level. To wrap up the concept, c-Myc can function as a double-edged sword wherein the threshold sensitivity level of ER-stress can direct it to handle both apoptosis and proliferation of tumor cells wherein the physiological results of this contribution are significantly related to perceived stress level within a tumor cell. We used some documented shreds of evidence to analyze the cognate contribution.

C-Myc upregulation is associated with aggressive proliferation and poor clinical outcomes, but based on molecular subtypes of breast cancer especially in the basal-like subtype it provides different results. To be more precise, c-Myc together with OCT4, AKT, GRP78 and the physiological shifting of the NMD pathway can dictate a lower proliferation rate and increased apoptosis in tumor mass in the favor of upregulated cancer stem cell (CSC) production and metastasis during therapy implementation as provided by MTT assay, immunofluorescence staining and flow cytometry (p-value <0.05). Meanwhile, the cellular translation of the mentioned threshold effect is so critical for providing CSC enrichment within tumor mass in the later phases of cancer progression and therapy implementation. Here we provided that in the first phase of therapy implementation, the expression level of c-Myc and NMD elements can modify cellular sensitivity to apoptosis and proliferation.

Keywords: NMD; breast cancer; c-myc, cancer cell reprogramming

Poster Presentation

1st International Congress of Biomarkers

PN: 1287

New spotlight to diverse incidence of therapy resistence in breast cancer; introducing new biomarker potential

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ABSTRACT

The selection between apoptosis and autophagy-related reprogramming for a cancer cell can drastically modify the outcome of therapy regimens. C-Myc alone is a major factor for orchestrating this revenue since its expression can be manipulated by calpain (calcium-activated cysteine proteases) and GRP-78 with a specific spotlight on the synchronized feedback contributions in the favor of either tumor mass survival or effectiveness of cancer treatments. It was demonstrated that high levels of calpain-1 and -2 are strongly associated with poor clinical outcomes and pathological adverse effects, respectively, from where the c-Myc active protein level can be handled during these changes.

GRP78, as the pivotal contributor to unfolded protein response (UPR) entrance into the cytoplasmic autophagy cycle, can be manipulated by c-Myc in different landscapes toward providing promising impacts for achieving conflicting outcomes from hormone therapy. Indeed, a low level of GRP78 has an impact on the efficacy of implemented endocrine therapy through the reduction of UPR stress responses and accordingly inhibiting pro-apoptotic CHOP induction along with its deactivating function on proapoptotic BCL-2 which itself can be regulated by ATG-5, known as a balance rheostat of apoptosis and autophagy.

We used some documented shreds of evidence to analyze the cognate contribution by considering the results of MTT assay, immunofluorescence staining, and flow cytometry (p-value <0.05).

ATG-5 and GRP-78, act as crosstalk operator factors for the outcome of cellular stress signaling by considering the collected data (p-value <0.05). Here, we imply that the theoretically designed regulatory ratio of GRP78/calpain-1,-2,-9/ATG-5 may have the potential to stratify patients based on the beneficial efficacy of receiving endocrine therapy and c-Myc gene expression profiling (GEP) for a specific subset of patients.The correlation between GRP78, calpain-9, and c-Myc can provide manipulable drivers for some extends of drug resistance in breast cancer.

Keywords: breast cancer; autophagy; apoptosis; cancer adaptation

Poster Presentation

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PN: 1288

The implementation of salivary biomarkers in cancer detection

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ABSTRACT

Recent evidence, has witnessed the use of salivaomics (comprehensive analysis of saliva) in biomarker discovery for the diagnosis of different diseases including cancer. Saliva is an available, non-invasive and low-cost sample that could be applied in the detect biomarkers with clinical relevance. Saliva-related "omics" applied sciences that encompass proteomics, transcriptomics, metabolomics and microbiomics, have promptly developed and might be useful in point-of-care diagnosis, liquid biopsy and nanomedicine. The improvements in analytical techniques has enhanced the scope and implementation of salivaomics from solely the oral cavity to the whole body, and correspondingly to personalized medicine. Therefore, recent advances in analytical strategies to recognize and detect biomarkers in saliva and their potential application as theranostic markers should be discussed.

Keywords: Cancer, Biomarker, Saliva

Poster Presentation

1st International Congress of Biomarkers

PN: 1289

Bioinformatic analysis of hsa-miR-204-5p and hsa-miR-22-3p as therapeutic biomarkers for breast cancer

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ABSTRACT

Breast cancer has become the most common form of malignancy among women, which occurs in epithelial tissues of the breast gland. MicroRNA (miRNA) regulates the expression of related genes in breast cancer. As a result of their interaction with factors such as the cyclin protein family, protein kinases and their inhibitors, and other growth promoters or suppressors, miRNAs play a regulatory role in the multiple cell proliferation and cell cycle progression pathways in breast cancer. Moreover, as miRNAs are found in blood and tissues, therefore they can be selected as biomarkers by either oncogenic or tumor-suppressing functions. Data were selected from the dataset GSE199135 based on a single study of expression profiling by microarray. The samples included 9 tumor tissue samples compared to 9 adjacent normal tissue samples. The primary analysis was performed by R analysis program through the criteria of Log FC > 2 and p-value < 0.05. After that, several databases (String V 11.5, David v2022q2, Genemania, mirTargetlink 2.0) and software (Cytoscape 3.9.1, cytoHubba 0.1) were used to perform in-depth analysis, including gene network construction, gene hub along with regulation were used. Identification of miRNAs and construction of mRNA-miRNA network. The " Degree " algorithm of cytoHubba was used to determine hub genes. Finally, the tissue specificity of the identified genes was checked by The Human Protein Atlas reference database to validate our analysis. In total, among 198 upregulated genes, a network comprising 138 nodes and 150 edges was built from which 7 hub genes (NTRK2, CXCR4, FGF2, ESR1, ANK2, CXCL9, and LEP) were selected. Based on the system biology “Calcium Signaling pathway” and two related biological processes “regulating cytosolic calcium ion concentration” and “cellular calcium ion homeostasis” were selected as the most crucial pathway. From miRNA-mRNA network analysis, two main regulatory miRNAs were identified. As hsa-miR-204-5p targets both NTRK2 and CXCL4, hsa-miR-22-3p regulates ESR1 and NTRK2 similarly. Our research predicts that hsa-miR-204-5p and hsa-miR-22-3p and LEP tissue gene may have the potential to be used as diagnostic, monitoring and therapeutic biomarkers in breast cancer.

Keywords: Bioinformatics; Breast Cancer; Systems Biology; hsa-miR-22-3p; hsa-miR-204-5p

Poster Presentation

1st International Congress of Biomarkers

PN: 1291

Investigating the effect of capectiabine drug on Ls_180 protein molecular docking

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ABSTRACT

Capecitabine (Xeloda) is an oral prodrug that is converted into fluorouracil(fu_5) in body tissues, the function of this drug is to slow down or stop the growth of cancer cells, especially cancer, and it is prescribed in the treatment of metastatic colorectal cancer.

Protein Ls-180 is a regulatory subunit of alpha_lactalbumin, this protein is encoded in different organisms, which we examine in this study of LALBA genes in the homo sapiens(humans)organism, This protein is involved in colon cancer. In this present descriptive and analytical study, we investigate the effect of capecitabine on Is_180 protein by molecular docking. In this study, we get drug information from the site pubchem.ncbi.nlm.gov and get protein information from the site www.uniprot.org.we also made corrections based on the Chimera1.15 software, and docking was done by PyRx. Among the studied compounds, the best molecular docking result was related to capecitabine, which was the most negative connection level(-8/5kCal/mol)

According to the results of docking and efficacy, it can be concluded that capecitabine has a favorable effect on Ls-180 protein.

Keywords: Capecitabine, ls_180**;** molecoular docking

Poster Presentation

1st International Congress of Biomarkers

PN:1292

Reconstruction of the miRNA-mRNA regulatory network in dysplasia progressing to oral squamous cell carcinoma

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ABSTRACT

Oral squamous cell carcinoma (OSCC) is a frequently encountered neoplasm of the head and neck region and has a poor prognosis. MicroRNAs (miRNAs) play a critical role in different biological processes involved in cancers. This study aimed to reconstruct the miRNA-mRNA regulatory network from dysplasia to OSCC. The gene expression profiles (GSE30784) were downloaded from the GEO database. Differentially expressed genes (DEGs) were analyzed with Transcriptome Analysis Console (TAC) software in two groups: OSCC and dysplasia compared with the control group and filtered with P-value < 0.05 and |log fold change| > 2. Finally selected common genes in both groups. We established a protein-protein interaction (PPI) network of the DEGs through the STRING database and functional and pathway enrichment analyses were performed by the ToppGene database. From the PPI network, the top 20 nodes with the highest degree were detected as hub genes and were analyzed with Gephi software.

Then we used the ToppGene database to identify miRNAs related to the hub genes and reconstructed the miRNA-mRNA regulatory network with Cytoscape software. Then determined the miRNAs & mRNAs with the highest degree. A total of 646 DEGs were identified which were common in dysplasia and OSCC. Furthermore, hub mRNAs (COL5A2, COL3A1, COL1A2, COL1A1, COL4A1, COL6A3, COL5A1, MMP2, THBS1, LOX) and hub miRNAs (miR-29b, miR-29c, miR29a, let-7f, miR-767, let-7d, let-7e, miR-98, let-7a, let-7c, let7g, let-7i, let-7b) were also identified. Gene ontology analysis showed significant enrichment of genes such as extracellular matrix organization and collagen fibril organization in biological process, extracellular matrix structural constituent, and platelet-derived growth factor binding in molecular function.We reconstructed the miRNA-mRNA regulatory network that may show crucial functions in dysplasia progressing to OSCC. Our finding suggested that extracellular matrix-related factors have the most prominent role in the progression of dysplasia to OSCC.

Keywords: MicroRNA‹Oral squamous cell carcinoma‹Regulatory Network‹Dysplasia

Poster Presentation

1st International Congress of Biomarkers

PN: 1293

Inflawell® improves neutrophil-to-lymphocyte ratio and shortens hospitalization in patients with moderate COVID-19, in a randomized double-blind placebo-controlled clinical trial

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ABSTRACT

COVID-19 is a significant global threat to public health. Despite the availability of vaccines and anti-viral drugs, there is an urgent need for alternative treatments to help prevent and/or manage COVID-19 symptoms and the underlying dysregulated immune response. We hypothesized that administration of Inflawell® syrup, a Boswellia extract formulation enriched for boswellic acids (BAs), can reduce the excessive or persistent inflammation and thereby prevent disease progression. BAs are medicinally activated triterpenoids found in the resins of *Boswellia spp*., and possess an immense therapeutic potential due to their anti-inflammatory and immunoregulatory activities. We investigated the effect of Inflawell® syrup, on moderate COVID-19 patients along with the current standard of care treatment.

A randomized placebo-controlled double-blind clinical trial was conducted, following definitive Confirmation of COVID-19. Forty-seven hospitalized patients with moderate COVID-19 were enrolled and received either the Inflawell® syrup or placebo. Clinical symptoms and markers of inflammation were evaluated at baseline and completion of the trial.

Our clinical trial revealed an increase in the percentage of oxygen saturation level in patients that received the BAs compared to placebo ($P < 0.0001$). In addition, the average duration of hospitalization was significantly shorter in the BAs group compared with the placebo group ($P < 0.04$). Concomitantly, some improvement in the clinical symptoms including cough, dyspnea, myalgia, headache, and olfactory and gustatory dysfunction were detected in the BAs group. Hematologic findings showed a significant decrease in the percentage of neutrophils ($P < 0.006$) and neutrophil-to-lymphocyte ratio (NLR) levels (*P*

< 0.003), associated with a significant increase in the percentage of lymphocytes in the BAs group compared with the placebo ($P < 0.002$). Additionally, a significant decrease in CRP, LDH, IL − 6 and TNF − α levels was detected in the BAs group. Following the intervention, fewer patients in the BAs group were PCR-positive for COVID-19 compared to placebo, though not statistically significant.
Overall, the treatment with Inflawell® resulted in shorter hospital stay, alleviation of COVID-19 clinical symptoms and decline in the level of pro-inflammatory cytokines. Trial registration: The trial has been registered in https://www.irct.ir with unique identifier: IRCT20170315033086N10 (https://en.irct.ir/trial/51631). IRCT is a primary registry in the WHO registry network (https://www.who.int/clinical-trials-registry-platform/network/primary-registries).

Keywords: COVID-19; Clinical trial; Boswellic acids; Inflammation; Inflawell® syrup

Poster Presentation

1st International Congress of Biomarkers

PN: 1295

Bioinformatics study to find genes whose expression is decreased in Hepatocellular adenomas compared to normal liver tissue

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ABSTRACT

Hepatocellular adenomas (HCA) are rare benign tumors that occur mainly in women after 2 years of oral contraceptive use. HCA are also related to other risk factors (obesity, vascular diseases, androgen and alcohol intake) or to different genetic diseases (Mac Cune Albright syndrome, ...). Bleeding and malignant transformation to hepatocellular carcinoma (HCC) can occur as severe complications observed respectively in 30-50% and 5% of the cases. Recently, in silico studies provide valuable information regarding aberrant gene expression profiling and introducing novel biomarkers. We used R programming to analyze the GSE88839 dataset containing HCA liver tumors corresponding to 35 patients. In all cases, tumor samples were frozen (-80°C) after hepatic resection at diagnosis. Normal liver samples were used as reference samples. Afterward, the downexpression gene of the hepatocellular adenoma (HCA) group compared to the normal group (p-value <0.001, adj.p-value <0.05, and log Fc = 1) was calculated with R software. Eventually, the Cytoscape software was used to construct the interaction network, and the top ten genes (ranked by Degree method) were found using the cytoHubba plugin. The result of the R analyze represented 405 genes of hepatocellular adenoma (HCA) group have Decreased gene expression with Log FC =-1 compared to the normal group. Based on the system biology, Retinol metabolism pathway was selected as the most crucial pathway. In addition, cytochrome P450 family 26 subfamily A member 1(CYP26A1) and UDP glucuronosyltransferase family 2 member B17(UGT2B17) the most significant Molecular Functions (MF). Finally, CYP2B6, CYP2C19, UGT2B17, CYP26A1, CYP3A43, SLCO1B3, CLEC4G, RBP1, CLEC1B, FCN2 were selected as top ten genes in network string interactions, including 50 nodes and 150 edges. This study set out to better understand hepatocellular adenoma pathogenesis. Moreover, the hub genes could be considered as possible prognostic/diagnostic biomarkers.

Keywords: Hepatocellular adenomas (HCA); Bioinformatics study; System Biology

Poster Presentation

1st International Congress of Biomarkers

PN: 1296

The regulatory role of microRNAs in the development, cyclic changes, and cell differentiation of the hair follicle

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ABSTRACT

A variety of studies have been evaluated the role of miRNAs in the development and cyclic changes of hair. It is well-documented that miRNAs play a vital role in the differentiation of hair follicle stem cells (HFSCs). Dicer and Drosha-DGCR8, the key components of microRNA biogenesis, were demonstrated to be expressed in the hair follicle (HF). Dicer has an essential role in the morphology and development of the anagen phase of hair. HF cycling is governed by miRNAs that regulate gene activation and silencing. MicroRNAs including miR-24, miR-125b, and miR-22 may synergistically promote hair regression. Other microRNAs, such as miR-148b can stimulate the Wnt/β-catenin signal pathway to enhance hair growth. Furthermore, some studies confirmed the important role of miRNAs in controlling the stemness and differentiation of HFSCs in vitro. Of note, studies are highlighting the role of other novel miRNAs in the biology of HF. Therefore, the present review aimed to investigate the importance of microRNAs in the control of HF biology in some species of mammals.

Keywords: microRNAs; Hair follicle; Cyclic changes; Signaling pathways & Differentiation

Poster Presentation

1st International Congress of Biomarkers

PN: 1298

Inflammatory cytokines as an indicator for early diagnosis of peri-implantitis; A systematic review

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ABSTRACT

Peri-implantitis is a site-specific infectious destructive disease that causes an inflammatory process in soft tissues, and bone loss around an osseointegrated implant and cause its failure of it. The aim of this study was to review the cytokine profiles in the peri-implant crevicular fluid (PICF) as an early indicator of disease. Published articles were accomplished from PubMed, Google Scholar, Wiley, Springer, ScienceDirect and Elsevier from 2004 to September 2022. Approximately 60 articles were initially found and then relevant articles (about 26 articles) to the aim of the study were identified and reviewed.

High levels of interleukin (IL)-1 beta (β) in the PICF of implants affected by PI (test) compared to healthy (control) sites. over-expression of IL-6 and IL-8 in the PICF of implants affected by PI compared to healthy implants. One study showed an increased secretion of IL-6, IL-8 and matrix metalloproteinase-1 by fibroblastic cells cultured from the test- compared to control sites. High levels of tumour necrosis factor-alpha (TNF-α) levels in the PICF from test sites (sites with PI) compared to the control sites. The positive association between polymorphism of IL-1 gene and PI. Raised levels of proinflammatory cytokines are exhibited in the PICF of patients with PI. Interleukin-1ß was detected in the crevicular fluid of implants in all three groups (healthy = 59.47 ± 15.55 pg/site; early peri-implantitis = 460.77 ± 35.67 pg/site; and advanced peri-implantitis = 191.10 ± 21.60 pg/site [mean ± SEM]). These results indicate that interleukin-1ß is present in implant gingival crevicular fluid and may be modulating attachment loss in implants suffering from peri-implantitis. Thus, interleukin-1ß may be used to monitor disease progression. Peri-implantitis posses clinical characteristics same as periodontitis disease.

A positive correlation was noted in the control group between IL-1β and TNF-α and between MIP-1α and IL-8 in the group with early mucositis. The results suggest that cytokines could be prognostic markers of implant failure.

Keywords: Cytokine; crevicular fluid; implant & peri-implantitis

Poster Presentation

1st International Congress of Biomarkers

PN: 1299

Effects of Hydroxytyrosol on the expression of *miR-21*, *MMP-2*, and *TIMP-1* genes in HepG2 cell line

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ABSTRACT

Hepatocellular carcinoma (HCC), one of the most common types of cancer in the world, accounts for almost 90% of all primary liver malignancies. Most cancer-related deaths are due to cell survival and the spread of cancer cells to other organs in the body. Hydroxytyrosol (HT) is a natural compound that has numerous activities, like the ability to inhibit metastasis by regulation of microRNAs and the genes associated with the invasion of cancer cells. The dysregulated expression of numerous microRNAs, including microRNA-21 in HCC, has been informed in multiple studies. Matrix metalloproteinases (MMPs) include a family of proteolytic enzymes capable of degrading components of the extracellular matrix and basement membrane. Of all the MMPs, MMP-2 cleaves collagen IV in the extracellular matrix, which is regulated by a family of proteins called tissue inhibitors of metalloproteinase (TIMPs). Therefore this study aimed to investigate the effect of HT on the expression of *miR-21*, *MMP-2*, and *TIMP-1* in HepG2. In this study, following the MTT assay, hepatocellular carcinoma cell line HepG2 was treated with different concentrations of hydroxytyrosol for 24 hours. RT-qPCR determined expression levels of *miR-21*, *MMP-2*, and *TIMP-1*. The results showed that HT significantly downregulated *miR-21*, and *MMP-2* in different treatment groups compared to the control group. In addition, *TIMP-1* gene expression was considerably reduced in two different concentrations of hydroxytyrosol. Findings indicated that HT plays an important role in inhibiting the invasion of hepatocellular carcinoma cells by downregulating *miR-21*, *MMP-2*, and *TIMP-1*. Thus, we concluded that hydroxytyrosol may be useful in preventing the proliferation of cancer cells.

Keywords: Hepatocellular Carcinoma, Hydroxytyrosol, MicroRNA, Matrix Metalloproteinase, Tissue Inhibitor of Metalloproteinases.

Poster Presentation

1st International Congress of Biomarkers

PN: 1300

The miR-135b as a Diagnostic Biomarker for Endometriosis

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ABSTRACT

Endometriosis is defined as an estrogen-dependent disorder in which endometrial cells that are in the normal state of the uterus are seen outside the uterus. In addition to existing therapies, the use of epigenetic factors, and in particular, assessment of the expression of microRNAs is effective in the diagnosis and treatment of the disease. The aim of this study was to investigate the expression of miR-135b in endometriosis so that it can be used as a diagnostic and therapeutic biomarker by identifying changes in these microRNAs.From 25 cases with endometriosis and 25 healthy subjects (control) tissue and serum samples were taken. First, cDNA synthesis for microRNAs was done in two steps. In this experiment, cDNA synthesis kit (Bonyakhteh Company, Iran) was used. In the first step, a large number of A nucleotides were added to the ends of small RNAs with the help of polymerase enzyme A, and in the second step, the first strand of cDNA was synthesized based on the specific instructions of the desired kit. and the expression of miR-135b was investigated by poly A reverse transcription-polymerase chain reaction method and with ABI device (Applied Biosystem, USA).The expression of mir-135b significantly was up-regulated in endometrial tissue of patients with endometriosis in both ectopic and uterine tissues compared to healthy women; while the expression of this microRNA in the serum samples of patients was down-regulated compared to control group.Considering significant changes in both eutopic/ectopic samples and serum samples in patients with endometriosis compared with controls, miR-135b may be considered as a diagnostic and therapeutic biomarker for endometriosis.

Keywords: Endometriosis; Serum; miR-135b

Poster Presentation

1st International Congress of Biomarkers

PN: 1301

Allium saralicum green-mediated silver nanoparticles: formulation, characterization and assessment of ovarian cancer activities

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ABSTRACT

The biosynthesis of metal nanoparticles using medicinal plants is not only economical but also environmentally friendly as well as having miscellaneous biomedical applications. The ovarian cancer activities of AgNPs@A. Annua were evaluated using MTT assay. The nanoparticles were formed in a spherical shape in the range of 36.2 to 69.5 nm for the particle size. On the other hand, the MTT assay was run to evaluate ovarian cancer activity of AgNPs@ Allium saralicum. In the cellular and molecular part of the study, the cells treated with AgNPs@ Allium saralicum were assessed by MTT assay for 48 h to determine the cytotoxicity and ovarian cancer properties on normal (HUVEC) and ovarian cancer cell lines, i.e. WiDr, SW1417 [SW-1417], and DLD-1. In the present study, gold nanoparticles were green-synthesized using an aqueous extract of Calendula officinalis. The synthesized AgNPs@ Allium saralicum was characterized by analytical techniques including EDX, FE-SEM, XRD, UV-Vis., and FT-IR. The IC50 values of AgNPs@ Allium saralicum were 440, 342, and 384 µg/ml against WiDr, SW1417 [SW-1417], and DLD-1 cell lines, respectively. In the antioxidant test, the IC50 values of AgNPs@ Allium saralicum and BHT against DPPH free radicals were 224 and 122 µg/ml, respectively. The viability of the malignant colorectal cell line decreased dose-dependently in the presence of AgNPs@ Allium saralicum. After the clinical study, silver nanoparticles containing Allium saralicum leaf aqueous extract may be used to formulate a new chemotherapeutic drug or supplement to treat several types of ovarian cancer.

Keywords: Allium saralicum green-mediated silver nanoparticles; Chemotherapeutic; Ovarian cancer

Poster Presentation

1st International Congress of Biomarkers

PN: 1302

Evaluation of Gene Expression and Serum Levels of Interleukin-17 and Interleukin-22 in Mild and Severe Covid-19 Patients

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ABSTRACT

Hyper-inflammatory response induced by SARS-COV-2 is a major cause of disease severity and death. Interleukin-17(IL-17) and Interleukin-22(IL-22) were linked to several inflammatory diseases. Prognostic biomarkers regarding disease progression and severity are critically lacking. Thus, we proposed to assess the serum levels of IL-17 and IL-22 in mild and severe patients. In this study, COVID-19 patients admitted to Taleghani hospital were divided into two groups with 45 participants in every group: the mild group (PCR-positive and mild symptoms) and the severe group (PCR-positive with acute pulmonary symptoms and inflammation). Patients with chronic respiratory diseases (asthma and COPD), underlying diseases (blood pressure, diabetes, cancer, cardiovascular diseases, etc.), and inflammatory diseases (autoimmune diseases, Rheumatoid Arthritis) were excluded from the study. We evaluated gene expression and serum protein levels of IL-17 and IL-22 in two groups. Mean expression levels of the Dct17 were 2.56±2.82 and 8.96±7.69 in the mild and severe disease groups, respectively which had a significant difference between the two groups. While, the mean expression levels of the Dct22 in the mild and severe patients were 4.22±2.784and 4.15±1.86, respectively, which was not statistically significant. Besides, the serum levels of IL-17 and IL-22 in the mild and sever groups were not significant. This study showed that the levels of IL-17 and IL-22 in the mild and severe disease groups were not affected. However, our study results were limited by the low sample size.

Keywords: Covid-19; Pulmonary Inflammation; Interleukin-17; Interleukin-22

Poster Presentation

1st International Congress of Biomarkers

PN: 1303

miR-182 as a biomarker for Cu, N-CDs treatment in HCT-116 colorectal cancer cells

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ABSTRACT

Colorectal cancer (CRC) is one of the most common malignant diseases and the third leading cause of cancerous mortality worldwide. Carbon dots (CDs), as new nanomaterials for cancer therapy, may influence the expression pattern of miRNAs (miR). Recent documents indicate that dysregulated microRNAs-182 (miR-182) influenced CRC progression and tumorigenesis. Therefore, we aimed to evaluate the expression of miR-182 as a cancer biomarker in HCT-116 CRC cells treated with Cu, N-doped carbon dots (Cu, N-CDs). The Cu, N-CDs synthesized and Fourier transform infrared (FT-IR), transmission electron microscopy (TEM), ultraviolet-visible (UV-Vis) spectroscopy, energy dispersive X-ray (EDS) and fluorescence spectroscopy were performed for characterizing of them. HCT-116 cells cultivated in DMEM supplemented with 10% FBS and kept in a conventional cell culture incubator. 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide (MTT) assay performed. Cells were co-cultured with IC50 value of Cu, N-CDs over a time of 24 h. RNA extracted and cDNA synthesis and quantitative polymerase chain reaction *(*q-PCR) were performed according to the guidelines of a commercial miRNA kit. Data analyzed as fold changes. The Cu, N-CDs size, structure, surface functional groups, and optical properties were determined. The 24h MTT test indicated 0.40 mg/ml IC50 for Cu, N-CDs in the HCT-116 cell line. The expression of miRNA-182 was significantly decreased in treated cells versus control cells (0.738 ± 0.18 fold; $p<0.05$). Data indicate that the expression levels of miR-182 were changed in cells treated with Cu, N-CDs, suggesting possible biomarker application in colorectal cancer.

Keywords: miR-182; HCT-116; Cu; N-CDs

Poster Presentation

1st International Congress of Biomarkers

PN: 1304

The significance of miR-21, miR-155, and miR-182 as biomarkers for Cu, N-CDs treatment in HT-29 colorectal cancer cells

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Abstract

Colorectal cancer (CRC), an important health problem, has the third-highest incidence among the cancer-causing condition. Carbon quantum dots (CQDs) are being used in various biomedical fields including drug delivery systems. Various miRNAs (miR) contribute to regulate tumor progression. We aimed whether Cu, N-doped CQD (Cu, N-CQD) can regulate expression of miR-21, miR-155, and miR-182 in HT-29 cells. The Cu, N-CQDs synthesized and characterization methods like fourier transforms infrared (FT-IR), transmission electron microscopy (TEM), ultraviolet-visible (UV-Vis) spectroscopy, energy dispersive X-ray (EDS) and fluorescence spectroscopy were performed. The gene expression of miR-21, miR-155, and miR-182 were done via quantitative polymerase chain reaction *(*q-PCR) from HT-29 treated with Cu, N-CQD (IC50 24h that obtained from 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide (MTT) assay). The data reported as fold change. The Cu, N-CQDs characterization tests results showed their size, the structure, surface functional groups, and optical properties. The 24h MTT test indicated 0.334 mg/ml IC50 for Cu, N-CQDs in HT-29 cell line. The expression of miR-21 (0.29 ± 0.14 fold change), miR-155 (0.3 ± 0.12 fold change), and miR-182 (0.53 ± 0.25 fold change) was significantly decreased in treated HT-29 cells ($p<0.05$) compared to untreated (control) cells. It was concluded that Cu, N-CQDs could influence HT-29 cells through the downregulation of miR-21, miR-155, and miR-182, which can be as potential biomarker for following up of the treatment of CRC with Cu, N-CQDs.

Keywords: miR-21; miR-155; miR-182; HT-29; Colorectal cancer; Cu; N-CDs

Poster Presentation

1st International Congress of Biomarkers

PN: 1305

Correlation between Placental growth factor as a biomarker and pregnancy-related complications during the pregnancy

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ABSTRACT

Placental growth factor (PlGF) is a multi-tasking cytokine and can stimulate endothelial cell (EC) growth, migration, and survival. PlGF binds to vascular endothelial growth factor receptor 1 (VEGFR-1) and acts as the antagonist of VEGF on Flt-1 receptors. It is an angiogenic growth factor, which is produced by placenta. PlGF rises during pregnancy and inconsonance in the level of it causes complications, therefore it may be used as a biomarker to predict, diagnose and treat the pregnancy-related complications. In this review article, we want to find a correlation between PlGF as a biomarker and pregnancy-related complications.

Keywords: Placental growth factor, biomarker, pregnancy, cytokine, angiogenic

Poster Presentation

1st International Congress of Biomarkers

PN: 1306

Osteogenic differentiation of adipose-derived stem cells on dihydroartemisinin electrospun nanofibers

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ABSTRACT

Adipose tissue-derived stem cells (ASCs) are promising candidate in stem cell therapies, and maintaining their stemness potential is vital to achieve effective treatment. Natural-based scaffolds have been recently attracted increasing attention in nanomedicine and drug delivery. In this study, Dihydroartemisinin (DHART)-loaded polycaprolactone collagen nanofibers (PCL/Col NFs) were constructed as effective biocompatible scaffolds through adjusting the proportions of hydrophobic/ hydrophilic polymers for enhanced osteoblastic differentiation of human adipose-derived stem cells (hADSCs). DHART-loaded PCL/Col NFs were manufactured through an electrospinning procedure. The proportions of hydrophobic/hydrophilic PCL/Col polymers were adjusted as DHART carriers, and their morphology and functional properties were examined. The prepared PCL/Col/DHART NF scaffolds inhibited the crystallization of DHART and demonstrate their remarkable promise as a sustained DHART drug delivery system. Furthermore, the efficiency of these electrospun NFs for osteoblastic differentiation was evaluated by detecting stem cell proliferation, calcium secretion, alkaline phosphatase activity, and the expression mRNA levels of kay osteoblast differentiation markers. The designed NFs were characterized through FTIR, XRD, TGA, FE-SEM, and tensile testing. DHART-loaded PCL/Col electrospun NFs provide an ideal solution, with the potential of sustained drug release as well as inhibition of drug re-crystallization. Interestingly, inhibiting DHART re-crystallization can improve its bioavailability and provide a more effective therapeutic efficacy. Besides, the data set found through FE-SEM, MTT, PicoGreen, qPCR, and alkaline phosphatase (ALP) assays revealed the improved adhesion and proliferation rate of hADSCs cultured on PCL/Col/ DHART (5%) NFs after 14 and 21 days of incubation. These findings confirmed the potential of the designed NF scaffolds for sustained/controlled release of DHART therapeutic molecules toward bone tissue regeneration and engineering.

Keywords: Dihydroartemisinin; Polycaprolactone/Collagen; Nanofibers; Osteoblastic differentiation; Sustained release

Poster Presentation

1st International Congress of Biomarkers

PN: 1308

miR-455-3p and miR-296-3p as biomarkers for regulated apoptosis in bulls with asthenozoosermia

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Abstract

Sperm miRNAs regulate many cellular processes, including motility and apoptosis. Various miRNA and molecular signaling pathways are involved in asthenozoospermia (AS), which is thought to be one of the factors of infertility with reduced sperm motility. To investigate the role of apoptotic miRNAs in asthenozoospermia, 32 semen samples from four Holstein bulls (normozoospermic (NS); total motility > 70%) and 32 semen samples from four bulls (asthenozoospermia; total motility <40%) were collected. Samples were then diluted with a Tris egg yolk extender and aspirated into 0.5 mL straws. After the freeze-thaw process, sperm kinematic parameters, DNA fragmentation, apoptosis status and expression of apoptosis-associated miRNA (miR-455-3 and miR-296-3p) were evaluated. According to the results, miR-455-3pp expression was up-regulated in the NS group, but miR-296-3p expression was up-regulated in the AS group. Live cells were significantly correlated with miR-296-39 in two study groups (r = -0.51805, P 0.05). Researchers found a significant correlation between miR-296-3p and necrotic cells (r = 0.67753, P 0.05) in two study groups. The normozoospermic group outperformed the asthenozoospermic group on most functional and flow cytometric indicators. With regard to sperm motility and apoptotic status, expression levels of miR-296-3p and miR-455-3p correlated significantly.

Keywords: Bulls; Asthenozoospermia; Normozoospermia; Apoptosis; miRNA

Poster Presentation

1st International Congress of Biomarkers

PN: 1309

Multi-omics Data Mining on Gene Ontology terms and Signaling Pathways of Cancer Stem Cells

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ABSTRACT

Data analytics are commonly employed to assist biomedical research in all fields, notably on the most pertinent clinical problems, such as cancer stem cells. Bioinformatics methods have been utilized to describe the molecular features of diseases and disease-related cells/stem cells. In recent years, multiple cancer stem cell research based on single and multi-omics data have been conducted. Network analysis of stem cell signaling pathways provides curated visual data to identify hub genes in stemness properties and cancer progression. Gene ontology (GO) investigation could underline specific terms that navigate cancer stem cells from naive lineage to progressive cancers. This study aims to provide a novel data mining approach on GO and signaling pathways of cancer stem cells. These analyses highlighted the most stemness regulator and cancer-related pathways parallelly. Also, the GO investigation has specified the distinct biological process and cellular component of cancer stem cells. Multi-omics data mining could facilitate raw data processing and visualize the informational data.

Keywords: Data mining; Omics; Gene ontology; Cancer stem cell; Network analysis

Poster Presentation

1st International Congress of Biomarkers

PN: 1311

Terminological status of searched contents in the subject areas of stomach, skin, prostate, breast, colon cancers using Google Trends service in Iran and USA

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ABSTRACT

Most internet users continuously use search engines and subject guides as a tool for searching and accessing information. Today, search engines provide many services to provide statistics about the amount of usage, behavior and recognition of user preferences. These statistics, in addition to helping website managers to optimize user searches (SEO), show the gap between special users (subject matter experts) and usual users in the point of view and how dealing with specific subjects. This research is practical in terms of purpose and content analysis approach.In this paper, the contents searched in the subject areas of cancers (stomach, skin, prostate, breast, large intestine) were analyzed in the Google search engine in Iran and USA in five years period. The tool in this study was Google Trends service. This service provides all the statistics related to the searches made based on the keywords used by all the users based on the country and region. The results showed that in the last 60 months, the most searches and concerns of Iranian users were about stomach, skin, prostate, breast, and colon cancers, respectively, and similar to the above conditions in the United States, namely Breast cancer, Prostate cancer, Colon cancer, Skin cancer, and Gastric cancer. It seems that a high percentage of the similarity and sameness in the search methods in the five years have been existed and also the interests of the search at the local level (Iran and USA) are similar in the time under review, in terms of ranking keywords. It can be said that from the point of view of Iranian users, the most concern is stomach cancer, and from the point of view of USA users, breast cancer is the most concern. Although there is a significant difference between the number of searches made regarding these five cancers. Also more users have used the words: signs and symptoms for searching these cancers, which shows their concern about the incidence and side effects of these diseases.From the above findings, it can be concluded that the interest and need to have information about incurable diseases such as types of cancers is increasing in all geographical regions of the world. According to the amount and manner of searches performed in the Google search engine, it can be concluded that providing correct and reliable information can greatly increase people's awareness of various cancers. These information increase people's awareness of various issues related to different cancers and solve their problems by making preventive decisions.

Keywords: Search engines; Google trends; Gastric cancer; Skin cancer; Prostate cancer; Breast cancer; Colon cancer.

Poster Presentation

1st International Congress of Biomarkers

PN: 1312

Omega-3 DHA targets cell proliferation, differentiation markers and colony forming capacity in colorectal cancer stem-like cells

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ABSTRACT

Colorectal cancer (CRC) is one of the major health problems in Iran. Despite receiving conventional therapy, many CRC patients develop resistance to chemotherapy compounds. In this regard, CRC stem cells (CRCSCs) as a small subpopulation of tumor cells with high proliferation rate and poor differentiation are responsible for chemotherapy resistance in CRC patients. Unfortunately, the efforts to develop effective drugs that target CRCSCs remain challenging. Therefore finding novel and safe compounds with the ability to target proliferation and differentiation markers in these cells has high value. Here, we investigated the effect of omega-3 DHA on the cell proliferation rate, colony forming capacity and differentiation markers in CRC stem-like cells. Caco2 cells as CRC stem-like cells were treated with 50-150 µM/L DHA. Next, cell proliferation rates, self-renewal capacity, cytokeratin 20 (Ck20), Mucin 2 (Muc2) and CD133 expression as differentiation markers were evaluated by MTT assay, colony-forming assay and real-time RT-PCR method respectively. 48 h treatment with 50-□to 150 µM/L DHA resulted in 28.4% to 39% decreases in cell proliferation rates followed by remarkable decreases in self-renewal capacity ranged from 195- to 10 colonies per well after 2 weeks. Treatment with 100 µM/L DHA significantly increased the expression level of Ck20 and Muc2 by 3.3- and 2 fold respectively. Furthermore, in the malignant cells treated with 150 µM/L DHA, a remarkable decrease in CD133 expression level were observed by 0.63 fold compared to untreated control cells. Omega-3 inhibited cell proliferation rate of CRC stem-like cells. Differentiation markers Ck20, Muc2 and CD133 appear to be promising targets of omega-3. Our data may provide a new therapeutic approach for treatment of CRC patients through differentiation effects of DHA on the CRC stem-like cells.

Keywords: Colorectal cancer (CRC); Colorectal cancer stem cells (CRCSCs); Differentiation markers; Omega-3 DHA

Poster Presentation

1st International Congress of Biomarkers

PN: 1313

Effect of Vitamin D3 on the cell proliferation, differentiation markers and self-renewal in colorectal cancer stem-like cells

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ABSTRACT

Colorectal cancer (CRC) is the most common cancer in the world with resistant to the majority of the current treatments. Different studies have shown that colorectal cancer stem cells (CRCSCs) are responsible for resistance to conventional therapies. Therefore, effective targeting of CRCSCs is of great importance in CRC treatment. These cells are small subpopulation of tumor cells that possess rapid proliferation and poor differentiation. With these in mind, finding a safe compound with the ability to target cell proliferation, self-renewal and differentiation markers, has high value and may provide more sensitivity of CRCSCs to chemotherapy. In this study, we evaluated the effect of Vitamin D_3 as a safe compound on the cell proliferation, self-renewal capacity and differentiation markers in CRC stem-like cells. CRC stem-like cells (Caco2) were treated with different concentrations of Vitamin D3 after which cell proliferation rates, self-renewal capacity, cytokeratin 20 (Ck20), Mucin 2 (Muc2) and CD133 expression as differentiation markers were evaluated with MTT assay, colony-forming assay and real-time RT-PCR method respectively.

48 h post-treatment with 0.1 to 1 nM Vitamin D_3 resulted in 28.2 % to 66.4 % decreases in cell proliferation rates followed by remarkable decreases in self-renewal capacity ranged from 95- to 0 colonies per well after 2 weeks. Treatment with 1 nM Vitamin D3 dramatically increased the expression level of Ck20 and Muc2 by 2.9- and 2.6 fold respectively followed by a remarkable decrease in CD133 expression level by 0.35 fold of the untreated control cells. Vitamin D3 targeted CRC stem-like cells and successfully inhibited cell proliferation rate in these cells. Differentiation markers Ck20, Muc2 and CD133 appear to be promising targets of Vitamin D3. Our results may open up avenues for treatment of CRC patients using Vitamin D3-based differentiation effects on the CRC stem-like cells with lower toxicity on normal cells.

Keywords: Colorectal cancer; Colorectal cancer stem cells; Differentiation markers; Vitamin D3

Poster Presentation

1st International Congress of Biomarkers

PN: 1315

Introducing a special type of miRNA to diagnosis of ovarian cancer

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ABSTRACT

The most common gynecologic cancers detected in women in Turkey are uterine cancer, ovarian cancer, and cervical cancer. Identification of the molecular pathogenesis of ovarian cancer, and discovery of new moleculer biomarkers which facilitate the ovarian cancer treatment are required for an effective ovarian cancer treatment in clinics. The miRNAs are reported to be the possible biologic indicators for various cancer types. We aimed to investigate a miRNA which were suggested to have effect in ovarian cancer in our (previous) monozygotic twin study from the miR-1260 microRNA family who's association with ovarian cancer yet has not been reported in the literature. We investigated the expression levels of miR-1260b miRNA, in the peripheral blood lymphocytes of 150 familial and sporadic ovarian cancer patients, and of 100 healthy individuals of the control group who were matched for age, sex, and ethnicity with the patient group, and investigated their possible property of being a biologic indicator for ovarian cancer. The expression results of ovarian cancer patients were evaluated by comparison of the results of the control group in the study. The expression level of miR-1260b in ovarian cancer patients was found highly increased compared with the levels in the control group. The miR-1260b expression level in ovarian cancer patients was detected to have increased approximately 33fold compared with the levels in the control group. The String Analyses showed that the miR-1260b was associated with CHEK2 protein which was a member of the serine/threonine-protein kinase family. It should be investigated for larger cohorts in benign ovarian diseases and in different stages of patients receiving ovarian cancer treatment whether this molecule is a noninvasive biomarker and therapeutic target to be used especially in the early diagnosis and prognosis of ovarian cancer in the future.

Keywords: miRNAs, miR-1260, Ovarian cancer, CHEK2 protein

Poster Presentation

1st International Congress of Biomarkers

PN: 1316

Identification of the particular type of miRNA which promises early diagnosis of ovarian cancer

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ABSTRACT

The most common gynecologic cancers detected in women in Turkey are uterine cancer, ovarian cancer, and cervical cancer. Identification of the molecular pathogenesis of ovarian cancer, and discovery of new moleculer biomarkers which facilitate the ovarian cancer treatment are required for an effective ovarian cancer treatment in clinics. The miRNAs are reported to be the possible biologic indicators for various cancer types. We aimed to investigate a miRNA which were suggested to have effect in ovarian cancer in our (previous) monozygotic twin study from the miR-1260 microRNA family whose association with ovarian cancer yet has not been reported in the literature. We investigated the expression levels of miR-1260a miRNA, in the peripheral blood lymphocytes of 150 familial and sporadic ovarian cancer patients, and of 100 healthy individuals of the control group who were matched for age, sex, and ethnicity with the patient group, and investigated their possible property of being a biologic indicator for ovarian cancer. The expression results of ovarian cancer patients were evaluated by comparison of the results of the control group in the study. The expression level of miR-1260a in ovarian cancer patients was found highly increased compared with the levels in the control group. The miR-1260a expression level in ovarian cancer patients was detected to have increased approximately 17fold compared with the levels in the control group. The String Analyses showed that the miR-1260a was associated with the ribosomal protein family which was known to be effective in the translation stage of cell. It should be investigated for larger cohorts in benign ovarian diseases and in different stages of patients receiving ovarian cancer treatment whether this molecule is a noninvasive biomarker and therapeutic target to be used especially in the early diagnosis and prognosis of ovarian cancer in the future.

Keywords: miRNAs, miR-1260, Ovarian cancer, CHEK2 protein

Poster Presentation

1st International Congress of Biomarkers

PN: 1319

Identification of a novel autoantibody to the RNA-binding domain of Nucleolin as a potential biomarker in the detection of cancers

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ABSTRACT

Nucleolin expression and localization are often abnormal in malignancies, and ectopic expression and overproduction of it may lead to the generation of autoantibodies; detecting such autoantibodies is predicted to be essential for early diagnosis and prognosis of patients. In this study, we employed an *E. coli* expression system to clone the recombinant nucleolin protein and an indirect ELISA to evaluate its reactivity to cancer patient sera to that of healthy individuals. Lung cancer patients' autoantibodies had the greatest seroreactivity with our recombinant protein, with an area under the curve of 0.948 and a sensitivity and specificity of 85 and 96.67 %, respectively ($P < 0.0001$, Accuracy = 92%). Lung tumor size ($r = 0.793$, $P < 0.0001$), TNM staging ($r = 0.643$, $P = 0.002$), and proliferation ($r = 0.744$, $P = 0.0001$) were significantly correlated with anti-Nucleolin autoantibodies. Moreover, unlike other tumor sera, this autoantibody distinguished patients with early-stage lung cancer significantly from healthy control sera ($P = 0.0009$). As a result of our findings, anti-Nucleolin autoantibodies may be a potentially useful biomarker for the diagnosis of a wide variety of human cancers, particularly early-stage lung cancer, and because its level correlates strongly with tumor size, pathological staging, and proliferation, it may be used to evaluate therapy response.

Keyword: Immunoreactivity, Autoantibody, Nucleolin, Cancer, Biomarker, ELISA assay.

Poster Presentation

1st International Congress of Biomarkers

PN: 1320

Nucleolin; A tumor associated antigen as a potential lung cancer biomarker

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ABSTRACT

Lung cancer is a primary cause of mortality in many communities. The poor prognosis and clinical outcome of this cancer are mostly attributable to its advanced stage upon diagnosis, and as a result, it places a significant cost on public health across the globe. The majority of patients experience severe adverse effects from conventional therapies that involve nonspecific invasion of both healthy and malignant cells. Furthermore, no particular tumor marker has been developed to evaluate the patients' status and prognosis. NCL as one of the vital nuclear proteins is involved in various cellular activities, including ribosome assembly and rRNA processing. Research have shown that following malignant transformation in lung cancer cells, both the cytosolic and plasma membrane levels of this protein rise dramatically. Furthermore, signaling generated by the surface nucleolin significantly enhances tumor proliferation, differentiation, and angiogenesis. On the other hand, findings showed that altering the size and other properties of tumor cells may influence the expression pattern of nucleolin. Therefore, in the current study, we intend to review the role of nucleolin in the development and progression of lung cancer cells and also evaluate its potential as a prognostic, therapeutic as well as diagnostic marker in lung cancer patients.

Keywords: Nucleolin, Lung, Cancer, Biomarker, Prognosis, Diagnosis, Therapy

Poster Presentation

1st International Congress of Biomarkers

PN: 1321

Potential of biomarkers in multiple sclerosis

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ABSTRACT

Multiple sclerosis (MS) is a demyelinating and inflammatory disorder that outbreaks in neurons and axons of the central nervous system (CNS). Lesions in different regions of the CNS, for instance: the brain and spinal cord, are typically required for the diagnosis of MS. The number of promising MS therapies has significantly increased in recent years. The optimum course of treatment is often determined by a customized plan based on a patient's prognosis and treatment risks. Making crucial decisions about MS therapy requires the use of biomarkers that can forecast the progression of disabilities, track ongoing disease activity, and evaluate treatment response. This review discusses MS biomarkers that are currently used in clinical practice. It also summarizes and examines recently published research on prospective MS biomarkers that may be clinically relevant. We performed a search of PubMed, Scopus, and Google Scholar database of Abstracts of Reviews of Effects. This search was limited to English language publications and yielded a total of approximately 900 articles, which were reviewed by title and abstract for potential relevance.

Keywords: Multiple Sclerosis, neurodegenerative disease, biomarker.

Poster Presentation

1st International Congress of Biomarkers

PN: 1322

Sensitive and convenient detection of miRNA-145 using a gold nanoparticle-HCR coupled system: computational and in vitro validations

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ABSTRACT

As a challenging disease, multiple sclerosis (MS) requires accurate diagnosis and treatment in a timely manner. The aim of this study was to develop a novel ultrasensitive optical biosensor that detects microRNA-145 (miRNA-145) as MS biomarker using hybridization chain reaction (HCR). In order to construct such a sensor, HCR occurred between hairpin probes MB1 and MB2 probes, owing to the poly-cytosine nucleotide loop in MB1 and the poly-guanine nucleotide loop in MB2. Long-range dsDNA polymers are made by adding miR-145 as a target sequence. The HCR product was then incubated with positively charged gold nanoparticles (AuNPs), which electrostatically adsorb onto the dsDNA polymers. This resulted in the precipitation of the AuNPs. By incubating different concentrations of miR-145 with AuNPs, the changes in the UV-vis spectrum of the supernatant were analyzed. The proposed biosensor showed great ability to detect miR-145 in a wide linear range of 1 pM-1 nM with an excellent detection limit of 0.519 nM. Moreover, the developed biosensor showed considerable selectivity in discriminating between miR-145 and mismatched sequences. It's interesting to note that miRNA-145 could also be detected in diluted serum samples using the proposed method. For the detection of circulating microRNAs, our sensor shows remarkable selectivity and specificity, which is promising for translation to clinical applications.

Keywords: Hybridization chain reaction; Colorimetric detection; miRNAs; Positively charged gold nanoparticles; Multiple sclerosis; Biosensor

Poster Presentation

1st International Congress of Biomarkers

PN: 1323

A Review of Exosome Therapy in the Treatment of Neurodegenerative Disease

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ABSTRACT

One of the main challenges in the neurodegenerative diseases is their ineffective treatment. Discovery of biomarkers in disease for prognostic purposes, clinical monitoring, and evaluation of treatment response is a major research endeavor in neurodegenerative disease. Extracellular vesicles, are biologically relevant, considering their cargo of RNAs, proteins, and surface receptors and they have potential to be used as biomarkers in both physiological and pathological states. Exosomes were first introduced as nanoscale vesicles. Today, most studies focus on exosomes as carriers of the drugs and they are naturally used as biological carriers. Exosomes were initially thought to be secreted by some cells as a compensatory response, but later it was determined that various cells such as hematopoietic, non-hematopoietic, nerve tissue, epithelial and even cancer cells actively secrete exosomes. Exosomes are present in biological fluids such as plasma, cerebrospinal fluid, bile, and even saliva. The kinetics of exosomes change depending on the conditions and different functions. EV's production by p53-regulated transcript genes is controlled, detected by electron microscopy due to their morphology. The role of exosomes in angiogenesis, apoptosis, inflammation, coagulation, drug delivery, cell-cell communication, cell migration, and message transmission, as well as pathological conditions. Exosomes influence the response of other cells. In this review, Google Scholar and PubMed databases have been used and keywords for "neurodegenerative", "biomarker", "exosome" have been searched. The papers were found based on a related topic. So that, we focus on the immunomodulatory and neuroprotective effects of EVs within in vivo and in vitro models of nerve disorders.

Keywords: Neurodegenerative disease; Biomarker; Exosome

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A comparative study of the myofibroblasts and macrophages frequency between the oral and skin squamous cell carcinoma

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Abstract

Oral squamous cell carcinoma (OSCC) is one of the 10 most common malignant tumors and SCC accounts 94% of all oral malignancies. Mast cells are regarded as complex and multifunctional cells, playing a significant role in immunopathology. The aim of this study is to comparative evaluation of the frequency of myofibroblasts and Macrophages between oral and cutaneous squamous cell carcinomas. In this descriptive-analytic cross-sectional study, 60 paraffin were comprised including 20 cases of OSCC and 20 cases of CSCC and 10 cases of normal skin and 10 cases of normal oral mucosa. To evaluate the prevalence of myofibroblasts, α-SMA staining and CD163 markers for macrophages were used. In this study, the data were analyzedusingWilk Shapiro and t-testsinSPSS 19. The *p* value was less than 0.05. The average of myofibroblast scores in skin squamous cell carcinoma was 20.05 and the mean myofibroblast score in oral squamous cell carcinoma was 20.95. There was no significant difference between the means (P> 0/05). The average of macrophages in the skin was 28.125 vs. 49.67 for the mouth. This difference was statistically significant (P < 0/05). There is no significant difference between the presence and accumulation of macrophages and myofibroblasts in oral and skin squamous cell carcinoma, but intensity accumulation and color pattern in OSCC and CSCC is more than normal skin and mucosa (p<0.05). According to the findings of this study, it does not seem that the difference in biological behavior of squamous cell carcinoma of the oral cavity and skin depends on myofibroblasts. In case of the macrophages in this area also requires designing and conducting more studies.

Key word: cutaneous squamous cell carcinoma, macrophage, myofibroblast, oral squamous cell carcinoma

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Prognostic biomarkers influencing survival rate in head and neck Squamous Cell Carcinoma: a systematic review

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ABSTRACT

Head and neck Squamous cell carcinoma of the (HNSCC) is a group of related tumors that develop in the epithelial lining of the oral cavity, larynx, and many other regions in head and neck area. The use of prognostic factors has been one of the most important management strategies for selecting the appropriate treatment plan for HNSCC patients. There is an urgent need to identify new biomarkers influencing prognoses in the HNSCC, and to assess whether they can serve as a guide to risk classification and treatment decisions. Considering that different biomarkers have been proposed to predict the prognosis of patients with squamous cell carcinoma of the head and neck, the aim of this study was systematically review of these biomarkers. After extracting the articles from the targeted databases(pubmed,google scholar) using the specific keywords(Head and neck neoplasms , Biomarkers , Prognosis , Survival rate , Overall Survival , Disease Free Survival) , they were selected by the subject expert in 3 steps. The abstract and full text of the articles studied. After the final selection of studies, the articles sorted by publication date and after careful study and extraction of required information, the results of each study reported separately. Out of 4727 studies, a total of 128 studies were included in this study. In this 128 study, results of prognostic biomarkers affecting the survival rate of patients with squamous cell carcinoma of the head and neck were reported in the form of various parameters such as survival rate (OS), risk ratio (HR). Descriptive specifications and data obtained from these 128 articles which included: name of the first author, year of publication, sample size, average of parameters was reviewed and classified. Different biomarkers have been expressed as selected biomarkers in various studies. The collection of these biomarkers can be considered as a group of appropriate biomarkers in predicting and making the right decision to follow the treatment of patients with squamous cell carcinoma of the head and neck. HOXA5 biomarker with survival rate of 83.30, VEGF-C biomarker with risk ratio (univariate) of 14.68, SCC-Ag biomarker with risk ratio (multivariate) of 11.109, PSMA biomarker with 60 risk ratio and OPN biomarker with RR of 1.8 were identified as successful biomarkers among their peers .

Keywords: Head and neck neoplasms, Biomarkers, Prognosis, Survival rate, Overall Survival, Disease Free Survival

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Comparison of Ki-67 Marker Expression betweenDentigerous Cyst and Calcifying Odontogenic Cyst

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ABSTRACT

Odontogenic cysts are the most common cysts in the jawarea, and one of the most common cysts is Dentigerous Cyst (DC) and Calcifying Odontogenic Cyst (COC). Calcifying odontogenic cyst has significant variation in clinical and histopathological features. In some cases,it is in the form of a benign cyst, and in some cases, it may have an aggressive biological behavior and show tumoral changes. Dentigerous cystis the most common facial developmental cyst that originates from reducedenamel epithelium and is mostly associated with impacted teeth and is usually clinically asymptomatic, but it has the potential to enlarge andcause bone changes, as well as the potential it has tumoral changes. The most common behavior of any lesion is generally reflected by its growth potential. The growth potential is determined by measuring the cell proliferation activity, among which the immunohistochemical method (IHC) is the most common method. In this study, we will compare the rate of cell proliferation and growth potential of these two cysts by Ki-67 marker.

Keywords: immunohistochemical, Dentigerous cyst, Calcifying Odontogenic Cyst, Ki-67 marker

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