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The Future of Medicine is Personalized

The International Personalized Medicine Congress of Iran

Personalized Medicine Journal

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Telephone: +98 (21) 88985293

Email: info@PersonalizedMedicineJournal.com

Address: NO.2,St.Italia, Tehran, Iran

Message of Congress Chairman

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Chairman of National Institute of Genetic Engineering & Biotechnology

With greetings and high respect to colleagues, scientists, professors and all audiences who are active in the field of medicine. It gives us the greatest pleasure to invite you to join us at the next International personalized medicine congress of Iran.

We are proud to announce that with the grate grace of God Almighty and the best efforts of scientists and scholars the second International personalized medicine of Iran will be held on 13-15 of January 2018 in Tehran, Iran.

As the whole medicine societies believe Personalized Medicine is the future of medicine and its various fields and the human beings will benefit from its advantages in near future. International personalized medicine of Iran is a pragmatic event directed at filtering through the information overload of the digital age to deliver targeted information.

We hope that with the help of Allah, we can provide the new opportunity to address serious problems of progress, notifications, exchange up to date knowledge, trade, benefit from results of previous studies and make a productive cooperation of professors and experts for seminar and consultation in an intimate setting and away from any biases in order to get the goal of novel science and technologies improvement.

We kindly appreciate the all endeavors of our partners and colleagues from Iran and round over the world that helped us to make this event more effective and even possible.

Looking forward to welcome you in Tehran.

Warm regards,

Massage of Congress Secretaries

Dr. Mohammad Ali Saremi

Dr. Massoud Houshmand

Dr. Reza Nekouian

Personalized Medicine: the most effective way to evaluate which medical treatments will suit best for each patient.

Dear Distinguished Colleagues,

It is a great pleasure and an honor to extend to you a warm invitation to attend the 2nd International Congress of Personalized Medicine, to be held January 13 – 15, 2018 in Tehran, Iran. The 2018 Congress is jointly organized by the Baghiyatallah University of Medical Sciences and the with the cooperation of Iran University of Medical Sciences and National Institute of Genetic Engineering and Biotechnology.

Personalized medicine is an evolving field which makes the transition from a one-size-fits-all world to one that is based on delivering the right treatment and drug to the right patient at the right time. The concept of personalized medicine provides the best tools for physicians to apply diagnostic tests to identify specific biological markers, often genetic, that help determine which medical treatments and procedures will work best for each patient. In this new field of medical science, targeted and effective therapy, reduces side effects and prevention plans might be named as some of the personalized medicine achievements. Over recent years pharmacogenomics that uses an individual's genome to provide a more informed and tailored drug prescription has been developed extensively which help prevent adverse events, allow for appropriate dosages, and create maximum efficacy with drug prescriptions. Heavy investments in pharmaceutical industries to make effective drugs which suit the genetic make-up and individual's circumstances of the patients reflects the need to transform approaches of health care system. Preventive care might be the ultimate goal of personalized medicine to be achieved which would be possible by using genotyping for many diseases like different cancers and metabolic disorders.

We hope you will join us for a symphony of outstanding science, and take a little extra time to enjoy the spectacular and unique beauty of this region.

With best wishes,

Message of Personalized Medicine Research Center & Journal Board

Dr. Mohammad Ali Saremi

Chairman of Personalized Medicine Research Center

Nayyere Moslehi

Editor In Chief Personalized Medicine Journal

Greetings from us and our executive colleagues of 2nd Personalized Medicine Congress.
With honor we are happy to be placed once more in the pathway of science promotion and expansion of the research era.
Personalized Medicine Journal is the first medical journal of Iran in individualized medicine which has the pleasure to print the Personalized Medicine Congress papers for the second year.
This journal invites the universities scientific boards members of the fields of cancer, genetics, psychology, molecular medicine, pharmacogenomics, nutrition and fitness, cell therapy, bioinformatics, , traditional medicine, omics and etc.
We wish to thank all of our colleagues in the office of AmitisGen Med TECH Group that their efforts make this event background.
We also warmly welcome Iranian and foreign gusts and with appreciation of the scientific and executive committees, speakers, financial sponsors, supporting organizations we hope to see this congress holding in next years.

Aknowledgment

2nd International Personalized Medicine Congress of Iran wishes to thank the following people for their kind effort s and endeavors to do the event:

Dr. Kazem Malakouti

Dr.Gholamhossein Alishiri

Dr. Sadegh Ghasemi

Dr. Hassan Saadat

We do also thank you the permanent secretariat collogues:

Najme Shojaei

Nayyere Moslehi

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and

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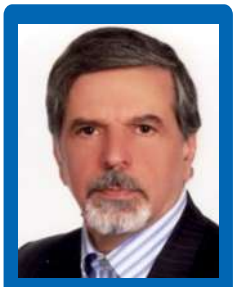

Dr. Mohammad Reza Zali

Congress Main Topics

- Cancer Genetics
- Tumor & Cancer Immunology
- Cancer : Genomics & Metabolomics
- Targeted Cancer Therapy
- Stem Cell Therapy
- Cancer Biomarkers
- Cancer Case Reports
- Novel Approaches to Cancer Therapeutics
- Precision Medicine & Cancer Therapy
- Cancer Management & Prevention
- Cancer Pharmacology
- Organ Specific Cancers
- Radiation Oncology
- Surgical Oncology
- Cancer Drugs
- Complementary and Alternative Cancer Treatment
- Cancer Clinical Trials
- Cancer & Lifestyle
- Cancer: Psychological & Social Aspects
- Cancer Diagnostics & Diagnostic Market

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Dr. Mitra Zarrati

The International Personalized Medicine Congress of Iran

Key Speakers

KO1001

Recombinant Antibody and CAR-T cell cancer Therapy

Dr.Davoud Ahmadvand

Davoud Ahmadvand

Assistant of Professor of clinical biochemistry, school of Allied Medical sciences, Iran University of Medical Sciences
Neuroscience Research Center, Iran University of Medical Sciences, Tehran, Iran

Abstract:

T cell therapy, which involves the adoptive transfer of tumor-antigen specific T lymphocytes into cancer patients, offers excellent opportunity for modern cancer therapy. Really CARs structure are composed of an antigen-specific single chain antibody variable fragment (scFv) that is linked via a spacer to the intracellular signal transduction domains derived from ζ chain of the TCR complex or γ chain from FcεRI. CAR-T Cell is a genetically modified autologous T-cell immunotherapy. Each dose is a customized treatment created with a patient's own T-cells, which are collected and sent to a manufacturing center where they are genetically modified to include a new gene that contains a specific protein—a chimeric antigen receptor or CAR—that directs the T-cells to target and kill leukemia cells that have a specific antigen (CD19) on the surface. Once the cells are modified, they are infused back into the patient to kill the cancer cells. Fortunately CAR T-cells had demonstrated dramatic results in clinical trials in patients with relapsed/refractory hematologic cancers, who have limited or lack any therapeutic options. In some cases, one dose of the treatment has eradicated the disease. The overall remission rate was more than 85% in treated subjects. Based on these promising clinical trial results on August , 2017 , FDA approved the first chimeric antigen receptor (CAR) T-cell therapy that Novartis called it tisagenlecleucel (Kymriah) for pediatric and young adult patients with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse. Recently on October, 2017 FDA approved the second T-cell therapy that uses chimeric antigen receptor (CAR) technology. Axicabtagene ciloleucel (Yescarta, Kite Pharma) has received FDA approval for the treatment of patients with relapsed/refractory aggressive B-cell non-Hodgkin lymphoma (NHL) who are ineligible for autologous stem cell transplant. Kymriah is going to be introduced on the market at a price of $475,000 for a single infusion by Novartis.

KO1002

Personalized Medicine approach in breast cancer

Prof.Esmaeil Akbari

Esmaeil Akbari
Head of Cancer Research Center, Shahid Beheshti University

Abstract:
One of the aspirations(Everlasting wishes) of humankind is the deep recognition of health risk factors, Preventing them and, if so, their treatment. This desire was augmented by the advancement of molecular, mental, and social knowledge, and various variables were found in individuals who could not respond to the actual causes of the diseases and how to care for them in all peoples. For this reason, human beings have embraced the science of numbers in the form of epidemiology of diseases, including the incidence, prevalence, survival and death of breast cancer and In any case, the factors of diagnosis and treatment have come to the fore with this science, which obviously implies that it contains all the personal factors of a human being associated with the diseases. However nowadays, But today, with the advancement of molecular, psychological and social science, more are known. Many omics have been discovered, such as genomics, transcriptomics, proteomics, metabolomics, etc., each of which expresses one of the molecular and cellular domains. In psychological and spiritual affairs, there are many factors such as patience, kindness, confidence, socialism, forgiveness, sacrifice, etc., and distinguish humans from eachother. In social affairs and social determinants of health (SDH), they have entered the health field in a powerful way that today, without considering them, talking about personalized medicine, is a lack of knowledge and a lack of belief in science. With this description, we hear different definitions in the international literature for personalized medicine.
If a geneticist defines it, his or her words may vary a lot with a dietitian defines that also is completely different from what a surgeon, psychologist or social worker interprets it.
I hope we discuss a few of these issues in this short panel and introduce Precision Medicine as a dense, integrated, comprehensive content to you successfully.

KO1003

The Approach of Medical Ethics in Personalized Medicine

Dr.Gholamhossein Alishiri

Gholamhossein Alishiri
Personalized Medicine Research Center of BUMS

Abstract:
Personalized medicine is a branch of medicine focusing on incorporation of molecular genetic insights into treatment of patients and prognosis strategies selection. As passing the second decade following the Human Genome Project parallel to developing in technologies such as gene expression assays and next-generation sequencing, evidence base of personalized medicine has become settled in a growing number of clinical fields. Shifting into personalized medicine is confronting many challenges including ethical and social problems. Since personalized medicine could not get prosper as ethical problems stay unresolved, there is need to broaden the focus of work on this filed of medication to overcome the ethical hindrance including informed consent science gap.
The significant increment in amount of health information associated with personalized medicine will raise need for addressing issues such as privacy, availability, stigmatization, discrimination, liability, physician/patient relationships, implementation, data banking, confidentiality and unauthorized disclosure. Furthermore, individual/social benefit versus science development beside health disparities exacerbation such as cost and input/output problem should be balanced. Therefore, the need for proper ethical ground rules is indispensable in order to illustrate structure of policy making and strategy planning in field of ethical issues surrounding personalized medicine. Considering the importance of individualized therapy, the next decade in personalized medicine should be the time of extensive alterations in the medication trend comprising ethical, social, legal and economical modifications to create a positive impact on quality of healthcare system.

KO1004

Measuring the Genetic Damage in Some Iraqi Breast Cancer Patients During Chemotherapy with Three Genetic End-Points

Dr.Abulsahib K,Ali

Abulsahib K, Ali[1], Abd AL-Ameer, N. AL_Rekaby[2], Sara J. Kadhim[2]

1) Ministry of Science and Technology, Central Labs. Directorate, Baghdad, Iraq.
2) Ministry of Higher Education and Scientfic Research,AL-Mustansiriya University , College of Science, Baghdad, Iraq.
sahib1966@ yahoo.com

Abstract:

This study was carried out on twenty four Iraqi women patients with breast cancer patients during chemotherapy treatment at Al-Amel National Hospital for cancer Management in Baghdad during time 1-15 years , non-smokers and non- alcoholic , aged (30 - 69 year),with stage (grade) I - IV, as well as twenty four apparently healthy individuals females collected randomly from population living Baghdad , aged (30 - 69 year) which are non-smokers non- alcoholic as control group. Using three molecular genetic end-points parameters were studied to determine genotoxic effects of some anticancer drug in peripheral blood lymphocytes of some Iraqi breast cancer patients during chemotherapy and compared with control groups. Investigations were carried out by using the micronuclei (MN) frequency in binucleated lymphocytes, nuclear division index (NDI) and Hypoxanthine guanine phosphoribosyl transferase (HPRT) mutation assay were performed on peripheral blood lymphocytes for breast cancer patients and control groups. The results of the MN frequency in binucleated lymphocytes a significant increase ($p< 0.05$) in breast cancer patients during chemotherapy as compared with the control group. The increase frequencies of MN in breast cancer patients increased with the cumulative effect of chemotherapy. However, the results of the average of NDI were significant decrease ($p > 0.05$) in peripheral blood lymphocytes patients with breast cancer after chemotherapy treatment as compared with control group. The decline in the NDI test is based on the fact that this marker that this decline refers to the increased cellular toxicity of chemotherapy. Meanwhile, it was found the results of the average mutation frequency for HPRT (Mf-HPRT) gene showed a significant increase ($p<0.05$) in the breast cancer patients during chemotherapy as compared with the control groups. In conclude, the results indicated that there is a possibility of using the changes at the level of HPRT gene mutation as useful biomarkers for the detection of the effect of chemotherapy in peripheral blood lymphocytes for cancer patients. In addition, the results of MN, NDI and Mf-HPRT were compared in the ages and grade of the studies groups.

KO1005

The effect of naturally-occurring dietary compounds on Cancer Stem Cells

Dr. Fatemehsadat Amiri

Fatemehsadat Amiri
Assistant Professor, Department of Nutrition, School of Public Health, Iran University of Medical Sciences

Abstract:
The first use of chemotherapeutic agents to treat cancer was in the early twentieth century, which became the basis of discovery and development of most current anti-cancer drugs. Although a large majority of chemotherapeutic drugs can considerably shrink tumor sizes, they often fail to eradicate tumors. The cancer may eventually develop drug resistance and recurrence.
In recent years, a great deal of research has demonstrated the existence of cancer stem cells (CSCs) or tumor-initiating cells (TICs) in several human cancers. However, most currently available therapeutic approaches, including chemotherapy and radiotherapy, lack the ability to effectively kill these CSCs. Therefore, this CSC population has become a target for cancer prevention and therapy.
The CSC theory asserts that many types of cancer are initiated from and maintained by a minor population of tumorigenic cells that are capable of continuous self-renewal and differentiation. This cell population undergoes unlimited proliferation and gives rise to differentiated cells, developing new tumors phenotypically recapitulating the original tumors. In addition, recent studies indicate that CSCs may be responsible for tumor relapse and resistance to therapy. So far, several major pathways including Wnt/β-catenin, Hedgehog, and Notch have been identified to play pivotal roles in CSC self-renewal.
It is suggested that targeting CSCs could be achieved by several strategies including sensitizing them to chemotherapeutic agents, induction of differentiation, and inhibition of self-renewal signaling.
A plethora of naturally-occurring dietary compounds have been proven to be promising chemoprevention agents against various types of cancer. A number of studies have found that some dietary compounds including "Curcumin, Sulforaphane, Soy Isoflavone, Epigallocatechin-3-Gallate, Resveratrol, Lycopene, Piperine and Vitamin D3" can directly or indirectly affect CSC self-renewal pathways. These naturally-occurring dietary compounds are advantageous in several aspects as chemoprevention agents: (1) they are present in commonly consumed food, which is readily available to most people in daily life; (2) they usually have very low or no toxicity, in contrast to most chemotherapy drugs; (3) many of these compounds have shown potential as an adjunct to chemotherapy drugs in some clinical trials. Investigating the efficacy of the dietary compounds against CSCs will provide rationale for preclinical and clinical evaluation of these compounds or potentially their native food extracts for chemoprevention of CSCs. These studies will eventually enable us to discover more effective strategies for cancer treatment to reduce cancer resistance and recurrence and to improve patient survival.

KO1006

Personalized medicine in hematologic malignancy

Dr.Nafise Ansarinejad

Nafise Ansarinejad
Hematologist and Medical Oncologist, IUMS

Abstract:
Personalized medicine is the cornerstone of medical practice. It tailors treatments for specific conditions of an affected individual. The borders of personalized medicine are defined by limitations in technology and our understanding of biology, physiology and pathology of various conditions.
Current advances in technology have provided physicians with the tools to investigate the molecular makeup of the disease. Translating these molecular make-ups to actionable targets has led to the development of small molecular inhibitors.
Also detailed understanding of genetic makeup has allowed us to develop prognostic markers, better known as companion diagnostics. Current attempts in the development of drug delivery systems offer the opportunity of delivering specific inhibitors to affected cells in an attempt to reduce the unwanted side effects of drugs.
Targeted therapies or small molecular inhibitors block the proliferation of cancer cells by intercepting their specific target.
First of all, most of the small molecular inhibitors currently available in clinics are targeting protein kinases. These are an essential cellular component and blocking these molecules could result in cellular compensation.
Chronic myeloid leukemia (CML) and Chronic lymphocytic leukemia (CLL) are the best hematologic malignancy for describe historical role of personalized medicine in hematologic malignancy. Maybe the first diseases that used new science for diagnosis, risk assessment, treatment and prognosis.

KO1007

The effect of Conjugated linoleic acids on tumor cells suppression and probably mechanisms of their effect

Dr.Naheed Aryaeian

Naheed Aryaeian

Associate Professor, Department of Nutrition, School of Public Health, Iran University of Medical Sciences, Hemmat Broadway, Tehran, Iran - aryaeian.n@iums.ac.ir

Abstract:

Conjugated linoleic acids (CLAs) are composed of positional and stereo isomers of octadecadienoate (18:2). They find in foods derived from ruminants (beef and lamb as well as dairy products from these sources). When a mixture of isomers is fed to experimental animals, chemically induced Cancer, tumorogenesis in mammary, prostate, colon and skin is decreased. Also CLA treatment has contributed to improvement disease outcomes in children with HPV-induced laryngeal papillomatosis during one-year crossover study, Mechanisms of inhibition of carcinogenesis may include reduction of cell proliferation, induction of apoptosis and alterations in the components of the cell cycle. In addition, CLAs modulate markers of immunity and also eicosanoid formation in numerous species as well as lipid metabolism and gene expression. It is likely that CLAs exert inhibitory properties in carcinogenesis via one or more of these pathways. This review will explain recent advances in Explore of putative mechanisms of reduction of carcinogenesis by CLAs.

KO1008

Personalized Medicine In Metastatic Colon Cancer

Dr.Farzaneh Ashrafi

Farzaneh Ashrafi
Hematologist, Oncologist, Isfahan University Of Medical Sciences

Abstract:
Progress in the treatment of metastatic colorectal cancer in terms of personalized medicine, has been slow. We know a couple of markers that tell us what not to use, and now more recently, one that we know is proactive and tells us what to use. In terms of how it fits, for the longest time, KRAS at codons 12 and 13 and now what are called all-RAS, or NRAS, are a series of different mutations in the RAS gene. These are all biomarkers that largely tell us which patients are very unlikely to benefit from the EGFR antibodies. They give us some prognostic information as well. So, those are two biomarkers that tell us what not to use.

The BRAF mutation is an important biomarker, which we now understand to be a particularly negative factor. This is something that should guide us to treat patients differently than standard, because patients on average do poorly if they're treated with standard therapy with a BRAF mutation. BRAF mutations do not exist in patients with RAS mutations.

MSI-High, the so-called microsatellite instability, is a marker of a genetic predisposition to cancer, a familial cancer risk gene that has some bearing in stage 2 colon cancer. But in terms of metastatic colorectal cancer, its importance relates to the use of checkpoint inhibitors. In metastatic colorectal cancer, about 3% of patients with metastases are what's called MSI-High. Those patients have a reasonably good chance of benefiting from the checkpoint inhibitors.

KO1009

Multiple myeloma a heterogeneous challenge

Dr.Mojan Asadi

Mojan Asadi
hematologist-oncologist,assistant profesor of Alborz university of medical science

Abstract:
about 10% of hematological malignancies is multiple myeloma. despite relatively low incidence , ecomonic impact is high.
we surely cannot treat all patients in the same way.risk stratification is mandatory and it will be influence on prognosis,clinical trial selection and therapy.
with the availability of novel therapies, new markers are now more important than ever in predicting not only risk and outcome but also treatment selection.
here is a short review of this heterogeneous disease and usage of personalized medicine for risk stratification and treatment modality.

KO1010

Precision Medicine for Endocrinology

Dr.Fereidoun Azizi

Fereidoun Azizi
Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences

Abstract:
In recent decades, major biotechnological advances have been achieved following the sudden escalation of disease-related molecular information, with the potential for greatly advancing patient care. The human genome was depicted in 2000 and followed by the completion of the Human Genome Project in 2003. Scientists have ignited a firestorm of breakthroughs and upsure genomic information, by laying out, in order, the 3.2 billion units of human DNA. Innovative omics technologies including whole-genome single nucleotide polymorphism (SNP) chips, RNA interference high-throughput screening, microarrays and next-generation sequencing have also rapidly surfaced offering enormous potential in this field. This genomic revolution era offers unlimited possibilities and unlimited possibilities including the development of individualized medical necessities for each human based on his unique genomic information.
Personalized medicine today is commonly defined as a combination of molecular profiling and traditional diagnostic and therapeutic strategies precisely adapted to the individual requirements of patients. The fundamental idea behind personalized medicine is to couple large amounts of data available from the human genome with established clinical-pathological indexes to devise diagnostic, prognostic, and therapeutic policies specifically adapted to each patients needs and the ensuing research wave of the molecular basis of disease. Eventfully, precision medicine facilitates more accurate diagnosis and therapy at the intrinsic molecular level, promoting the individual bation and this allows the customization of healthcare and incorporation of electronic medical information obtained both on an individual and on the more comprehensive global scale.
The success of precision medicine faces many challenges. First, the establishment of frameworks for organizing, compiling, and elucidating the influx of data that can keep apace with rapid scientific innovations. Second, the shift toward a deeper understanding of disease, based on molecular biology, requires necessitates reclassification of disease states incorporating this knowledge, i.e modernization of the World Health Organization's International Classification of Diseases, for which there is a need for a reconsidered categorization classification based on intrinsic biology and traditional signs and symptoms. Thirdly, precision medicine will require promotion of handling of multi-parametric data and some proficiency in interpreting "-omics" data, dealing with the anticipated complexity and volume of new information. Addressing these challenges will require effective clinical decision support tools and new educational models.
It is anticipated that the initiative for precision medicine has two main components: A near-term focus on cancers and a longer term objective to generate data pertaining to all aspect of health and disease. This requires keeping upright research advances that will facilitate better evaluation of disease risk, comprehension of pathophysiology and prediction of favorable treatments for many more illnesses, with the aim of expanding the advantages of precision medicine into innumerable aspects of health and health care, which will undoubtedly motivate the next generation of scientists to develop novel innovative approaches for identifying, measuring, and analyzing a wide range of information data, including molecular, genomic, cellular, clinical, behavioral, physiological, and environmental frameworks.

Is it possible that the concept of precision medicine be extended to endocrine disorders? Let's consider diabetes, a disease that is today a major health problem worldwide and an epidemic in 21st century. It is estimated there are 330 million people with diabetes worldwide, almost half of whom are undiagnosed. This disease is a major cause of cardiovascular disease, renal failure, blindness and nontraumatic amputation and is the seventh leading cause of mortality. It is noteworthy that these figures are not only for developed countries, but prevelance of diabetes in many developing countries is increasing and imposes considerable medical expenses on the health budget. In the Islamic Republic of Iran, a developing country in south-west Asia, with 76 million population, the estimated diabetes population has increased from 3.6 million in 2005 to 4.5 million in 2011; corresponding figures for pre-diabetics have been 4.4 and 5.8 million, respectively. In Tehran, incidence rate of type 2 diabetes has been 1% per year. Diabetes mellitus among men ranked number 25, 13 and 22 for years of life lost (YLLs), years lost due to disability (YLDs) and disability-adjusted life years (DALYs) in 1990 and 12th, 5th and 10th in 2010, respectively. Diabetes as a cause of death has increased 40% in the last 20 years.

There has been great progress in understanding of pathophyiology and management of diabetes. However, despite availability of several classes of drugs for diabetes, both oral and insulin preparations, treatment is often on a trial and error basis or on the availability or affordability of medications, rather than the underlying pathophysiology; hance most diabetics do not achieve proper blood glucose control, mainly because all guidelines aim at management of the average patient, rather than at personalized, precision medicine. With increasing knowledge of the molecular causes of diabetes, we need to increase and update our tools for indentifying patients at very early stages, even before prediabetes, to begin early preventive measures to abort or delay the onset of disease. The advent of precision medicine for diabetes will require handling, incorporation and interpretation of massive amounts of genomic, metabolic, lifestyle, environmental, and clinical and para-clinical data, all of which need comprehensive investigations, progressive education and manpower training. With rapid progression of related sciences, there is prediction for soon appearance of precision diabetes clinics.

Another example of the impressive benefits of precision medicine in endocrinology is the treatment of thyrotoxicosis. Antithyroid drugs have been the mainstay of treatment of hyperthyroidism for years. However, with fixed doses of this drugs, some patients become euthyroid, some develop hypothyroidism and others still remain hyperthyroid after few weeks. In addition, if antithyroid medications are given to pregnant women in the first trimester of pregnancy, although safe for most, it causes fetal malformation in some. Would it be possible to identify the exact dose of anti-thyroid medication for each indivial patient and avoid giving it to the pregnant women, whose genomic and molecular study shows definite possibility of adverse effect on the fetus? Some scientific developments have taken the first step towards precision medicine for antithyroid drug-induced agranulocytosis. Pharmacogenomics is the study of how a person's reactions to medications is affected by their genetic constitution. It integrates pharmacology and genomics to develop efficient, safe medications and doses individualized to a person's genetic makeup. A sub-discipline of functional pharmacogenocalledmics, pharmacoproteomics, is a study of how the protein content of a cell or tissue changes qualitatively and quantitatively in response to treatment of disease, and how a person's protein variants in quality and quantity affect a person's reaction to a medicine. Using this technique in precision medicine may help to answer the challenges of anithyroid therapy, such as what has been proposed for metformin pharmacogenomics.

It must be accepted that some people from the medical community feel that unstinting focus on precision medicine is a mistake and a diversion from the main aim/target of producing a healthier population; they are not convinced that investing in biomedical research will result in unlimited rewards in financially and the health of people, and they emphasize that the challenges we are confronted with to improve population health do not include the frontiers of science and molecular biology; for them, it requires development of the scope and will to address certain incessant social realities, and an unstinting focus on factors, indispensable to the production of population health. They worry that an openhanded focus on precision medicine by trusted spokespersons for health is a mistake and a distraction from the goal of producing a healthier in reality; health care stakeholders must be made aware that precision medicine is no longer just a blip on the horizon and ensure that it lives up to its promise.

Endocrinologists are called upon to participate take part in the development of precision medicine for endocrine disorders and the management of their patients, by accepting the complexities and heterogeneities of these disorders and their burden in the population health. This will be a worthwhile investment with significant positive medical and socioeconomic outcomes for achieving "Health for All".

KO1011

Using zebrafish models of rar diseases to accelerate orphan drug discovery

Dr.Alexander D.Crawford

Alexander D.Crawford

Luxembourg Centre for Systems Biomedicine, Belval, Luxembourg
Norwegian University of Life Sciences, Oslo, Norway
Institute for Orphan Drug Discovery, Weihenstephan, Germany
Theracule, Belval, Luxembourg
alexander.crawford@uni.lu

Abstract:

Only a small minority of the estimated 7,000 rare diseases have an approved drug, creating the urgent need for new approaches to accelerate orphan drug development. Zebrafish are a powerful model organism, ideally suited for the rapid generation of biomedically relevant and predictive in vivo bioassays for a wide range of human genetic diseases. Because of the small size of their embryos and larvae with which most bioassays are developed, zebrafish models of human diseases enable the high-throughput, microscale in vivo screening of small molecule libraries. Zebrafish have therefore emerged as a promising tool for modeling rare diseases and supporting orphan drug discovery. In my presentation, I will review how we and others are using zebrafish to model rare diseases, and will highlight our recent progress in using genetically-modified zebrafish models to identify new orphan drug candidates. The need to expedite orphan drug development has created an urgency for identifying new uses for existing drugs (drug repurposing). As a result, the development of animal models able to support the screening of approved libraries of compounds in multiple rare disease-relevant assays has become a key priority and a limiting step in the development of orphan drugs. As the field of medicine moves towards more patient-specific models and shorter development timelines, zebrafish are rapidly becoming a key drug discovery tool with the potential to revolutionize not only orphan drug discovery but also personalized medicine.

KO1012

Whole-genome sequence variation, population structure and demographic history of the Iran: Iranian reference Genome Research (IrGR) project

Dr.Maryam S Daneshpour

Maryam S Daneshpour

PhD, Cellular and Molecular Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, I.R. Iran - Daneshpour@sbmu.ac.ir

Abstract:

The oldest and largest bio-bank with definite phenotypes in Iran belongs to the Tehran Lipid and Glucose Study (TLGS) a family based cohort. One of the aims of TLGS is to enrich biobanks with different types of molecular and phenotype data. Here in, we describe the Iranian reference genome research (IrGR) project, a whole-genome-sequencing project in a representative sample consisting of 1191 samples (trio+ families=34, trio families= 84, Parent-sibling= 56, Parent-child=109, Siblings= 141, Unrelated individuals=582) from all provinces of Iran. The aims is to characterize DNA sequence variation in the Iranian population. The parent–offspring trios include adult individuals ranging in age from 23 to 62 years from TLGS cohorts 1955–1994. Sequencing was done on blood-derived DNA and accomplished coverage was 35x. We found 44 million SNPs and 9 million insertions-deletions (indels). Both family-based and unrelated person designs represent unique resources to assess the frequency of regional variants, accurately reconstruct haplotypes by family-based phasing, characterize short indels and complex structural variants, and determine rates of loss of function and de novo mutational events. IrGR will also serve as a reference panel for imputation on genome-wide association studies in the Tehran cardio-metabolic genetic study (TCGS) and other Iranian cohorts to refine association signals and uncover population-specific variants. IrGR will create a catalog of human genetic variation in this sample that is uniquely characterized with respect to micro-geographic location and a wide range of phenotypes. The resource will be made available to Iranian national researchers and the medical community to guide the interpretation of sequencing, clinical and randomized clinical trial projects in Iran. The present paper summarizes the global characteristics of the project.

KO1013

An update of personalized medicine issues in breast cancer

Dr.Rezvan Esmaeili

Rezvan Esmaeili
PhD, Molecular genetics, Head of Genetics department, Breast cancer research center, Motamed cancer institute, ACECR, Tehran, Iran

Abstract:
Treatment of cancer involves patients with side effects that detriments their quality of life. Moreover, the efficiency of them may not enough to prevent recurrence and metastasis. Personalized medicine in breast cancer like other diseases uses information about a person's genes, proteins and environment to prevent, diagnose and treat disease. Recent genes and molecules are about to predict not only treatment response, but also the severity of common cancer related symptoms. In this talk the personalized options for optimal treatment choice and dosage and managing the related symptoms in order to enhance the quality of life of breast cancer patients will discussed. The following areas are discussed properly. Treatment related issues such as Gene Expression Profiling Techniques in the Optimization of Drug Choice, Use of Pharmacogenomics in Predicting Response to Chemotherapeutic Drugs, Circulating Tumor Cells, MicroRNA in Triggering Drug Release, Biomedical Engineering Tools in Intervention Design, Optimizing Radiation Dose in Radiotherapy, and quality of life issues such as Premature Menopause or Chemotherapy-Induced Menopause, Chemotherapy-Induced Peripheral Neuropathy, Cognitive Dysfunction.

KO1014

Ethics in Personalized Medicine

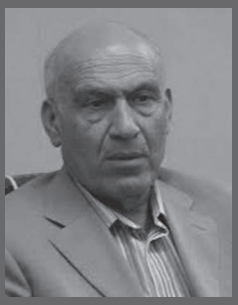
Prof.Dariush D. Farhud

Dariush D. Farhud
Prof. of Medical Genetics & Anthropology
Member of WHO Committee of Ethics- Geneva
Member of Iranian Academy of Medical Sciences- Tehran/ Iran
Member of Third World Academy of Sciences (TWAS)- Triest/ Italy

Abstract:
Background: Personalized medicine is a novel perspective in medicine and it is in challenge with potential classical perspective of medicine against patients. For analyzing the basics of ethics in personalized medicine, the accurate definition is provided. Personalized medicine points to design and presentation of medical services to individual in different areas; presentation, diagnosis, treatment and care fit to the genetic, cellular and molecular of each person.
Undoubtedly, four basic principles are discussed in personalized medicine:
Autonomy is defined as respect to ideas and acceptance of patient's decisions. Also, it seems that health and welfare of each one is the attractive principle in personalized medicine. Undoubtedly, this perspective focuses on the ethical principle called beneficence.
One of the basic goals of personalized medicine is increase of security and decrease of impairment of drugs and distinction between patients who benefit and do not benefit from one treatment. It is clear that decrease of risk or non-maleficence is another principle of medicine ethics. Therefore, non-maleficence in personalized medicine means as preventing from impairments of diagnostic and treatment services and minimizing the possible injuries.
Finally, justice means as provide fair and equal diagnostic and treatment services for all patients and clients. It is an important aim of medical ethics. Unfortunately, it cannot be met in personalized medicine as other expensive medical services. This is where we find the role of effective insurance.
Conclusion: Personalized medicine's projects have arguable ethical consideration in individual and social level. Expected beneficence of this project for people and groups can be followed by undesirable and unwanted results. Therefore, ethical issues must be considered carefully. The notable point is that; considering ethical issues in personalized medicine is depending to social health policies as scientific developments.

KO1015

Personalized Care in Colorectal Cancer



Prof. Ardeshir Ghavamzadeh

Ardeshir Ghavamzadeh
Hematologist, Oncologist
Head of Hematology, Oncology and Stem Cell transplantation Research Center, Tehran University of Medical Sciences

Abstract:
Colorectal cancer (CRC) is one of the most common cancers worldwide. Today, various techniques are available to detect CRC in its early stages or as precursor lesions, thereby preventing aggressive treatment. Approaching 60% of patients diagnosed with CRC will not die from the disease within the following five years. The range of drugs available to treat metastatic CRC is rapidly expanding and, in this area of cancer as in others, major advances are being made in our ability to assign specific treatments to subgroups of patients who are most likely to benefit.
It has been needed to differentiate the individual characteristics of each tumor based on its biology as well as on the specific clinical situation. To understand the evolution of the disease, obtaining specimens of tumor tissue is crucial. This helps in optimizing the care of individual patients. It also enables us to develop more successful treatments in general by allowing the design of new clinical trials based on the molecular features of CRC.
Typically, receptor-blocking drugs are large molecules based on our immune system and called monoclonal antibodies. The anti-EGFR monoclonal antibodies cetuximab and panitumumab are the two most important examples. The advantage of using drugs that target VEGF is that the need for blood vessels is common to all colorectal tumors.
Even when a relevant molecular abnormality is identified, the subgroup of tumors which are positive on this test needs to be further dissected to establish which cancers among them are sensitive and which resistant to targeted drugs. And to truly personalize therapy for metastatic CRC, we may have to look not for the presence or absence of one, two or even three markers.
The recent advances in molecular biology and the genetic classification of CRC are essential to individualize these therapies and will be basic for improving the treatment in the next years.

KO1016

Drug resistance and personalized medicine

Dr.Roya Ghods

Roya Sajed[1], Roya Ghods[1,2]

1) Department of Molecular Medicine, Faculty of Advanced Technologies in Medicine, Iran University of Medical Sciences, Tehran, Iran.
2) Oncopathology Research Center, Iran University of Medical Sciences, Tehran, Iran.

Abstract:

Drug resistance is one the causes of limited efficacy of cancer therapy and could be intrinsic or acquired. In fact, heterogeneity in gene dosage and signaling pathways in cancer cell populations renders them intrinsically more resistant to therapeutic approaches. For instance, colorectal cancer patients harboring mutation in KRAS do not respond to EGFR inhibitors such as Cetuximab and panitumumab. Resistance to drugs could be acquired through various mechanisms: 1- secondary genetic variations in drug targets; an example is BCR-ABL amplification seen in imabtinib-resistant CML patients. 2- pathway independent resistance. A typical example is the impact of tumor microenvironment on the efficacy of inhibitors of polo-like kinase and Janus-activated kinase-2. 3- drug resistance acquired through activation of alternative mechanisms. 4- resistance due to the existence of cancer stem cells (CSC).

Hence, identifying drug resistance-related mechanisms in the case of every patient prior to commencing the treatment is of major importance. Making use of NGS, proteomics and metabolomics data would be of great help in this regard. To investigate drug resistance, different approaches can be adopted, among which are: 1- examination of the sensitivity of patient biopsy-derived cells to drug. In this case, patients' biopsies are treated with different drugs and generally, the level of cell death is measured. 2- patient-derived xenograft tumor model, in which, patient biopsy is implanted orthotopically into an animal model and the in vivo impacts are assessed. 3- In situ assessments, which are based upon intratumoral injection of microdasage of drugs with the help of newly designed devices. In fact, personalized medicine provides the opportunity for applying the appropriate drugs with the perfect timing and at a suitable dosage with minimal or even no toxicity.

KO1017

Clinical proteomics in cancer: a focus on personalized medicine

Dr.Mohammad Reza Haghshenas

Mohammad Reza Haghshenas
Shiraz Institute for Cancer Research, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

Abstract:
Many physiological and pathological processes in cancers are controlled by protein complexes and protein-protein interactions. Proteomics technologies investigate and identify the expression and function of proteins in large scale. Clinical proteomics refers to the utility of data obtained from proteomics in clinic. A detail characterization about molecular mechanisms underlying the development of diseases, particularly in cancer, may be essential in terms of diagnosis and treatment. In this context, proteomics creates the bridge between molecular diagnostics and therapeutics, and their integration will be imperative to improve monitoring of patients for development of personalized medicine. Some identified proteins via the proteomics studies have been recently implemented in clinical trials for evaluation of response to drugs, some identified proteins are under development in clinic laboratories and some others are commercially available in clinic to personalized cancer management.

KO1018

Title: Cell therapy in diabetic foot ulcer

Dr.Nahid Hashemi Madani

Nahid Hashemi Madani, Rokhsareh Aghili
Institute of Endocrinology and Metabolism, Iran University of Medical sciences

Abstract:
Foot ulcer is a major complication of diabetes that not only does impair physical and mental health of the patient, but also imposes an economic burden on the society. Non-healing diabetic ulcers are more challenging. The standard clinical treatment of diabetic ulcer includes wound dressing, repeated debridement of necrotic tissue, off-loading, and antibiotics in the presence of infection. However, despite recent advances in such therapeutic modalities, a large number of diabetic foot ulcers end up to amputation. Recent evidences derived from clinical and basic science studies show that stem cell therapy can be a good solution. In this presentation we will report the short-term results of stem cell therapy in three patients with non-healing wound ulcers, in whom amputation was the only option. Then we will discuss the advantages and limitations of stem cell therapies in diabetic ulcers.

KO1019

Thyroid Cancer and Personalized Medicine

Dr.Mehdi Hedayati

Mehdi Hedayati

Cellular and Molecular Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract:

During the last decade, the incidence of thyroid nodules and cancer is increased and a higher demand for the diagnosis of thyroid nodules, and the treatment of this aggressive disease appeared. Molecular biology has given important contributions in the understanding of the mechanism of thyroid cancer, and it is used for the diagnosis, treatment, and prognosis of thyroid cancers successfully. Testing of fine needle aspiration (FNA) samples, from thyroid nodules, for a panel of mutations (typically includes BRAF, RAS, RET/PTC, VEGFR, EGFR, and PAX8/PPARg), proteomics, and metabolomics aimed by many researchers. The low-cost of individual genomic analysis provides a new era of personalized, patient-specific care. The lack of effective therapies for DTC, resistant to radioiodine and traditional therapies, is now being overcome by the development of targeted novel compounds in the context of personalized medical treatment. The increasing complexity of the diagnostic and therapy of thyroid cancer needs increased effort to personalize the diagnosis and the treatment, to reach the best and maximum success, and avoiding unnecessary and potentially harmful treatments. Nowadays, ctDNA results will be a useful and additional tool, while tumor biopsy will remain the gold standard, as it yields important information about tumor type, morphology, and origin of tumor, genetic or epigenetic alterations. A liquid biopsy is defined as circulating tumor cells (CTCs) and fragments of circulating tumor DNA (ctDNA) shed into the bloodstream from primary and metastatic tumor deposits. Using of ctDNA is superior to a non-invasive and cost-effective solution to identify reliable biomarkers for measuring tumor growth, metastasis and response to treatments. Molecular imaging based personalized therapy has been a fascinating concept for individualized therapeutic strategy, which is able to attain the highest efficacy and reduce adverse effects in certain patients.

Finally, for molecular diagnosis, molecular imaging, and molecular treatment of the thyroid cancers, more and more, personalized medicine made a hopeful light in this ear and the future of this field will belong to personalized medicine in a belief of cancer researchers.

KO1021

Personalized medicine in diabetes

Dr.Maryam Kabootari

Maryam Kabootari

Prevention of Metabolic Disorders Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran - maryam_kabootari@yahoo.com

Abstract:

Type 2 diabetes (T2D) is a heterogeneous disease, with genetic background, underlying pathogenic mechanisms and clinical features markedly varying among patients and with an ascending trend in both the developed and developing countries. In the Islamic Republic of Iran, the estimated diabetes population has increased from 3.6 million in 2005 to 4.5 million in 2011; corresponding figures for pre-diabetics have been 4.4 and 5.8 million, respectively.

Personalized medicine in diabetes refers to the utility of genomics data of a patient with diabetes to provide the most effective diagnosis strategies and treatment plans.

The current guidelines for the treatment of T2D do not include any genomics information. Diet, exercise and metformin are recommended as first-line therapy, although there is considerable variability in patients' responses to them. By considering common variations in certain genes, in the form of single nucleotide polymorphisms (SNPs) in an individual's genetic architecture, pharmacogenomics can promise new drug selection process in order to optimize pharmacokinetics and pharmacodynamics to eventually increase drug efficacy and decrease adverse drug reactions.

Moreover, type 2 diabetes mellitus encompass microvascular and macrovascular complications. Studies of human genetics offer powerful tools for delivering robust mechanistic insights into diabetic complications, which have a substantial genetic component. Identification of genetic variants with robust effects on the risk of developing diabetic complications will accelerate efforts to develop more effective strategies for treatment and prevention.

Personalized medicine is growing and gnomics data together with the potential of other "Omics" and clinical evidence-based data will lead to diabetes care improvement in the context of personalized medicine in the future.

KO1022

Personalized Medicine Importance and Necessity in Iran

Prof.Ali Karami

Ali Karami
Professor of Medical Biotechnology and Molecular Biology Research Center, Bagyiatallah University of Medical Sciences, Tehran. Iran

Abstract:
Recent development in molecular biology, molecular genetics, Omics, Marker findings, microbiom , Bioinformatics, system biology, Medicine and personal genomics has opened a new avenue to enhance our healthcare system from prevention to accurate treatments. New findings have revealed personal differences that will impact on precision diagnosis, prevention and treatments. Several hundred years of knowledge and experiences of Iranian traditional medicine on the basis of personal differences and temperament and its combination with personal medicine will have tremendous impact on health system of IRAN. In this paper we will discuss and address real importance and necessity of developing personalized medicine in medical faculties and research centers. We have main infrastructure basis in our medical science universities, high quality medical educations, experts in both medical and applied sciences, physicians, Molecular biologists, Genetics, Bioinformatics and high level and advanced research centers and laboratories. We need to evaluate our great capabilities on healthcare and medical experiences and Bioresearch works to develop Personal medicine departments and faculties to enhance our healthcare system as soon as possible.

KO1023

Application of Network Science in Drug-Protein-Disease Interaction and Drug Repositioning

Dr.Kaveh Kavousi

Akram Ahmadi[1,2], Amir Hosein Khanmohammadi[1,2], Najmeh Khedmatgozar[1,3], Vali Derhami[3], Maseud Rahgozar[4], Sajjad Gharaghani[1], Masoumeh Karamali[1,4], Ali Moeini[2], Kaveh Kavousi[1*]

1) Department of Bioinformatics, Institute of Biochemistry and Biophysics, University of Tehran, Tehran, Iran
2) Faculty of Engineering Science, College of Engineering, University of Tehran, Tehran, Iran
3) Computer Engineering Department, Yazd University, Yazd, Iran
4) Faculty of Engineering Science, College of Engineering, University of Tehran, Tehran, Iran

Abstract:

Network science is exploited in various disciplines for better understanding and analysis of components of a complex system. In recent years, several studies in the fields of computational prediction of drug-target, drug-disease, and drug-drug interaction as well as drug repositioning based on network modeling have been done in the laboratory of Complex Biological Systems and Bioinformatics (CBB), Institute of Biochemistry and Biophysics (IBB), University of Tehran, with collaboration of some other research labs. In this article, a brief review of these research works is presented. Prediction of Drug-Target Interaction (DTI), plays important role in drug design. In our recent research, drug interactions with four groups of target proteins has been investigated. These groups include Enzymes, Ion Channels, G-protein Coupled Receptors (GPCR) and Nuclear Receptors. In one of studies, a recommendation system was designed, named DTI- BECM (Drug Target Interaction Based on Eigenvector Centrality Measure). This recommender system uses well-known SIMCOMP algorithm for similarity measurement between chemical structures of drugs. Also, it uses the generalized Eigen vector centrality measure for bi-partite graphs. In a complementary study, molecular descriptors of drugs were used for improving the performance of system. These methods, successfully repositioned some known drugs for new targets. One of the latest projects, was performed to establish a framework for discovering unknown Disease-Drug Interactions. A random walk algorithm with restart was developed on a three-layer heterogeneous network to prioritize candidate diseases associated with drugs. Nine different networks (drug similarity, target similarity, disease similarity, gene similarity, drug-target interaction, target-pathway interaction, pathway-gene interaction, gene-disease interaction and drug-disease interaction network) were composed to shape a single heterogeneous network. The proposed method predicts therapeutic indices for existing or new potential drugs.

Proposing a solution for Drug-Drug Interaction (DDI), is another discipline in the drug research field that we have focused on it. Drug-Drug Interaction (DDI) is an unsafe drug side effect occurs unexpectedly when more than one drug is utilized. Identification of drugs with undesirable interactions with experimental methods is almost impossible. In the proposed method, different features are extracted from drugs for DDI prediction. These features include the fingerprint of chemical structure, label side effect, reported side effects, drug targets, and Anatomical Therapeutic Chemical (ATC) classification codes. Besides, we used the molecular descriptors of drugs as a new source of information for DDI prediction. Applying appropriate feature selection methods and using Support Vector Regression (SVR), alongside integration different information sources, showed significant results in comparison with other methods.

KO1024

Advanced Differentiated Thyroid Cancer: Molecular Targeted Therapies

Dr.Mohammad E Khamseh

Mohammad E Khamseh , Maryam Honardoust
Institute of Endocrinology and Metabolism, Iran University of Medical sciences

Abstract:
Thyroid cancer is the most common endocrine malignancy, Differentiated thyroid carcinoma (DTC) arises from follicular cells and are further classified as either papillary (PTCs, 75-80%) or follicular thyroid cancers (FTCs, 5-10%). The survival rates of patients are highly variable and depend on the histotype and the degree of differentiation.
Generally, in 10% of cases, the patients have an advanced stage of the cancer at the time of diagnosis, with local invasion and/or distant metastases. In about one-third of advanced DTCs, the metastatic lesions have a very low avidity for iodine at the time of diagnosis and 131I therapy has no effects.
Risk stratification in thyroid carcinoma is crucial to avoid overtreatment of low-risk and undertreatment of high-risk patients. Initial risk stratification, based on histopathological data is carried out just after primary surgery.
During the follow-up, patients are rest ratified considering their response to treatment to one of the following categories: excellent response, biochemical incomplete response, structural incomplete, or indeterminate response. This new approach is called dynamic risk stratification. It reflects a real-time prognosis and thereby substantially influences and personalizes disease management.
The advent of individual genomic analysis provides hope that we are entering a new era of personalized, patient-specific care. Reliable identification of mutations typically associated with thyroid cancer could alter the initial cancer treatment specially for high-risk patients and can potentially prevent the recurrences. The lack of effective therapies for PTC, resistant to radioiodine therapies, is now being overcome by the development of targeted novel compounds in the context of personalized treatment. Using approved targeted therapies such as anti-BRAF (V600-E) selective inhibitors and tyrosine kinase inhibitors (single or in combination) based on the individual characteristics of each patient may help to improve overall survival rates.
In general, good candidates for targeted therapies are those thyroid tumors that are defined as radioactive iodine resistant (RAI-R) according to well-defined criteria. This group generally includes approximately 66% of DTCs that have distant metastases at the time of diagnosis, which cannot be cured with 131I because they were initially or become RAI-R over time. Only patients with an advanced and progressive disease should undergo a treatment with targeted therapies.
Sorafenib and lenvatinib have been approved by the FDA and the EMA for the treatment of progressive RAI-R-DTC. Determining the right time to start targeted treatments represents a goal for future clinical research.

KO1025

Personalized medicine in acute leukemia

Dr. Mahshid Mehdizadeh

Mahshid Mehdizadeh
Associate professor of ped hematology and oncology, Shahid Beheshti university of medical sciences

Abstract:
Personalized medicine in acute leukemia has become a reality. The diagnostic procedures, including immunophenotyping, cytogenetics,molecular genetics, and new genomics, have allowed the definition of new ALLand AML sub-entities which, in some cases, has translated into specific therapies. A great achievement is the possibility of evaluating minimal residual disease (MRD) of ALL patients. MRD is the most important prognostic factor and thus a major component of a personalized treatment algorithm. Progress has also come from targeted therapies,extending the existing backbones of chemotherapy and stem cell transplantation .Targeted therapy in philadelphia chromosome-positive ALL with tyrosine kinase inhibitors and immunotherapy with monoclonal antibodies targeting surface antigens expressed on leukemic blast cells have extended .A new promising approach is the activation of patients' Tcells directed against their own leukemic blast cells either through a bi specific antibody, or chimeric antigen receptor modified T cells.
In Acute myeloid leukemia for decades, pretreatment karyotype evaluation has served to identify subgroups for risk-adapted post remission therapy, but the initial treatment approach has been largely unchanged. Nowadays AML is categorized into biologically defined groups .Identifying the genetic abnormalities and biological drivers prior to AML treatment will be important as we work to individualize therapy and improve outcomes.

KO1026

Bioresonance: a personalized approach to diagnosis and treatment

Dr.Alireza
Madjid Ansari

Alireza madjid ansari
tegrative oncology department, breast cancer research center, motamed cancer institute, ACECR, Tehran, Iran

Abstract:
The torso of human beings and all other creatures has been drawn up of molecules and sub molecular particles which skitter all the time like all other components of the world. These movements have their specific pattern and periodic cycles which make frequencies. This fact makes it possible to specifically affect these movements by using the waves with the same frequency. Also, the confluence of waves can reflect specified measurable signal which describes maternal frequency and their parental overheads. That means we have a big pool of data only by sending a simple signal and interpretation of receiving reflection. On the basis of this hypothesis many data banks have been made in therapeutic Bioresonance texts which are known as the bible of Bioresonance therapists. While a specific frequency revealed for a disordered organ in an individual, using an effective wave can reorganize the abnormality or to force it up to self-repair. This is the basics of Bioresonance as an individualized diagnostic and therapeutic method. Although many diagnostic and therapeutic centers are providing these services to the people worldwide, the current epidemiology still has concerns about the reliability of this hypothesis.

KO1027

Personalized Medicine in Breast cancer: Where we are in practice?

Dr.Keivan Majidzadeh

Keivan Majidzadeh
Associate Professor of Medical Biotechnology

Abstract:
Breast Cancer is the most prevalent cancer among women worldwide. It is also the leading cause of cancer mortality around the world. In our country the situation is the same, the incidence is significantly less than western countries though. Meanwhile the mean age of patients is a decade lower than North American and European countries which implies to specific characteristics of the patients in our country.
BC patients are classified; based on their biomarker profiles; into different categories. This classification has had a great impact on the identification of risk, prediction of prognosis and response to therapy and also on survival of patients. Biomarkers are the cornerstone of personalized medicine and their role in guiding clinical decisions has got greater importance than the past.
Biomarker is the biologic or molecular condition that distinguishes one patient group from another. Biomarkers are classified into different groups including: risk categorization (eg, determination of germline mutations as a marker of susceptibility), screening, differential diagnosis, prognosis, prediction, or monitoring.
In this talk the present situation of using biomarkers in clinical practice of Breast Cancer is being discussed.

KO1028

Palliative care for cancer patients

Dr.Reza Malayeri

Reza Malayeri
Paliative Care Ward, Firoozgar Hospital, Tehran

Abstract:
It is well known that palliative care is a necessity in cancer patients, as early on, as the time of diagnosis. Palliative care should not be mistaken with end of life care. Palliative care for cancer patients means caring for patients from all aspects. Besides best medical treatment, patients receive adequate psychological, spiritual, social, nutritional care etc. The focus is on the patient, i.e. real personalized medicine.
Iran has a population of around 80 million people and, according to the official cancer registry, a yearly cancer incidence of around 100 thousand. We currently have around 8 active palliative care units for cancer patients and one palliative care ward in Iran, all run by charities. In these palliative care units, we have oncologists, palliative care specialists, pain specialists, psychologists, spiritual care specialists, social workers and dieticians. A total number of 3677 patients, ages between 16 and 94 (Median 61), of whom 3277 (89%) with a similar age distribution had a cancer diagnosis were referred to our palliative care unit in Firoozgar Hospital, which is run by the Ala Charity, in Tehran in the last two years. 1770 female (54%) and 1457 male (46%) cancer patients were referred. We have also a home care unit, supporting currently more than 200 patients monthly with palliative care at home.
Iran, like many other countries, needs many more palliative care units. As palliative care is not financially lucrative, charities play a major role in setting up, maintaining and expanding these units.

KO1029

Endocrinology and Precision Medicine

Dr. Mojtaba Malek

Mojtaba Malek
professor of internal medicine, Institute of Endocrinology and Metabolism, Iran University of Medical Sciences

Abstract:
Advancements in science and technology are changing the way we define disease, develop drugs, and prescribe treatments. The ability to predict the likely development of disease or appropriate response to therapy has been touted as a means to improve clinical outcome. Recently more personalized medicine products are available for patients than ever before. One in 5 FDA approvals in 2014 was for targeted therapies. An increasing number of treatments are personalized across a variety of therapeutic areas. About 6% of medication in endocrinology was for targeted therapies especially in thyroid cancer and osteoporosis. In the era of precision medicine, targeting the mutations driving cancer growth, rather than the tumor site itself, continues to be a successful approach for some patients. In the latest example, researchers found that treating metastatic thyroid cancer patients harboring a BRAF mutation with the targeted therapy. Also the evaluation of osteoporosis and fracture risk is moving from a risk stratification approach to a more individualized approach, in which an individual's absolute risk of fracture is evaluable as a constellation of the individual's environmental exposure and genetic makeup. In other field of endocrinology type 2 diabetes mellitus (T2DM) is recognized as a public health problem and increasingly prevalent illness. Despite medical advances in diabetes field, many people still suffer high rates of complications. Key elements of the guideline for diabetes care are based on evidence-based medicine approach and apply for population, not individuals. However, individualized care can improve diabetes management. Personalized medicine tries to find better prediction, prevention, and intervention for T2DM individuals. Precision medicine in diabetes refers to the utility of genomics data of a patient with diabetes to provide the most effective diagnosis strategies and treatment plans. Certain types of monogenic diabetes already present an excellent opportunity to practice personalized medicine. Proper genetic diagnosis and appropriate pharmacological treatment of these patients often prevent unnecessary insulin therapy, simplify and increase efficacy of treatment, and create opportunities for prediction and personalized treatment of diabetes in family members. In future building knowledge networks to store data and building cohorts of patient data for further investigation and updating research infrastructure help us to translating basic science into practice guidelines for clinicians and translating genetic testing results into meaningful patient results.

KO1030

Circulating tumor cells as a novel cellular biomarker in breast cancer

Dr.Sepideh Mansouri

Sepideh Mansouri
Recombinant Proteins Department, Breast Cancer Research Center, Motamed Cancer Institute, ACECR, Tehran, Iran

Abstract:
As the standard of care in primary breast cancer includes regular physical examinations and annual mammography, the micrometastasis cannot be detected during present patients' follow up. Cancer calls can spread through vessels not only in advanced breast cancer, but also in early ones. Cancer management is challenged by metastasis which is based on primary cell potential to escape from treatment strategies and spread through vessels. Circulating tumor cells, which carry certain tumor specific characteristics, have ability to invade extra cellular matrix, migrate in the blood vessels, escape from immunity system, and finally home in the specific target organs. Based on evidence, CTCs have prognostic impact which can predict the patient's response and survival. However, administration of CTCs as cellular biomarkers deals with issues such as technical difficulties in detecting and characterization of these cells which can affect the accuracy of the present tests. By means of technical improvement in CTCs characterization, there is a hope that they can be useful in personalized decision making for breast cancer patients.

KO1033

Recent update on “checkpoint inhibitors” for cancer immune therapy

Dr.Nazanin Mojtabavi

Mojtabavi Nazanin
Immunology department, Iran University of medical sciences

Abstract:
T cell exhaustion is a phenomenon that occurs during chronic antigen exposure and cancers. Exhausted T cells have dampened effector function and proliferative capacity, decreased production of inflammatory cytokines and over expression of inhibitory receptors which are known as checkpoints. Exhausted T cells are defective in controlling tumors, which causes the glory of cancer against immune system. Until now, various approaches to re- invigorate the immune system exist to attack the cancer cells. In recent years, basic, translational and clinical data have been integrated into checkpoint inhibitor development programs at many pharmaceutical and biotechnology companies. Production of this checkpoint inhibitors is an indispensable parts of the drug development process.

This lecture will focus on recent cancer treatment via inhibition of prominent candidate of immune check points such as PD1, PDL1, CTLA-4, GITRs which are enrolled in clinical trials for treatment of diverse types of cancer. In addition the advantage of combination therapy with check point inhibitors will be discussed.

KO1034

Guided management for Cancer

Dr. Seyed Akbar Moosavi

Seyed Akbar Moosavi
Iran University of Medical Sciences

Abstract:
Today cancer considered being a major killer in modern and developed countries throughout the world, and a major clinical dilemma in patient cares for health industries. Various challenges interfere with proper and effective care for the cancer patient as well as dealing with identifying the primary cause, diagnosis, prognosis, and selection of effective therapy against the cancer. There is no consistent algorism and pathways in solving those aforementioned problems. The National Comprehensive Cancer Network (NCCN) has developed evidence based guidelines for every cancer to resolve many obstacles facing the cancers. The NCCN guidelines describe various effective methods and algorisms for accurate diagnosis and prognosis based on initial physical examination followed by conventional and genetic lab tests, and also specific imaging analysis. Based on information provided by these identifying testing and images a comprehensive patient profile is made to start the treatment process. Nonetheless the profile is used to select a specific treatment that suit the patient's disease process. Moreover the drug dose will be tailored and assessed later for the patient to evaluate the treatment and the follow ups.

KO1035

Pharmacogenomic management of malignancies using Integrated Clinical Genomics (ICG)

Dr. Kazem Mosavizadeh

Golnaz Ensieh Kazemi-Sefat[1], Mohammad Keramatipour[2], Kaveh Kavousi[3], Saeed Talebi[4], Mohsen Razavi[5], Mohammad Vaezi[6], Abdolrahim Hazini[7], Kazem Mousavizadeh[1,8*]

1) Department of Molecular Medicine, Faculty of Advanced Technologies in Medicine, Iran University of Medical Sciences, Tehran, Iran
2) Department of Medical Genetics, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
3) Department of Bioinformatics, Institute of Biochemistry and Biophysics, University of Tehran, Tehran, Iran
4) Department of Genetics and Molecular Biology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran
5) Department of Gynecology Oncology, Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran
6) Hematology-Oncology and Stem Cell Transplantation Research Center, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran
7) Palliative Care center, Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran
8) Cellular and Molecular Research Center, Iran University of Medical Sciences, Tehran. Iran

Abstract:

Next Generation Sequencing (NGS) technology by massively parallel sequencing significantly have reduced the cost and increased the speed of sequencing the nucleic acids from different biological sources.

In 90 to 95 percent of malignancies, genetic mutations occur secondary to an environmental factors and in the remaining the mutations are due to inheritance. Variations in cancer genes (driver mutations), make them the golden aim of genome and transcriptome analysis by WGS/WES and RNA Seq in terms of integrated clinical genomics (ICG). The analysis lead to multi dimensional view of different alterations such as fusion genes that can be targeted by specific FDA approved anti-neoplastics drugs (Pharmacodynamic) so impact on the clinical decision making. In addition this data provides the required information that is related to the Pharmacokinetic of different types of drugs. Therefore pharmacogenomic management of malignancies may be facilitated significantly using ICG. Pharmacogenomics assess the role of genome on the drug response. It relates the personalized genetic features to the treatment response. This field evaluates the effect of acquired and inherited genetic variations to the drug response in patients by correlating single nucleotide variations and gene expressions to the pharmacokinetics and pharmacodynamics. The term pharmacogenomics and pharmacogenetics are often used interchangeably. However pharmacogenetics evaluates the effect of a single gene on a drug but the pharmacogenomics approach is usually genome wide and relates the effect of multiple genes on the drug response. Recently the U.S. Food and Drug Administration has approved Pembrolizumab for cancer treatment according to the particular genetic features in the first line treatment of solid malignancies. It seems FDA will gradually approve using drugs which are specific for genetic alterations independent of tumor types. Therefore in near future by decreasing the cost of NGS we hope that pharmacogenomic management using ICG to be an important part of personalized treatment of malignancies which has a potency to improve progression-free survival without enhancing the health care costs.

KO1036

A Novel Approach to the Nutrigenetics and Nutrigenomics of Breast Cancer

Dr. Azadeh Mottaghi

Azadeh Mottaghi

Assistant Professor of Nutrition
Research Center of Prevention of Cardiovascular Disease, Institute of Endocrinology and Metabolism, Iran University of Medical Sciences, Tehran, Iran

Abstract:
Breast cancer is the major cause of cancer death in women worldwide. However, several epidemiological studies have shown that incidence of this cancer is specifically higher in developed than in developing countries. Geographic variation, lifestyle habits and diet diversity can justify difference in incidence rate. Many of the changes that occur in the DNA methylation patterns like gene-specific promoter hypermethylation or hupomethylation which lead to gene silencing or activation, can be reversed and responsive to environmental factor such as diet. In addition to DNA methylation pattern, DNA methyltransferase (DNMTs) that catalyzing methylation reaction of DNA is important target for epigenetic chemoprevention. One of the strategies for cancer treatment is the use of DNMT inhibitors such as azacitidine and decitabine. However, the use of these drugs is not without side effects. For this reason using of some bioactive phytochemicals such as sulforphane (SFN) which present in cruciferous vegetables like broccoli, broccoli sprouts, cabbage and kale, especially when are used at low doses and within the range of physiological concentrations, seem to be safe. Several in vitro study have been demonstrated that SFN inhibits growth of phenotypically different breast cancer cells. Some chemoprotective mechanism presented to explain the effect SFN on inhibiting tumor cells growth are the repression of phase 1 detoxification enzymes and the induction of phase 2 enzymes, cell cycle arrest and apoptosis induction as well as inhibition of cell proliferation. In conclusion, it seems that SFN is novel chemopreventive agent that through indirect modulation of DNA methylation has role in epigenetic therapy of solid tumours along with synthetic drugs.

KO1037

Personalized medicine in BMT

Dr. Sayeh Parkhideh

Sayeh Parkhideh
Assistant professor of adult hematology and oncology, Shahid Beheshty University of medical sciences

Abstract:
HSCS and their transplantation has proved itself as an effective approach to treat different diseases.
From the very beginning HSC demonstrates the importance of individual/personal approach in all steps of the management of the disease.
Many disease specific transplant regimens are under development to improve transplant after HT.Depending on the disease and patient's status the source of the HSCS (autologus or allogenic) will be considered.
In allogenic BMT given the progress being made in GVHD biomarker identification, the clinical trial design will begin incorporating biomarkers.

KO1038

Circulating tumor DNA as an early marker of therapeutic in patients with metastatic colorectal cancer

Dr.Hossein Pashaiefar

Hossein Pashaiefar

Hematology, Oncology and Stem cell Transplantation Research Center, Tehran University of Medical Sciences, Tehran, Iran.

Abstract:

Colorectal cancer (CRC) is the third most common cancer and leading cause of cancer-related mortality in the world. Approximately half of CRC patients develop metastatic disease. Since the metastasis may be lethal, causing mass-impact and interfering with homeostasis, its development is a concern for clinicians and patients. Over the past decade, advances in systemic therapeutic options have improved outcomes of patients with metastatic CRC (mCRC). One important goal of treatment strategy of mCRC patients is to enhance survival while maintaining the life quality and avoiding unnecessary toxic impacts of an ineffective treatment. To achieve this point, the early assessment of therapeutic efficacy is a central aspect in the management strategy of patients. The gold standard for response assessment and treatment efficacy of CRC patients is the radiographic imaging. However, there are some limitations to its use. Recently, several attempts have been made to establish minimal or noninvasive biomarkers for evaluation of response to therapy.

Circulating tumor DNA (CtDNA), tumor-derived fragmented DNA, generally represents a small fraction (<1%) of the total circulating DNA. Recent studies have been shown that CRC patients had higher total concentration of circulating DNA compared with healthy people. Furthermore, patients with advanced or metastatic CRC had higher circulating DNA concentration compared with patients with localized CRC. It has additionally been demonstrated that a part of this circulating DNA is carrying specific tumor genetic alterations. The amount of tumor-derived DNA in the bloodstream was hence proposed as being a surrogate marker of monitoring tumor burden or response during treatment and tracking resistance and tailoring treatment.

KO1039

The importance of precision medicine for cancer patients

Dr. Ana Finzel Pérez

Ana Finzel Pérez
OncoDNA, Belgium

Abstract:
Every cancer case is unique. That means that even if two patients have the same diagnosis, the molecular make-up of their tumor will be distinct, and they would probably respond in a different manner to the same therapy. That's why, precision medicine should play a key role in cancer patient management.
OncoDNA has established during the last years a big evidence-based database and developed different tumor profiling solutions based on solid biopsies, liquid biopsies or a combination of both. According to the results of the patient profiling, we can predict sensitivity or resistance to approved or in development targeted therapies, chemotherapies, hormonal therapies and immunotherapies. Moreover, thanks to the use of liquid biopsies we are also able to monitor therapy efficacy and tumor relapse.

KO1040

Epigenetic modifications by dietary polyphenols in cancer

Dr. Seyedeh Tayebeh Rahideh

Seyedeh Tayebeh Rahideh
Assistant Professor, Department of Nutrition, School of Public Health, Iran University of Medical Sciences

Abstract:
Epigenetics describes heritable alterations of gene expression and chromatin organization without changes in DNA sequence. In mammals, epigenetic mechanisms include changes in DNA methylation, histone modifications and non-coding RNAs. Each year, tens of millions of people are diagnosed with cancer around the world, and more than half of the patients eventually die from it. Recent studies with various types of cancers revealed that the epigenetic modifications are associated with the food source corresponds to dietary phytochemicals. The chemopreventive potential of polyphenolic compounds in the recent years has clearly supported their health benefits, including anti-cancer properties. The effects of dietary polyphenols on epigenetic modifications may provide an effective strategy for reducing the health burden of cancer in humans. These dietary polyphenols have shown potential as DNA methyltransferase (DNMT) inhibitors, histone modifiers and vary miRNA level altering gene expression and restoring the expression of various tumor suppressor genes. For example, several studies have demonstrated that green tea polyphenols is a potent demethylating agent which inhibits enzymes involved in DNA methylation and is an effective histone modifying agent. This area of research requires more information on the relative potency of these effects of polyphenols alone and in combination with other drugs and natural products or dietary supplements. Apigenin, dietary plant flavonoid, exposure resulted in decrease expression of DNMT1, DNMT3A, DNMT3B and histone deacetylase (HDAC) 1–8 levels. Focusing on epigenetic pathways related cellular targets, SIRT1 and acetyl transferase p300 were reported to be the activated by Resveratrol. In conclusion, results from the studies indicate that the effects of polyphenols or bioactive food components on DNA methylation, miRNA expression histone methylation or chromatin remodeling complexes will contribute to cancer prevention and treatment.

KO1041

Genomic Diagnostics of Cancer

Prof. Olaf Riess

Olaf Riess
MD, Director Institute of Medical Genetics and Applied Genomics, Director Rare Disease Center Tübingen, University of Tübingen, Germany

Abstract:
Genomic diagnostics has become a major milestone in prediction and treatment of cancer. This is due to the steady decreasing prices of the recent "Next Generation Sequencing" technology allowing parallel analysis of hundreds of genes in a single patient, but also to the developments of new treatment approaches in cancer not responding to first line therapy.
About 10% of all cancers have a strong genetic background and are heritable cancers. Genetics has the responsibility to define these patients for better management of the patient commonly being interdisciplinary, and for advising family members. This goes far beyond the commonly BRCA1/2 testing in breast cancer and is more and more directed towards combination of different cancers in one family. About 100 inherited cancer genes are known which require special attention of the health care system. National and international networks have been formed to address these more complex prevention strategies and to define the true cancer risk for different organs in the respective families. However, genomic technologies today allow somatic mutation analysis of basically all genes in cancer tissue to predict response (resistance, susceptibility) to many newly developed drugs. Here genetics serves as companion diagnostics such as for melanoma, ovarian cancer, or lung cancer. These developments reach true individualized treatment strategies such as peptide vaccination against mutated proteins of a single tumor. In my talk I will give examples as well of cancer prediction and prevention as a general health strategy, but also for personalized cancer treatment.

KO1042

Personalized treatment in colon cancer

Dr. Leila Sadeghi

Leila Sadeghi
Hematologist , Medical Oncologist, Assisstant Professor of SBUM

Abstract:
Colon cancer is one of the most prevalent cancer worldwide. It is estimated that , CRC is responsible for over 200,000 deaths each year. Like many other cancer types , colon cancer is a very good candidates for personalized treatment , since it`s cancer cells uses many molecular alterations for proliferation and defencing against apoptosis .
It is so important to know that the purpose of precision medicine in oncology is not to classify cancers only by site of origin , but to define the genomic alterations in the cancer DNA sequencing .Personalized cancer treatment use so many molecular testing to identify which type of cancer with which specific cancer genome is good candidate for a special targeted therapy .Therefore we will have the opportunity of having a unique treatment based on specific mutation and other cancer related change in the DNA programming of the malignant clone. In this way of attacking cancer cells , normal cells can be unaffected , and we will have more specific treatment besides less toxicity.
Now our knowledge in studying molecular alteration in colorectal cancer is growing , and we do have many biomarkers for targeting , such as genetic mutations like KRAS and NRAS for anti EGFR , BRAF , PIK3CA, microsatellite instability high and may have more targets in near future.

KO1043

Personalized lung cancer treatment

Dr. Babak Salimi

Babak Salimi
Medical Oncologist and Hematologist

Abstract:
The identification of molecular subtypes of non-small-cell lung cancer has transformed the clinical management of this disease. This is best exemplified by the clinical success of targeting the EGFR or ALK with tyrosine kinase inhibitors in the front-line setting. Our ability to further improve patient outcomes with biomarker-based targeted therapies will depend on a more comprehensive genetic platform that can rationally interrogate the cancer genome of an individual patient. Novel technologies, including multiplex genotyping and next-generation sequencing are rapidly evolving and will soon challenge the oncologist with a wealth of genetic information for each patient. Although there are many barriers to overcome, the integration of these genetic platforms into clinical care has the potential to transform the management of lung cancer through improved molecular categorization, patient stratification, and drug development, thereby, improving clinical outcomes through personalized lung cancer medicine.

KO1044

Immunotherapy in colon cancer

Dr. Farhad Shahi

Farhad Shahi
Hematologist and Oncologist, MD, Tehran University of Medical Sciences

Abstract:
Immunotherapeutic approaches to cancer therapy are based upon the premise that the immune system plays a key role in surveillance and eradication of malignancy, and that tumors evolve ways to elude the immune system. Historically, mCRC was considered non-immunogenic, that is, incapable of inducing immune-mediated tumor destruction. However, the importance of the immune system in the biology of CRC is underscored by the finding that infiltration of the tumor by specific T cell immune infiltrates is highly correlated with better disease-free and overall survival at all tumor stages.
These data suggest that an immune response to specific tumor antigens might drive improved outcomes. However, most tumor-associated antigens in CRC, while expressed at higher levels within tumor, are also expressed in other tissues. As a result, the tolerance mechanisms that suppress the immune response to self-antigens to minimize autoimmune disease may also serve to suppress the immune response to these tumor antigens. Based upon data on the immunogenicity of mutated antigens in melanoma, it has been hypothesized that "neoantigens" generated from tumor-specific mutations of self-antigens within CRC may be recognized by the immune system as foreign and could therefore trigger an antitumor immune response.
Approximately 3.5 to 6.5 percent of stage IV CRCs are characterized as having high levels of microsatellite instability (MSI-H), which is the biologic footprint of deficiency in DNA mismatch repair enzymes (dMMR). Tumors that lack the mismatch repair mechanism harbor many more mutations (ie, they are hypermutated) than do tumors of the same type without such MMR defects, and as noted above, the neoantigens generated from mutations such as these have the potential to be recognized as "non-self" immunogenic antigens.
One option for treatment at progression for patients who have MSI-H/dMMR tumors is immunotherapy with an immune checkpoint inhibitor that targets the programmed death receptor-1 (PD-1; ie, nivolumab, pembrolizumab). In clinical trials, objective response rates with these two PD-1 inhibitors are 30 to 50 percent, and some responses are durable.
On May 23, 2017, the FDA granted accelerated approval to pembrolizumab for the treatment of patients with advanced MSI-H or dMMR mCRC that has progressed following conventional chemotherapy and in August 2017, the FDA extended the approval of nivolumab to MSI-H or dMMR mCRC that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan .
From Uptodate(online)
Systemic chemotherapy for metastatic colorectal cancer: Completed clinical trials

KO1045

Molecular pathology of gastric carcinoma

Dr. Amir Sheykholeslami

Amir Sheykholeslami

Abstract:
Gastric carcinoma (GC) is a biologically heterogeneous disease involving numerous genetic and epigenetic alterations. A very small proportion of GCs can be caused by a specific germ-line mutation of the E-cadherin gene (CDH1). Sporadic GC is developed through multistep processes that begin with Helicobacter pylori-induced atrophic gastritis. Epstein-Barr virus is another infectious cause of GC, and the above two infection-associated GCs are characterized by global CpG island methylation in the promoter region of cancer-related genes. Mutations of tumor protein p53 (TP53) and β-catenin (CTNNB1) genes occur early in the development of GC and contribute to gastric carcinogenesis. Furthermore, significant numbers of GCs show loss of Runx3 due to hemizygous deletion and hypermethylation of the promoter region. Aberrant Cdx2 expression has been shown in precancerous lesions as well as GC. However, it remains unclear whether Cdx2 plays an oncogenic role in gastric carcinogenesis. GC with microsatellite instability is also a well-defined subset exhibiting distinctive clinicopathologic features. Targeted therapy against GC with ERBB2 amplification recently improved the prognosis of patients with advanced GC. In addition, epigenetic changes in GC could be attractive targets for cancer treatment with modulators. A genome-wide search has been undertaken to identify novel methylation-silenced genes in GC, which will help us understand the overall molecular features of GC and further provide novel opportunities in the treatment of GC.

KO1046

Nutrigenomics of Omega 3 fatty acids

Dr. Farzad shidfar

Farzad shidfar
Head of School of Allied Medical Sciences, Iran University of Medical Sciences, Tehran, Iran

Abstract:
Dietary components can alter gene expression directly or indirectly, showing a beneficial or harmful physiological effect. ω-3 long-chain polyunsaturated fatty acids)LC-PUFAs(such as eicosapentaenoic acid (EPA, C22:5 ω -3) or docosahexaenoic acid)DHA, C22:6 ω -3) are synthesized de novo in the organism from the essential polyunsaturated fatty α-linolenic acid ω -3 (C18:3 ω -3) or acquired from the diet especially marine sources(fish,shrimp,oysters). Cellular function regulation by these FAs can occur at different levels such as modulation of signal transduction by the bioactive effect over the cell membranes and regulation of gene transcription, among others.It is well known that ω -3 long-chain polyunsaturated fatty acids (LC-PUFAs) control some key molecular cell mechanisms, resulting in a beneficial role in inflammatory diseases. Such mechanisms are complex and reflect the diversity of their functions, mainly as modulators of the dynamic properties of membranes, regulators of gene expression ,i.e regulation of sterol regulatory element-binding protein (SREBP), peroxisome proliferator-activated receptors (PPARs), carbohydrate response element-binding protein (ChREBP) and nuclear factor-kappa B (NFkB), mainly to regulate target gene transcription that encodes proteins involved in lipid and carbohydrate metabolism, thermogenesis and inflammatory processes (EPA and DHA are potential analgesics because they attenuate the acute inflammatory response, resulting in improvement of clinical outcomes ,it means that perioperative administration of enteral DHA may reduce the use, dose, and duration of buprenorphine analgesic requirements in neonates undergoing surgery; therefore, administration of DHA reduces
pain) and precursors of active mediators.

KO1047

Ethics in personalized Medicine

Reza Shirkoohi

Reza Shirkoohi
Cancer Biology Research Center, Cancer Institute, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran

Abstract:
In recent years high throughput technologies and enormous informatics analysis have been developed in the medical sciences. The huge amount of data generation by Next Generation Sequencing (NGS) is increasing the responsibility of data storing and analysis. In case of Whole Genome Sequencing (WGS) there will be huge amount of data with other information rather than a relationship with disease. These information publishing, could be very critical for patient (including behavioral, race, ethnicity and etc). On the other hand, different aspects of personalized medicine (PM) such as research, prevention, diagnosis and treatment could be considered in the ethical issues. Furthermore, bio and informatics material banking should also be included. The decision making for a disease based on the personalization is not only related to genotyping and genetic profiling but also the other mechanisms such as epigenetics and functional analysis. For example there are also tumor cell signaling analysis which is critical for decision making of PM in oncology. Other interfering mechanisms can make the decision fragile and the outcome could be totally different. In this case, two major goals for such procedure (increasing the quality of life and the duration of disease free period) will not be achieved. Considering the high cost of such services especially in low income countries, will increase the decision makers responsibility in such critical situations. Other point would be financial support for low income patients. In this case the high throughput technologies could only serve patients who are able to pay the expenses. The rapid rate of technological advances, huge amount of data gathering and expenses indicates the importance of ethics in PM.

KO1048

The treatment landscape for advanced prostate cancer is rapidly evolving

Dr. Mehdi Tabarraee

Mehdi Tabarraee

Assistant Professor, Adult Hematologist and oncologist in Shahid Beheshti University

The treatment landscape for advanced prostate cancer is rapidly evolving. In metastatic hormone-sensitive prostate cancer (mHSPC), the CHAARTED trial showed that androgen deprivation therapy (ADT) plus docetaxel increased overall. survival (OS) compared with ADT alone. Most recently, the STAMPEDE arm G and LATITUDE clinical trials demonstrated. That ADT plus abiraterone acetate (abiraterone hereafter) significantly improved outcomes in mHSPC compared with ADT alone. However, no biomarkers are routinely used in the clinic to predict response to these agents and personalize treatment selection. The most immediate need is for a biomarker to help select men for treatment with abiraterone vs docetaxel in the setting of newly diagnosed mHSPC. The HSD3B1 gene (OMIM 109715) encodes for the enzyme 3β-hydroxysteroid dehydrogenase-1 (3βHSD1), which catalyzes adrenal androgen precursors into dihydrotestosterone (DHT), the most potent androgen. A germline variant in HSD3B1 (1245A>C) renders 3βHSD1 resistant to polyubiquitination and subsequent proteosomal degradation, which significantly increases the half-life of the enzyme. the variant allele of HSD3B1 predicted shorter duration of response to ADT and a more rapid onset of castration-resistant prostate cancer (CRPC). If that is indeed true, the inherited HSD3B1 variant allele would have the potential to become the first biomarker to aid in clinical decision making in men with mHSPC choosing between abiraterone and docetaxel.

KO1049

Molecular signaling in nonfunctional pituitary adenoma

Dr. Tavakoli-Yaraki

Hamideh Akbari, Masoumeh Tavakoli-Yaraki
Institute of Endocrinology and Metabolism
Iran University of Medical sciences
Biochemistry Department school of medicine Iran University of medical sciences

Abstract:
It is well-illustrated that the promise of "personalized medicine," which is the tailoring of medical treatment to the individual characteristics, needs and preferences of each patient. Clinicians have long observed that patients with similar symptoms may have different illnesses, with different causes; and similarly, that medical interventions may work well in some patients with a disease but not in others with apparently the same disease. Clinically nonfunctioning pituitary adenomas range from those causing significant hypothalamic/pituitary dysfunction and visual field compromise to those being completely asymptomatic, detected either at autopsy or as incidental findings on imaging scans performed for other reasons (often referred to as pituitary incidentalomas). The molecular signaling pathways which are involved in the pathogenesis of nonfunctioning pituitary adenomas would shed light to the reality and complexity of disease and emphasis on the necessity of applying personalized medicine in new world of medication.

KO1050

Early Detection of Breast Cancer using a Panel of Circulating miRNA

Dr. Mehdi Totonchi

Hanieh Sadeghi[1], Bahareh Shayestepour[1], Arian Kamal[2], Andreas Keller[2], Ali Sharifi Zarchi[3], Hamid Gourabi[1,3], Habibollah Mahmoudzadeh[4], Ramesh Omranipour[4], Hamid Chitsaz[5], Marzieh Lashkari[4], Mehdi Totonchi[1,3*]

1) Department of Genetics, Reproductive Biomedicine Research Center, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran.
2) Clinical Bioinformatics, Saarland University, University Hospital Saarbrücken, Germany
3) Department of Stem Cells and Developmental Biology, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran.
4) Department of Radiation Oncology, Tehran University of Medical Sciences.
5) Computer Science Department, Colorado State University, Fort Collins, Colorado, 80523, USA.

Abstract:
Breast cancer (BC) is the most common type of cancer in women which leads to more than 500,000 deaths, annually. This type of cancer is a heterogeneous disease with diverse traits and sub-types reflected by various clinical outcomes. Therefore, identification of biomarkers that can accurately detect BC is a crucial step for early diagnosis of BC and choosing the optimal treatment for it. Circulating microRNAs have presented great potential as promising tools for BC detection. In this regard, we previously discovered a novel panel of circulating microRNAs based on the expression profiling analysis of 6017 patients with 14 cancer types including BC. Data from the cancer genome atlas (TCGA) database crossed with three large blood-based miRNome datasets from 5351 patients, resulted in identification of a list of microRNAs. Six out of nine microRNAs were subsequently validated in whole blood using qRT-PCR in a pilot study on 70 BC patients and a control group. The expression level of candidate microRNAs was higher in whole blood samples collected from patients with BC compared to controls. Notably, our panel successfully differentiated fibrocystic types from healthy individuals in a pilot study. These results demonstrated the potential of this promising combination of microRNAs for detection of BC at its earlier stages in clinical settings.

KO1052

Molecular biology of colorectal cancer & Antiepidermal growth factor receptor therapies

Dr.Marjan Yaghmaei

Marjan Yaghmaie
PhD in Medical Genetics, Assistant Professor
Hematology, Oncology and Stem Cell Transplantation Research center, Tehran University of Medical Sciences, Tehran, Iran
m-yaghmaie@sina.tums.ac.ir

Abstract:
Colorectal cancer (CRC) results from the progressive accumulation of genetic and epigenetic alterations that lead to the transformation of normal colonic epithelium to colon adenocarcinoma and can have different prognoses and different responses to treatment. The morphology of tumors and the pattern of molecular abnormalities vary depending on their anatomical location, with a probable gradual change in molecular characteristics between the right and left side of the bowel. There are thought to be at least three main mechanisms by which CRC occurs. The majority of cancers start as adenomas, which then undergo other mutational events such as loss of the adenomatous polyposis coli (APC) gene and p53 mutations and result in the chromosome instability (CIN) phenotype. In contrast, patients with Lynch syndrome (hereditary nonpolyposis CRC) have germline loss of DNA mismatch repair genes, most commonly MLH1 and MLH2. This results in the accumulation of DNA defects, predominantly in microsatellite areas and leads to the microsatellite instability high (MSI-high) phenotype. The Cancer Genome Atlas Network has recently published a comprehensive molecular characterization of CRC [Cancer Genome Atlas Network, 2012]. Specific signaling pathways or genes have been found to be commonly affected in CRC. Tumor heterogeneity means that it is challenging to elucidate the roles of individual mutations and poses significant challenges to personalized medicine. There may be significant differences not only within the primary tumor, but also between the primary tumor and metastases. Furthermore, anticancer treatment can affect tumor heterogeneity due to selection pressures. One of the major advances in the treatment of CRC has been the development of targeted therapies. Amongst the most well-established of these are the monoclonal antibodies cetuximab and panitumumab, which target the EGFR. Cetuximab has been shown to have efficacy both as monotherapy and in combination with chemotherapy for patients with pretreated metastatic CRC

KO1053

Personalized Medicine in Gastroenterology Disorders

Prof. Mohammad Reza Zali

Mohammad Reza Zali
Professor of Gastroenterology, Research Institute for Gastroenterology and Liver, Shahid Beheshti University of Medical Sciences

Abstract:
Medicine is now developing as personalized solutions for a particular patient's needs, and there is a cumulative attention to personalized medicine. Personalized medicine is an extensive field of healthcare subjects which is informed by each person`s unique clinical, genetic, genomic, and environmental information. Considerable progresses have taken place in biomedical science to make personalized medicine a feasible option. The translation of human genome information to clinical medicine needs answering three following questions: Which molecular factors are involved in the pathogenesis of a particular disease? Which individuals or patients will develop a particular disease? How a therapeutic regimen is developed that can be personalized to an individual with a unique biology? In gastroenterology, personalized medicine is mostly applied for management inflammatory bowel diseases, gastrointestinal malignancies, H. pylori associated diseases, and many other diseases. Study of microbioma structures in different people is an attractive field in personalized medicine. Pathogenesis and manifestation of gastroenterology and liver diseases are a direct result of the interaction of the human genome and the bacterial genome. In this regards, the characteristics of the host`s intestinal microflora is tremendously significant when beginning treatment of gastroenterology diseases because composition of gut microflora varies between different individuals. Applications of personalized medicine for the gastroenterology disorders are including: employment of novel therapeutic approaches, optimization of therapy, study of drug toxicity, development of efficient biomarkers for early detection of disease, identification of markers of response to therapy and study of virulency.

KO1054

Probiotics and suppression of cancer

Dr.Mina Zarati

Mitra Zarrati
Zarrati_ms@yahoo.com

Abstract:
Probiotics are 'live microorganisms that, when administered in adequate amounts, confer a health benefit on the host'. The popularity of probiotics has expanded exponentially recently, because of their health-promoting effects and their abilities to prevent or treat different diseases, including some types of cancers. These include microbiota modulation, immune modulation, reduced bacterial translocation, enhanced gut barrier function, anti-inflammatory and antipathogenic activity, with effects on reducing tumor formation and metastasis. The composition of gut microbiota has been associated with colon cancer risk. For instance, Fusobacterium nucleatum, Streptococcus gallolyticus and more recently Providencia have been found in human colorectal cancer tumors.
Concerning the mechanism of action, some studies reported that such suppressive effect was dependent on short chain fatty acids (SCFAs) production of probiotics. Apart from SCFA, tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) that induced apoptosis of tumors was also found to be upregulated by Lactobacillus casei ATCC 393, and the increased protein expression of TRAIL in tumors was associated with decreased tumor incidence in mice.
In most studies, tumors were either induced through administration of carcinogens, for example 1,2-dimethylhydrazine dihydrochloride or azoxymethane (AOM), or introduced through injection of tumor cells.Previous in-vitro studies have shown that proliferation of breast cancer cells, Michigan Cancer Foundation-7 (MCF-7), was inhibited by different isolated probiotics strain/supernatant from probiotic cultures. It was also reported that live Enterococcus faecalis and Staphylococcus hominis isolated from breast milk, as well as heat-killed cells and cytoplasmic fractions, caused cytotoxicity through the induction of apoptosis and G0/G1 phase cell cycle arrest Apart from the involvement of immune system, hypoxia-inducible factor (HIF) pathway that is associated with breast cancer was also reported to be suppressed by Lactobacillus cultures supernatant eight different Lactobacillus strains exerted the anti-proliferative effect on leukemia cells. Most of the heat-killed bacteria, cell wall extract and genomic DNA of the selected strains showed inhibition toward leukemia cells.
Administration of Bacteroides fragilis restored the CTLA-4 blockade effect, by affecting the interleukin (IL)-12- dependent Th1 immune response. Researchers reported a greater anti-melanoma effect of combined treatment of Bifidobacterium and programmed cell death-ligand 1 (PD-L1) blockade therapy, when compared with individual treatment.
Bifidobacterium species were suggested to exhibit protective effects through the activation of dendritic cells and thus the enhancement of antitumor immune response. Stimulation of T-cell responses was involved as revealed by the increased level of tumor-specific and antigen-specific T cells level.
The probiotics mixture reduced Th17 cells frequency and its recruitment to tumor, leading to a decreased production of IL-17. As IL-17A produced from Th17 favors angiogenesis, reduction of Th17 and IL-17 level may contribute to inhibition of cancer progression.
Human clinical trials of the application of probiotics as bio therapeutics against cancer are still lacking. Extensive clinical trials are necessary to identify potential strains, dosages and administration regimes for specific types and stages of cancer.

The International Personalized Medicine Congress of Iran

Oral Presenters

O002

Personalized Medicine in Pediatric Cancer

Dr.Amir Abbas Hedayati-Asl

Amir Abbas Hedayati-Asl

Ped. Hematologist Oncologist /BMT
Tehran University of Medical Sciences, HORC-SCT & Royan Institute
Cancer Personalized Medicine Program
Stem Cell Biology and Technology Department

Abstract:

The maturation of genomic technologies has enabled new discoveries in disease pathogenesis as well as new approaches to patient care. For most of its 70-year history, systemic cancer treatment has relied on drugs marginally more toxic to malignant cells than to normal tissues. Molecular markers to predict benefit or understand therapeutic resistance in the clinic have usually been lacking.

In pediatric oncology, patients may now receive individualized genomic analysis to identify molecular aberrations of relevance for diagnosis and/or treatment. Several recent clinical studies have begun to explore the feasibility and utility of genomics-driven precision medicine. Precision medicine is broadly defined by the National Institutes of Health as "an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person." We review the major developments in this field, discuss current limitations, and explore aspects of the clinical implementation of precision medicine, which lack consensus. Leading international researchers and pediatric cancer advocates will discuss opportunities and gaps in the research in 4 main tumor types: Brain cancers, Leukemia, Embryonal tumors, Sarcomas.

We discuss ongoing scientific efforts in this arena, which may yield future clinical applications. Precision medicine in pediatric oncology drug development: the right to accelerate innovation for children and adolescents with cancer and work together and re-invent partnerships. The goals of precision medicine in pediatric oncology increase genomics-based clinical and preclinical studies of cancer treatment: Expand genomics-based clinical trials, understand & overcome resistance to targeted drugs; drug combinations and build repository of patient-derived pre-clinical models for evaluating targeted therapeutics, create national cancer database to integrate genomic information with clinical response and outcome.

O005

Rare genetic variants in DNA repair genes in BRCA1 mutation carriers with early and late age at onset of breast cancer

Ilnaz Sepahi

Ilnaz Sepahi[1]*, Ulrike Faust[1], Marc Sturm[1], Kristin Bosse[1], Martin Kehrer[1], Tilman Heinrich, Kathrin Grundman-Hauser[1], Peter Bauer[1,2], Stephan Ossowski[1,3,4], Hana Susak[3,4], Raymonda Varon-Mateeva[5], Evelin Schröck[6], Dieter Niederacher[7], Bernd Auber[8] , Christian Sutter[9], Norbert Arnold[10], Eric Hahnen[11], Bernd Dworniczak[12], Shan Wang-Gorke[13], Andrea Gehrig[14], Bernhard H.F. Weber[15], Christoph Engel[16], Johannes Lemke[17] , Hoa Huu Phuc Nguyen[1], Olaf Riess[1], Christopher Schroeder[1]

1) Institute of Medical Genetics and Applied Genomics, Tübingen, Germany
2) CENTOGENE AG, Rostock, Germany
3) Centre for Genomic Regulation (CRG), The Barcelona Institute of Science and Technology, Barcelona, Spain
4) Universitat Pompeu Fabra (UPF), Barcelona, Spain
5) Institute of Medical and Human Genetics, Charité Universitätsmedizin Berlin, Berlin, Germany
6) Institute for Clinical Genetics, Dresden, Germany
7) Department of Obstetrics and Gynaecology, Düsseldorf, Germany
8) Institute of Human Genetics, Hannover Medical School, Hannover, Germany
9) Institute of Human Genetics, University Hospital Heidelberg, Heidelberg, Germany
10) Department of Gynaecology and Obstetrics and Institute of Clinical Molecular Biology, University Hospital of Schleswig-Holstein, Christian-Albrechts-University of Kiel, Kiel, Germany
11) Centre for Hereditary Breast and Ovarian Cancer, University of Cologne and University Hospital Cologne, Cologne, Germany
12) Institute of Human Genetics, Münster, Germany
13) Department of Gynaecology and Obstetrics, University Hospital Ulm, Ulm, Germany
14) Centre of Familial Breast and Ovarian Cancer, Department of Medical Genetics, Institute of Human Genetics, University Würzburg, Würzburg, Germany
15) Institute of Human Genetics, University of Regensburg, Germany
16) Institute for Medical Informatics, Statistics and Epidemiology, University of Leipzig, Germany
17) Institute of Human Genetics, University of Leipzig Hospitals and Clinics, Leipzig, Germany
* Corresponding author: Ilnaz Sepahi - Ilnaz.Sepahi@med.uni-tuebingen.de

Abstract:
Breast cancer is one of the major causes of cancer death among women with almost 31% heritability. Women carrying a mutation in BRCA1 have 57-65% risk of developing breast cancer by age 70. The lifetime risk varies between families and even within affected individuals of the same family. To find the cause for this variability in age at onset (AAO), we investigated the role of rare variants in different DNA-repair pathways in BRCA1 mutation carriers. DNAs were obtained from 139 carriers of BRCA1 mutation and either AAO below 35 (Early AAO cohort) or AAO above 60 (Late AAO cohort). Germline mutations in 311 DNA-repair genes were investigated by Next generation sequencing, using a customized sequencing panel. Forty-two truncating variants were found in 36 DNA-repair genes from different pathways. 25 patients in early AAO cohort (34.2 %; 95 %-CI 23.5 % - 46.3 %) carried at least one truncating variant compared to 18 women of the late AAO cohort (27.3 %; 95%-CI 17.0 % to 39.6 %). Germline DNA repair mutations load did not differ between the two cohorts (odds ratio: 1.4; 95 %-CI 0.7 to 2.9; p-value = 0.46). Additional truncating variants in DNA-repair genes did not explain the differences in AAO in this study. Further studies and larger cohorts are needed to further clarify the role of DNA-repair gene mutations on the age at onset among BRCA mutation carriers.

Keywords:
Hereditary Breast cancer, DNA-repair, Age at onset, Next Generation Sequencing, BRCA1, extreme phenotypes

O006

Mechanistic studies on ribonucleotide reductase regulation and DNA damage response-application in cancer research

Dr.Reza Rofougaran

Reza Rofougaran, PhD.
Institute of clinical neuroscience, Norrlands university hospital, Umeå, Sweden - rofougaranreza@yahoo.com

Abstract:
Targeting and damaging the DNA have been extensively used as an anti-cancer therapy in clinics. Nucleoside analogs such as gemcitabine diphosphate and clofarabine nucleotides target the large subunit of ribonucleotide reductase (RNR). This enzyme is one of the key enzyme that has been targeted for cancer treatment and is crucial for DNA replication, maintenance of a balanced dNTP pools and DNA repair. The fidelity of DNA replication requires an appropriate balance of dNTPs. DNA replication stress (RS) can be defined as incomplete single-stranded DNA, leading to either stalling, collapse of the replication fork or its slow replication progression. Many factors such as decrease in dNTP pools after treatment with ribonucletide reductase inhibitors such as hydroxyurea and gemcitabine contribute to RS.
The aim of the project was to investigate if there is any correlation between allosteric regulation of this enzyme and genomic stability (dNTP pool imbalance). In Our study, by using site-directed mutagenesis technique, we created a mutation in loop2 in the large subunit of RNR (Y285A) and after purification of the protein, the allosteric regulation of the Saccharomyces cerevisiae RNR was studied.
The results showed that the RNR Y285A activity has been reduced 3.07-fold and 12.3-fold in the presence of GDP and CDP, respectively in comparison with the wildtype RNR activity.
The consequence of Y285A mutation and dNTP imbalanced on DNA replication will be discussed.
In recent years, much effort has been put on the discovery and development of compounds that would exploit defects in DNA repair in cancer cells such as ATM and ATR inhibitors. Inhibition of ATR, which would normally keep non-deleterious levels of RS, induces intolerable RS levels for cancer cells.
The kinase ATR is activated by RPA-coated single-stranded DNA generated at aberrant replicative structures and resected double strand breaks. While many hundred candidate ATR substrates have been identified, the essential role of ATR in the replicative stress response has impeded the study of ATR kinase-dependent signalling. Using recently developed selective drugs, we show that ATR inhibition has a significantly more potent effect than ATM inhibition on ionizing radiation (IR)-mediated cell killing. Transient ATR inhibition for a short interval after IR has long-term consequences that include an accumulation of RPA foci and a total abrogation of Chk1 S345 phosphorylation. We show that ATR kinase activity in G1 phase cells is important for survival after IR and that ATR colocalizes with RPA in the absence of detectable RPA S4/8 phosphorylation. Our data reveal that, unexpectedly, ATR kinase inhibitors may be more potent cellular radiosensitizers than ATM kinase inhibitors, and that this is associated with a novel role for ATR in G1 phase cells. This will be very important role in the cancer field and might be used as an anti-cancer therapy in clinics.

Keywords:
DNA, anti-cancer therapy , DNA replication stress, ribonucleotide reductase

O009

Thwarting PTEN Expression by siRNA Augments HL-60 Cell Differentiation to Neutrophil-Like Cells by DMSO and ATRA.

Dr. Shahram Teimourian

Shahram Teimourian , Ehsan Moghanloo

Department of medical genetics Iran University of medical sciences Tehran Iran

Abstract:

Abnormal cell differentiation, in particular suppression of terminal cell differentiation, exists in all tumors. Therapeutic interventions to restore terminal differentiation ("differentiation therapy") are a very attractive way to treat cancer, especially leukemia. A variety of chemicals stimulates differentiation of leukemic cells, such as dimethyl sulfoxide (DMSO) and all-trans retinoic acid (ATRA). Tumor suppressor genes have a vital role in the gateway to terminal cell differentiation. In this study, we inhibited PTEN tumor suppressor gene expression by siRNA to investigate the effect of potentiating cell survival and inhibiting apoptosis on HL-60 cell differentiation by DMSO and ATRA. Our results show that PTEN siRNA increases HL-60 cell differentiation in the presence of DMSO and ATRA. At the same time, the presence of siRNA hampers accumulation of apoptotic cells during incubation. Our study suggests that manipulation of PTEN could hold promise for enhancing efficacy of differentiation therapy of acute myelogenous leukemia.

Keywords:

pten ,down regulation ,differentiation therapy

O020

Autologous Targeted Exosomes as a Drug Delivery System

Dr. Hosna Gomari

Hosna Gomari[1]*, Mehdi Forouzandeh Moghadam[1], Masoud Soleimani[2]

1) Tarbiat Modares University Medical Biotechnology group, Faculty of Medical Science, Tehran, Iran.
2) Tarbiat Modares University Hematology group, Faculty of Medical Science, Tehran, Iran.
* Mehdi Forouzandeh Moghadam - foroz@modares.ac.ir

Abstract:
Introduction: Exosomes are small (30 to 100 nm) membrane-bound particles that are released from many cell types. Like liposomes, they can be used as therapeutic drugs and it can be targeted to specific tissue by membrane modifications. Exosome from Mesenchymal Stem Cells (MSCs) have some advantages, MSCs have easy accessible source, and transplantation have been shown to be safe in numerous clinical trials.
Materials & methods: Exosomes which produce by transduced MSCs were purified by exosinp® kit. Doxorubicin was loaded in exosomes by electroporation. Her2+ cell line was treated by dox (doxorubicin) loading exosomes. Binding of targeted exosomes to HER2+ cells relative to HER2- cells were assessed by flow cytometry. Cytotoxicity of loaded exosome were measured by MTT.
Results: We produced Exosomes containing targeted protein on their surface, binding of labeled exosomes were quantified by flow cytometry, which was bound to HER2+ cells 56% and 1.6% to HER2- cells. Cytotoxicity of exosomes-loaded and free dox were compared by MTT assay and there was no significant differences in their results.
Conclusion: our results represented that, exosomes derived from engineering cells can be used as a targeted delivery systems, since they can preferentially enter HER2+ cell lines relative to HER2- cells. Furthermore, there is no significant differences in toxicity of exo-DOX and free DOX neither in BT-474 nor MDA-MB231 which indicated that encapsulation has no effect on DOX cytotoxicity but can reduce side-effect of it by decreasing in systemic absorption.

Keywords:
Targeted exosomes, Drug Delivery, Mesenchymal Stem Cells, Her2+, Doxorubicin

O021

Personalized Cancer Medicine: a Future Direction of Personal Genomics

Dr. Ehsan Ghayoor Karimiani

Ehsan Ghayoor Karimiani [1,2*]

1) Razavi Cancer Research Center, Razavi Hospital, Imam Reza International University, Mashhad, Iran
2) Innovative Medical Research Center, Faculty of Medicine, Mashhad Branch, Islamic Azad University, Mashhad, Iran
* Ehsan Ghayoor Karimiani - ghayoure@mums.ac.ir

Abstract:
Personalized medicine is significantly changing the fundamentals of healthcare. Genetic diagnostic tests are used in various parts of medicine from initial screening to the diagnosis and finally treatment. Investigations in fields of drug development indicate that oncology may lead other therapeutic areas in the number of targeted therapies on the marketplace as well as in the pipeline, expecting that within a few years, all oncology medications will have a related diagnosis. It has been shown that personal genomics will influence other important therapeutic areas, including the clinical decision making. In conclusion, personalized medicine is just getting started for hematology and respiratory medical therapies, as well as oncology.

Keywords:
Individualized Medicine; Genomics

O027

What are essential dimensions of personalized medicine which should be considered in policy making? A comparative study

Zeynab Foroughi

Zeynab Foroughi [1]*, Asra Asgharzadeh[2], Mahnaz Afshari[3]

1) Student Research Committee, School of Health Management and information Sciences Branch, Iran University of Medical Sciences, Tehran, Iran
2) School of Health Management and information Sciences Branch, Iran University of Medical Sciences, Tehran, Iran
3) School of Health Management and information Sciences Branch, Iran University of Medical Sciences, Tehran, Iran
* Corresponding author - foroughi.z@tak.iums.ac.ir

Abstract:
Implementation of personalized medicine without considering its challenges in different aspects will be resulted in imposing a lot of expenses to the health system and patients. Therefore, policymakers should investigate implementation of this approach from multiple aspects. This study present essential steps in investigating, promoting and legislation for transforming and adjusting personalized medicine in Iranian's context, considering institutions and different country's frameworks. This study is a comparative study between different frameworks of policymaking in personalized medicine. we detect 16 dimension that we should be considered in policy making for personalized medicine including: Creating required legislative authority, Guidelines for assessment and approval of PM medication, Educating healthcare providers, Developing ICT, Compliance with ethical issues, Create conditions for conducting research (such as HTA), Clinical and Analytical Validation of Biomarkers, Patients privacy and Personal Data Protection, Valuation of personalized medicine services, Developing and financing of required researches, Creating bio banks, Creating personalized medicine coalition, Creating new reimbursement mechanisms, Informing and participation of patients, Creating an integrated Patient centres approach, Providing required diagnostic equipment. in order to implementing personalized medicine in Iran we need to an integrated health system an creating changes in different aspects of it, trough coordination between institutions and organizations to informing and Create acceptance in society .So, it seeming that implementation of this strategy in Iran is time-consuming process and need to cooperating between different sectors. Implementation of personalized medicine only by relying on existing knowledge in country can cause a lot of harm to the health system and patients from financial, moral and legal issues.

Keywords:
Personalized Medicine, Policy making, Comparative study

O035

Assessment of micronuclei frequency in the peripheral blood lymphocytes in patients with gastric cancer before and after chemotherapy treatment

Ghazaleh Kamrani

Ghazaleh Kamrani[1], Bahareh Abbasi[2], Aziz Mahmoudzadeh[3]

1) National Institute of Genetic Engineering and Biotechnology, Shahrak-e Pajoohesh, km 15, Tehran - Karaj Highway, Tehran, Iran
2) National Institute of Genetic Engineering and Biotechnology, Shahrak-e Pajoohesh, km 15, Tehran - Karaj Highway, Tehran, Iran
3Department of Bioscience and Biotechnology, Malek-Ashtar University of Technology- Tehran, Iran
b.abbasi@nigeb.ac.ir

Abstract:
Cancer is one of the leading causes of illness and mortality in the world. There are different ways to treat cancer, the most common being chemotherapy and radiotherapy. On a positive note, these treatments produce some fatal chromosomal damages in tumour cells, but they also produce some chromosomal damages in healthy cells with long-term side effects. Some of these mutations can lead to a double-strand break in the to rejoin the daughter nuclei and turning into micronuclei (MN).
Previous researches, using cytogenetical studies, have proven that there is a specific relationship between the frequency of MN formation in the peripheral blood of healthy subjects and the possibility of cancer incidence. Therefore, it can be concluded that cytogenetical studies such as Cytokinesis Block Micronucleus assay (CBMN) can help cancer prediction and study of treatment caused complications.

In this study, blood samples of 25 gastric cancer patients undergoing chemotherapy treatment, were extracted before and after treatment and cultured in a complete culture medium (FBS 10%), with 200 microliters of PHA, for 44-45 hours in a 37˚C incubator. Then, 50 microliters of cytochalasin-B were added and the samples were left for a further 27 hours. At the 72nd hour, the cells were taken to the harvesting stage of the test. Finally, 1000 bi-nucleated cells were counted under microscope in order to find the amounts of micronuclei.

The average numbers of micronuclei, before and after treatment, was 310.76 with a standard deviation of 76.44 in 1000 lymphocytes. Also, the average survival rate was 13.56 months with a standard deviation of 2.21 months. It is also understood that patient's gender and age did not have a significant effect on MN frequency and life expectancy. ($P<0.05$)

This research shows that MN frequency has increased significantly after treatment. Also, it is noticeable from the results that the survival rate in different age and gender groups are under the influence of MN frequency; as the MN amount increases, the patient's life expectancy decreases.

Keywords:
Micronuclei- Lymphocyte- Peripheral blood- Gastric cancer- Chemotherapy.

O037

Prediction of drug sensitivity in AML subtypes in response to Mitoxantrone from global gene expression, an impact on personalized cancer chemotherapy

Farzaneh Mohamadi Farsani

Farzaneh Mohamadi Farsani, Mohamad Reza Ganjalikhany, Sadeq Vallian
University of Isfahan, Department of Biology, Faculty of Sciences, University of Isfahan, Isfahan, Iran
svallian@sci.ui.ac.ir

Abstract:
Introduction: Acute myelogenous leukemia (AML) is the most common acute leukemia affecting adults, and its incidence increases with age. A combination treatment with an anthracycline, combined with cytarabine (ara-C), has been the cornerstone of AML treatment since the 1960s.

The goal of the study: In line with personalized cancer chemotherapy, in the current study, using computational methods, possible drug sensitivity of AML subtypes to Mitoxantrone was predicted through gene expression and phylogenic analysis. Moreover, biological pathways related to drug resistance of AML cells to Mitoxantrone were investigated.

Methods: A global gene expression dataset from cells sensitive to Mitoxantrone and cells with resistance to this drug with the accession number of GSE48876 was obtained from the gene expression omnibus (GEO) database. Expression data of AML subtypes were also obtained from GEO with the accession number of GSE59808. The CEL files were normalized and summarized with RMA method. Differential gene expression analyses for genes in sensitive and resistance cells were performed using linear regression models in the Limma R package. For the phylogenetic tree construction, we only considered genes that show significant differences (determined with a one-way ANOVA) in their expression profiles. To perform the prediction of drug sensitivity in AML subtypes, we included expression data of sensitive cell as an out group for the phylogenetic tree construction. Pairwise distances of the cancer subtypes were computed with the Pearson Correlation Distance. The phylogenetic tree was constructed with Fitch-Margoliash methodand visualized with Dendroscope.

Results and Discussion: The results of phylogenetic studies showed that M0 and M7 subtypes of AML were placed closer to sensitive cell that others. With the Pearson Correlation Distance of zero from sensitive cells, we cloud consider M0 and M7 subtypes as sensitive types to Mitoxantrone. On the other hand, the phylogeny ranks the AML subtypes according to their dissimilarity from sensitive cell as M6, M1, M2, M3, M4 and M5. Moreover, the study showed that Insulin and Neurotrophin signaling pathways were the most important pathways were significantly affected by differential expressed genes in AML resistance cells to Mitoxantrone.

Conclusion: The results of this study could help prediction of the associated drug response, which could improve the efficiency of chemotherapy, and may improve cancer treatment.

Keywords:
Personalized cancer chemotherapy, Gene expression, AML subtypes, Drug sensitivity, Mitoxantrone

O052

Altered expression of TGF-beta signaling pathway components contributes to acute myeloid leukemia

Mohammad Hossein Mohammadi

Mohieddin Barzegar, Mehdi Allahbakhshian Farsani, Naser Shagerdi Esmaiele, Mohammad Hossein Mohammadi*

Laboratory hematology and blood banking, school of allied medical science, Shahid Beheshti University of Medical Sciences, Tehran, Iran
HSCT research center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
* Corresponding author - mohamad.mohamadi2@gmail.com

Abstract:
TGFβ signaling pathway is a crucial element with tumor suppressive effects, which its malfunction may lead to tumor formation. AML is a heterogeneous disorder caused by defective differentiation and enhanced proliferation in white blood cells and their precursors in the blood and bone marrow. In this study we measured gene expression levels of TGFβ, TGFβRII, smad3 and smad7 in peripheral blood and bone marrow samples of acute myeloid leukemia patients.
Methods & materials:
Peripheral blood & bone marrow samples of 93 newly diagnosed AML patients & 13 healthy subjects as control group were examined. The gene expression of TGFβ, TGFβRII, smad3 and smad7 were examined by Real time PCR (polymerase chain reaction). We used SPSS statistical software release 16.0 for analysis between different groups.
Results:
Expression levels of TGFβRII & smad3 were significantly increased in AML group versus control group. Also a significant decrease was observed in smad7 expression in AML patients compared with control group. There was no significant change in TGFβ expression between the two groups.
Conclusion:
According to upregulation of TGFβRII and smad3 and downregulation of smad7, it seems TGFβ signaling pathway is over-activated in AML patients, which suggests in despite of conventional role of TGF-b in normal cell cycle, it could be controversial role in the leukomogenesis of these patients.

Keywords:
Acute myeloid leukemia, TGFβ, signaling pathway

O056

Targeting the core regulatory network of stemness in an in vitro AML model using a GRN approach

Mahsa Mohammadi

Mahsa Mohammadi[1,2], Amirabbas Hedayati asl[2], Marzieh Ebrahimi[2], Mehdi Totonchi[2,3*]

1) Department of Stem Cells and developmental biology, University of Science and Culture, ACECR, Tehran, Iran
2) Department of Stem Cells and Developmental Biology, Cell Science Research Center, Royan Institute for Stem Cell Biologand Technology, ACECR, Tehran, Iran
3) Department of Genetics, Reproductive Biomedicine Research Center, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran.
*Corresponding Author's E-mail - m.totonchi@royaninstitute.org

Abstract:
Recent advances in hemato-oncology research have provided the chance to construct more personalized and pathophysiology-targeted therapeutic strategies. Despite the use of vigorous chemotherapy, relapse after remission and refractoriness to induction chemotherapy remain as the most common therapeutic failures in acute myelogenous leukemia (AML). It seems that a rare population of cells called Leukemia stem cells (LSCs), are responsible for initiating therapy resistance and relapse. Therefore, in this study we aimed to identify a precise list of biomarkers and target genes, which may play an effective role in targeting these cells. Gene Regulatory Network (GRN) is an adequate bioinformatics tool used in mapping gene interactions and also, pinpointing key genes which may regulate the stemness core in LSCs. In this study, our aim was to identify key genes which may be regulating the stemness core in LSCs.
In this study, 4 main steps were preformed: 1) Data collection: a data set of 495 Gene expression profiles (GSE76009) was obtained from GEO database. 2) Differentially expression analysis was performed between two defined groups of LSC+ and LSC- using limma package in R Software (3.4.2 version) with the following cut off; FC1.3, Adj.p-val < 0.05. 3) Network Reconstruction was conducted using ARACNE algorithm and Cytoscape software.4) Network analysis, in this stage hub genes were attained and confirmed in literature. Using this bioinformatics approach, we were able to attain a list of candidate genes which may have a significant role in regulating the stemness core in LSCs.

Keywords:
Personalized medicine, AML, Leukemia stemcells, Bioinformatics, Gene regulatory network

O057

Hematopoietic Differentiation of Induced Pluripotent Stem Cells (iPSCs) derived from Glioblastoma Cell Lines

Mousa Vatanmakanian

Mousa Vatanmakanian[1], Gholamreza Khamisipour[2], Masoud Soleimani[3], Shaban Alizadeh [1*]

1) Department Hematology, Faculty of Allied Medicine, Tehran University of Medical Sciences, Tehran, Iran.
2) Department Hematology, Faculty of Allied Medicine, Bushehr University of Medical Sciences, Bushehr, Iran.
3) Department Hematology, Faculty of Medicine, Tarbiat Modares University, Tehran, Iran.
* Alizadeh1982@gmail.com

Abstract:
Establishment of pluripotent stem cells provides a comprehensive model to study early hematopoietic development and has emerged as a powerful research tool to explore regenerative medicine. Owing to a shortage of donors and a limited number of the cells, hematopoietic cell induction from pluripotent stem cells has been regarded as an alternative source of hematopoietic stem cells (HSCs) and mature hematopoietic cells for intended therapeutic purposes. Generation of induced pluripotent stem cells (iPSCs) has been described as a powerful method to dedifferentiate the specialized cells to pluripotency. Particularly, the generation of induced pluripotent cancer cells (iPC) allows us to access a valuable experimental platform in order to mimic oncogenesis process and harbours a great potential regarding drug screening as well as differentiation studies and personalized medicine; however, obtaining iPCs is encountered to several barriers. To help overcome this difficulty in the iPC generation we have tried to set up an optimized method to generate iPC from in vitro transformed cell lines representing the aggressive form of brain tumor-glioblastoma- and to understand the potential barriers ahead of efficient generation of iPCs. Our findings confirmed a resistant identity of cancer cells to achieve the pluripotency markers. Furthermore, besides designing technical tricks to obviate the barriers ahead of iPC generation, we have suggested using the small molecule PD98059 to enhance the efficiency of iPC generation from glioblastoma cell lines. Our data also confirmed that while T653 cell line harbouring an overactive form of Ras oncogene reprogram into iPC cells the activity of oncoprotein Ras is significantly suppressed, a down-regulation which is sustained following the hematopoietic differentiation. Further studies are required to standardize the methods of iPC cell generation and differentiation for future regenerative medicine.

Keywords:
Hematopoietic differentiation, Induced pluripotent cancer cells, Glioblastoma

O058

The Effects of Anti-angiogenesis on Enoxaparin Cutaneous Emulsion on Induced Breast Cancer in Female Rats

Mona Bolandpayeh

Bolandpayeh M[1]*, Hassanpour Ezzati M[2] , Mousavi Z[3]

1) Department of Pharmacology& Toxicology, Faculty of Pharmacy, Pharmaceutical Branch ,Islamic Azad University, Tehran, Iran.(IAUPS)
2) Department of Physiology, Faculty of Sciences School, Shahed University, Tehran, Iran
3) Department of Pharmacology& Toxicology, Faculty of Pharmacy, Pharmaceutical Branch, Islamic Azad University, Tehran, Iran.(IAUPS)

Abstract:

Introduction: Studies have shown that there is a significant relationship between Heparin and female cancer. The present study examines the anti-angiogenesis effect of the enoxaparin skin lotion on breast cancer induced by dimethyl benzene anthracene.

Methods: In this experimental laboratory study, 50 female rats were divided into intact, control and animals treated with enoxaparin (40, 60 and 80 mg %). After one month after, breast tissue samples were provided and stained using hematoxylin-eosin staining method and tumor suppression rate was calculated. The data were analyzed using one-way analysis of variance (ANOVA).

Results: The percentage of tumor suppression significantly increased in groups treated with enoxaparin compared to control group ($P<0.01$), and also tumor suppression rate significantly increased in dose-dependent pattern with increasing of enoxaparin dose ($P<0.01$).

Conclusion: The results of this study demonstrate that enoxaparin has an inhibitory effect on the breast tumor size in a dose-dependent way; according to which, applying of enoxaparin in patients with breast cancer may have considerable role in considered in inhibition of tumor growth.

Keywords:

Enoxaparin, Anti-angiogenesis, Breast Cancer, Female Rat

O064

Early cancer detection based on guanine oxidation consequent to the hybridization between miRNA-21 and it's inosine substitute capture probe

Dr. Hossain-Ali Rafiee-Pour

Hossain-Ali Rafiee-Pour[1]*, Mohsen Behpour[2], Negin Nikzad[3]

1) Biotechnology Division, Department of Cell and Molecular Biology, Faculty of Chemistry, University of Kashan, Iran
2) Department of Analytical Chemistry, Faculty of Chemistry, University of Kashan, Iran
3) Biotechnology Division, Department of Cell and Molecular Biology, Faculty of Chemistry, University of Kashan, Iran
* Corresponding author - rafieepour@kashanu.ac.ir

Abstract:
Cancer is a one of the main cause of death in the world that its early diagnosis plays a critical role towards effective treatment outcome and patient survivals. Today biomarkers can provide a non-invasive approach for early detection of various types of cancers. These biological molecules give information about creation and development of cancer and can be measured simply, rapidly, reliably and cost effectively in body fluids. In this report, we used the advantage of nanomaterials along with the specificity of the nucleic acids to increase the sensitivity of miRNA biosensor. For this purpose, the glassy carbon electrode was modified by reduced grapheme oxide and gold nanoparticles (AuNPs/rGO/GC electrode). This electrode was modified with a self-assembled monolayer of mercapto acetic acid (MAA), as a linker to immobilization of the inosine substituted ss-DNA capture probe on the electrode surface (ss-DNA/MAA/AuNPs/rGO/GC electrode). The immobilization of mentioned components on ss-DNA/MAA/AuNPs/rGO/GC electrode surface was monitored by cyclic voltammetry (CV) method. The hybridization between ss-DNA and miRNA-21 was performed and oxidation of guanine during the hybrid formation was evaluated by differential pulse voltammetry (DPV). The observation of peak current increasing is related to hybridization process. We were able to directly detected 200 pM of synthetic miRNA-21 in buffer solution without the need of PCR and labeling reaction. Consequently this test will be valuable for sensitive, selective and label-free detection of miRNA and it's feasible for miRNA detection in serum and other biological samples.

Keywords:
Reduced graphene oxide, Gold nanoparticles, miRNA-21, Differential pulse voltammetry, Early cancer detection.

O070

Use of Biomarker Assessment of Nicotine Metabolism in Estimating the Risk of Cancer in People Who Smoke Tobacco

Dr. Arash nikkholgh

Arash nikkholgh
School of advanced technologies in medicine/Tehran university of medical sciences/ addiction studies, tehran, iran
arash.nikkholgh@yahoo.com

Abstract:
There are significant differences in the level of nicotine addiction, treatment, and the rate of relapse in different individuals, most of which attribute the effect of heredity.Accordingly, the use of biomarkers will allow the intensity of cigarette smoking as a relative indicator of the difference in the therapist's metabolism, in addition to predicting the situation of the person who consumes tobacco, will also be more influential on the decision to choose the appropriate treatment.Also, the risk of cancer is not the same among smokers. This is largely dependent on differences in the activity of cytochrome enzymes, especially cytochrome p450 Due to the involvement of this enzyme in the metabolism of nicotine in smokers and the clinical difference of individuals as a result of this difference, it seems that the use of clinical and biochemical criteria to differentiate individuals with slow and rapid metabolism (as a specific individual difference) is a way to evaluate The risk of developing cancer as a result of tobacco use and the differentiation of people at high and low risk of cancer for screening and paraclinical examinations is risk.
Materials and Methods: In this study, the sample size with the power of 80 per cent and 5 per cent errors were calculated using the same study data and calculated according to the following formula. 122 patients were studied and the biomarker assessed the severity of smoking with the evaluation of monoxocarbon gas; serum creatinine and the number of cigarettes with the prevalence of cancer (lung, gastrointestinal, bladder), grade one relatives were evaluated. In the two groups of nicotine replacement therapy, the status of the response to treatment in individuals was metabolized and investigated rapidly.
Results: There was a significant relationship between the rate of smoking biomarkers in people with fast and rapid metabolism and the prevalence of cancer in first-degree relatives, as well as nicotine replacement therapy through skin patches and those with fast metabolism and nicotine-binding > 0.001) was found.
Discussion and Conclusion: The evaluation of smoking intensive biomarkers in differentiating smokers with metabolic processes is a quick and slow way to be considered, which seems to be supported by supplementary studies with a higher sample size in terms of screening severity in smokers. Be practical.

Keywords:
Biomarker - Tobacco - Nicotine - Metabolism - Individual Difference

O080

Mutational Analysis of FLT3 Internal Tandem Duplication and D835 in De novo Adult Acute Myeloid Leukemia

Sahar Bayat

Sahar Bayat[1], Milad Gholami[2], Reza Mirfakhraie[3*], Farkhondeh Behjati[4*]

1) Department of Medical Genetics, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran
2) Department of Biochemistry and Genetics, School of Medicine, Arak University of Medical Sciences, Arak, Iran
3) Department of Medical Genetics, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
4) Genetics Research Center, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran
Reza_mirfakhraie@yahoo.com - Fbehjati@gmail.com
* Corresponding author

Abstract:
Aims: Acute myeloid leukemia is the most common acute leukemia in adult, resulting from genetic alterations in normal hematopoietic stem cells. Most studies focused on molecular genetic analysis of FLT3 gene. its mutations confer poor outcome to patients. This Cohort study presents a report concerning the frequency of FLT3-ITD and FLT3-D835 mutations in Iranian adult patients.
Methodology: We analyzed the frequency of FLT3 mutations (ITD and D835) in 91 de novo adult AML patients with conventional PCR and PCR-RFLP methods.
Results: we identified FLT3-ITD (27.47%) and FLT3-D835 (3.29%) in total 30.76 percent of patients. Furthermore, a significant correlation was observed between white blood cell (WBC) and blast cell count and the detected mutations (P-value<0.001). Except for the M6, FLT3 mutations were identified in other FAB type groups. Also mutations were observed in all three cytogenetic risk groups (favorable, intermediate and adverse). However, a significant correlation was detected between FLT3-ITD mutation and normal karyotype (P-value=0.032).
Conclusion: Collectively, our studies show that FLT3 activating mutations are recurrent in Iranian de novo adult AML patients. These findings indicate that mutational analysis of molecular markers such as FLT3 will help to explore more effective therapeutic strategies and prognosis base on categorizing of the patients and that PCR and PCR-RFLP is a reliable and cost-effective method.

Keywords:
Acute myeloid leukemia, FLT3, mutation, de novo

O082

The Effect of CXCR4-siRNA Nanoparticles on serum ALP and LDH levels in a mouse model of colorectal cancer Metastasis to the liver

Dr. Fatemeh Abedini

Fatemeh Abedini[1*], Mohammad Ebrahimi[2], Gholam Reza Shokri[1], Maznah Ismail[3]

1) Department of Research & Development, Agricultural Research, Education and Extension Organization, Razi Vaccine and Serum Research Institute, Karaj, Iran
2) Quality Assurance, Agricultural Research, Education and Extension Organization, Razi Vaccine and Serum Research Institute, Karaj, Iran
3) Laboratory of Molecular Biomedicine, Institute of Bioscience, Universiti Putra Malaysia, Selangor, Malaysia
*Correscpondence - ftmhabedini@yahoo.com

Abstract:
Previous researches showed that inhibition of CXCR4 and its ligand CXCL12 signaling by siRNA knock-down has been found to reduce metastasis breast cancer. The aim of this study was to investigate the effect of CXCR4 gene silencing on serum ALP and LDH levels in colorectal cancer by using CXCR4 siRNAs/ dextran-spermine nanoparticles. The fabricated nanoparticles were used in order to investigate whether down regulation of CXCR4 expression could affect on serum ALP and LDH levels in mouse models of colorectal cancer. In this study colorectal cancer was established in BALB/C mouse by IV injection of mouse colon carcinoma cells CT.26WT. CXCR4 siRNA targeting two sites of the CXCR4 gene was administered following injection of siRNA encapsulated into nanoparticles and naked siRNA. In vivo animal's data demonstrated that CXCR4 silencing by siRNA nanoparticles significantly down regulated CXCR4 expression when compared with naked CXCR4 siRNA. Interestingly, there was correlation between CXCR4 expression and serum ALP and LDH levels. Dextran-spermine was identified as an effective carrier for siRNA and inhibition of CXCR4 expression at the mRNA level by CXCR4 siRNAs nanoparticles.

Keywords:
Cationized dextran, Colorectal Cancer, Serum ALP Enzyme, serum HDL Enzyme, CXCR4, siRNA, Nanoparticles

O091

MicroRNAs: Promising Molecules against Resistance to Breast Cancer Therapeutic Drugs

Mina Mirian

Mina Mirian[1*], Homa Talabaki[1], Hamid Mir Mohammad Sadeghi[1], Nazita Tavazohi[1], Laleh Shariati[2]

1) Department of Pharmaceutical Biotechnology, School of Pharmacy, Isfahan University of Medical sciences, Isfahan, Iran.
2) Isfahan Cardiovascular Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, I.R. Iran.
mina.mirian@yahoo.com

Abstract:

Introduction and background: MicroRNAs (miRNAs) are single- stranded non-coding RNAs which could be considered as one requirement for development of personalized medicine. MiRNAs act as gene expression regulators in post-transcriptional level by binding to 3'untranslated region of the target genes. In this study, we introduce recent progresses in miRNA-associated chemoresistance studies which are the most common and serious problem in cancer treatment.

Methods: In this narrative review, a comprehensive search of PubMed database was carried out with the following Mesh term search using keyword: microRNA along with keywords: breast cancer treatment and drug resistance. Published data have been included since 2008 findings until September 2017, in the study. The inclusion criteria for the study were: all studies that introduced new microRNA associated with chemoresistance in breast cancer treatment.

Results: The final list consisted of 68 papers in respected journals that focus on chemoresistance in breast cancer treatment which were published in recent ten years conduct a comprehensive view of miRNAs associated with the response to chemotherapy in breast cancer.

Discussion and Conclusion: These findings illustrate that miRNA expression signatures play key role in development of drug resistance and consequently, breast cancer progression. These non-coding RNAs could mediate resistance to current breast cancer chemotherapy drugs such as doxorubicin, paclitaxel (Taxol), cisplatin, tamoxifen with control of various indispensable biological processes such as survival, cell cycle, apoptosis, gene regulation and histone modification. Here, we highlight the specific miRNAs involved in breast cancer resistance to treatment and targeted therapy. Moreover, this review critically assesses the challenges and opportunities of targeting miRNAs for emerging unique and more effective individualized therapies, improving the efficiency of drug, and for predicting patient response, monitoring their treatment and survival in breast cancer chemotherapy.

Keywords:

Breast cancer, MicroRNAs, Chemoresistance, Personalized medicine

O094

Impact of microsatellite status (MSI) with KRAS/NRAS and BRAF mutations for a colorectal cancer, a case report

Hamid Reza
A.NAGHASH

A.Naghash H[1,4], Ansarinejad N[2,4],Abbasi B[3,4] , Ramim T[4], Fardad F[2,4], Houshmand M[3]

1) Karaj Branch, Islamic Azad University,Karaj,Iran
2) Iran University of Medical Sciences,Tehran,Iran
3) National Institute of Genetic Engineering and Biotechnology (NIGEB),Tehran,Iran
4) Cancer Pharmacogenetics Research Group (CPGRG), Iran University of Medical Sciences, Tehran, Iran
Corresponding author: Hamid Reza A. NAGHASH - hamidnaghash@yahoo.com

Abstract:
Hereditary Non polyposis colorectal cancer (HNPCC) or Lynch syndrome is due to germ line mutation of one the DNA Mismatch Repair genes (MMR). In tumor cells, immunohistochemistry detects the loss of expression of either MLH1, MSH2, MSH6 or PMS2 protein, corresponding to the mutated genes. These mutations are associated with an unstable phenotype in tumor DNA characterized by new microsatellite alleles that are absent in matching normal DNA.
Genetic studies have demonstrated that mutations of the KRAS/NRAS and BRAF in the MAPK pathway, are detected in a high proportion of CRC patients, including those with defective MMR activity.
Elucidation of the microsatellite status of HNPCC patients may indicate what type of adjuvant chemotherapy is the most beneficial for a particular patient. Therefore, knowledge of MMR activity and KRAS/BRAF mutation status may provide further valu¬able guidance for planning therapeutic strategies.
A series of investigations led to the realization that MSI arises from defects in the DNA mismatch repair (MMR) system and the identification of the 4 genes that cause Lynch syndrome.
Particularly HNPCC patients with MSS and mutated KRAS or BRAF, who have poorer overall survival rates than patients with microsatellite instability. Knowledge of the microsatel¬lite status of patients and whether they harbor KRAS or BRAF mutations may enable more effective therapeutic strategies to be developed.
In the present study, the microsatellite status and genetic mutations of KRAS/NRAS and BRAF (V600E) were characterized in CRC tissue in a patient (age, 53; male, in Iran) as the clinical and pathologically diagnostic criteria for HNPCC.

Keywords:
Hereditary Non polyposis colorectal cancer, KRAS, BRAF, MMR, MSI, CRC

O103

Inhalation exposure of Manganese Dioxide nanoparticle induced oxidative stress in Melanoma

Vahidreza Esfehani

Vahidreza Esfahani, Dr.Parvane Naserzadeh, Dr Mehrdad Hashemi

Islamic Azad University of Medical Science Tehran,iran
Department of Pharmacology and Toxicology, Faculty of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Department of medical biotechnology Tehran Medical Science brunch Islamic azad university Tehran,iran
vahidstar26@gmail.com

Abstract:

1. With the ever-increasing use of manganese dioxide (Mno2) in health-related and engineering applications, the hazardous risks of this material have become a major concern. It is well known that Mno2 accumulate with cytotoxic and genotoxic levels within vital organs. It has also been shown that treating cell cultures with Mno2 resulted in cell cycle arrest and increased apoptosis/necrosis.
2. In this study, we investigated chronic exposed to Mno2 at the exposure chamber in mice. The animals were divided into two groups (control and exposed group to Mno2 at the concentration of 3 µg/m3 for 5 h/day,) in a whole-body inhalation chamber.
3. Our results showed that exposure to Mno2 induced the hematological and biochemical changes. The target organs for Mno2 were the melanoma in the mice, respectively. Also, NPs increased reactive oxygen species (ROS) generation, lipid peroxidation (LPO), the collapse of mitochondrial membrane potential (MMP), decreased a level of reduced glutathione (GSH) and finally increased a level of glutathione disulfide (GSSG) in melanoma tissues. Our results suggest that exposure to Mno2 can induce oxidative stress in the tissue mentioned.
4. These results suggest that exposure of researchers and workers with Mno2 probably increase a risk of respiratory, cardiovascular and cerebral disorders through oxidative stress. However, good ventilation, appropriate personal protective equipment and using of anti-oxidant compounds in daily diet of worker are suggested.

Keywords:
Mno2, chronic exposure, oxidative stress, reactive oxygen spices

O105

A New Anti-Era36 scFv to diagnose the Tamoxifen Resistant Breast Cancer

Leila Farahmand

Termeh Ghorbanian Bolouri, Leila Farahmand, Sepideh Mansouri, Shima Moradi Kalbolandi, Maliheh Salehi
Recombinant Proteins Department, Breast Cancer Research Center, Motamed Cancer Institute, ACECR, Tehran, Iran.

Abstract:
The estrogen receptor α has been identified in 1966, which has then led to the use of anti-estrogenic molecules in the treatment of breast cancer. Numerous studies also revealed a new cytoplasmic and membrane localized variant of ERα, named ERα-36, in breast tumor samples which does not process a complete ligand-binding domain, so that it is believed that this new variant can mediate estrogen non-genomic signaling through the rapid and transient phosphorylation of MAPK other than classical ERα ligands.
ERα-36 is a potential therapeutic target because Tamoxifen can't block ERα-36 mediated membrane-initiated estrogen signaling pathways, instead it stimulates cell growth. So targeting ERα-36 may have therapeutic results in tamoxifen resistance.
Materials and Methods: For targeting receptor, an expression cassette designed. VH and VL domains are linked with the 16 amino acids linker. Signal sequence added to the beginning (N terminus) of sequence for secretion of native protein. Then considering rare codon expression cassette optimized using optimizer online software to obtain favor codon in bacterial host.
Result: Expression cassette formed the anti ERα-36 scFv construct which cloned and expressed in bacterial hosts. This fragment is able to aim epitope of ERα-36 as an antigen.
Conclusion: Taken altogether, these observations help to conclude on the broader and more diverse ligand bonding spectrum of ERα-36 in addition to its potential for playing an independent role and being an important marker for diagnostic and therapeutic targeting.
Now the new constructed scfv may target the alpha Estrogen Receptors in order to recognize the subtype of the tumor more specifically, also the sensitivity of the tumor cells to the Tamoxifen now can be predicted by this scFv monoclonal antibody in order to Choose the appropriate treatment for the patient which may lead in personalized medicine.

Keywords:
Estrogen Receptor, Tamoxifen Resistance, anti ERα-36 scFv

O124

Challenges and Limitations of Personalized Medicine in the Treatment of Breast Cancer

Saba Hosseini

Saba Hosseini[1], Zeinab Imani Saber[2]

1) Medical Genetic Department, Tabriz university of medical science,Tabriz, Iran
2) Medical Genetic Department, Tehran university of medical science,Tehran, Iran
sabahosseine@yahoo.com - Zeynab.imanisaber@gmail.com

Abstract:
Personalized medicine is a medical method Which uses genomic and molecular diagnostic methods to make care decisions in the treatment of diseases, including cancers. This study attempts to investigate the challenges and limitations of personalized medicine treatment in breast cancer, which is a high prevalence in women. Examining these challenges can be important in managing and improving the crisis so that if we use this technique in Iran as an executive, we will be aware of the opportunities and threats we face.
Two common tests for breast cancer, BRCA1 Analysis and Oncotype DX have been used. The results of the tests can determine the risk of breast and ovarian cancers, improve the surgical consultation process, the risk of recurrence that helps in prognosis, and also the decision to chemotherapy .The three interviewed groups include physicians, reimbursers, and patient advocares. The results include two groups , timing and reimbursement. Doctors' priorities are accelerated in the treatment process, and one of the challenges is the timing of the testing process because the results are delayed by the physician, which jeopardizes the health and survival of the patient. Also payers and patient advocates group, payouts and financial issues have been considered, and if these challenges are in the best interest of the patient, the same routine treatments can be used, otherwise the benefit of the patient will be prioritized.
As a consequence poorly coordinated diagnostic testing are the current oncology reimbursement model are barriers to the use of Personalized medicine in cancer care.

Keywords:
genomic and molecular diagnostic, BRCA1 Analysis, Oncotype DX

O126

The new method of personalized chemotherapy with Notch inhibitor and mathematical model in melanoma mouse model

Faezeh Keighobadi

Faezeh Keighobadi[1,2], Vahab Nekoukar[3], Maryam Mehdipour[2], Marzieh Ebrahimi[4*]

1) Department of Biology, Faculty of Sciences, University of Science and Culture, Tehran, Iran
2) Developmental Biology, Department of Stem Cells & Developmental Biology at Cell Science Research Center, Royan Institute for Stem Cell Biology & Technology, Tehran, Iran
3) School of Electrical Engineering, Shahid Rajaee Teacher Training University, Tehran, Iran
4) Department of Stem Cells & Developmental Biology at Cell Science Research Center, Royan Institute for Stem Cell Biology & Technology, ACECR, Tehran, Iran
* Corresponding author - marzieh.ebrahimi@gmail.com

Abstract:

Introduction: Cell proliferation, drug resistance, and invasion are the main reasons for the severity of metastatic Melanoma. The aforementioned features have been attained by the over activation of several signaling pathways such as Notch. Recent studies have shown that Notch suppression using γ-secretase inhibitors has an effective role in decreasing cancer properties.

Materials and methods: In our study, we analyzed the primary effect of Notch pathway inhibition by DAPT on A375(Melanoma metastatic cell line). In the in vitro phase of the study, the effect of Notch inhibition on self-renewal properties of the cells was assessed. Also, in order to investigate cells behavior, we applied several tests such as colony formation, sphere formation, cell migration, Notch1 and Nestin protein expression. Furthermore, the expression of Notch down-stream genes (Notch1, Hes1, Hes5) and stemness genes (Oct4, Nanog, NESTIN) were examined by RT-PCR. In the in vivo model, every 72h, Notch inhibitor was injected via Intra tumoural(IT) and Intravenous(IV) to nude mice. Ki67, c-Myc, tumor cell death, and tumor pathology were measured after sacrificing the animals. What followed this, was designing a mathematical model for each tumor.

Results: we found the inhibitory effective dose of DAPT by MTS test and measuring both the down-stream genes of Notch and Notch1 protein expression in A375 cell line. Our study showed, in short period of time DAPT reduced migration and stemness properties. however, an increase of stemness property have observed after using DAPT for long period. Xenograft and mathematical models demonstrated that some tumors had reduction in growth with IT and IV injections, on the other hand, some other showed drug resistancy. We realized, lower dosage of DAPT as well as stop using it, lead melanoma tumors to drug resistancy. following our observation, we offered an appropriate dose of DAPT for the other tumors with the result that there were not any or bad effects, and all animals faced an effective cure.

Conclusions: This results showed that DAPT can be a unsafe choice in clinical stage for melanoma. because if the using dose of so-called treatment is not appropriate for cure, the drug resistancy and bad effects would appear. With mathematical model we can establish the best reduction in tumor size and abolish the drug resistancy. In addition, we can use this method for other drugs in chemotherapy and increase the health condition of most patients.

Keywords:

Personalized mwdicine, DAPT, Notch signaling pathway, melanoma, mathematical model, stemness, xenograft model

O131

Comparing the concentration of tamoxifen and its metabolites between different genotypes of CYP2D6 gene

Zahra Khalaj

Zahra Khalaj[1,2], Zohreh Baratieh[1], Parvaneh Nikpour[1,3], Fariborz Mokarian[4], Hossein Khanahmad[1], Rasoul Salehi[1,3], Mansoor Salehi[1, 2, 3*]

1) Department of Genetics and Molecular Biology, Faculty of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
2) Medical Genetic Center of Genome, Isfahan, Iran
3) Child Growth and Development Research Center, Research Institute for Primordial Prevention of Non-communicable Disease, Isfahan University of Medical Sciences, Isfahan, Iran
4) Cancer Prevention Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
* Corresponding author - m_salehi@med.mui.ac.ir

Abstract:
Tamoxifen has been extensively used for adjuvant endocrine therapy of ER-positive breast cancer patients. Tamoxifen acts as a prodrug that its effects are due to its active metabolites. Some of these metabolites have more anti-estrogenic effects in breast cancer tissue than tamoxifen, itself. The metabolism of tamoxifen is accomplished through two pathways called 4-Hydroxylation and N-desmethylation. CytochromeP450 2D6 (CYP2D6) is an important drug metabolizing enzyme involved in the pharmacokinetic metabolism of tamoxifen. Since the response of each person to tamoxifen is different from that of the human pharmacodynamics agent in tamoxifen metabolism, in the current study, for the first time in Iranian population, the concentration of tamoxifen and its metabolites in individuals with different CYP2D6 genotypes were compared.
The concentration of tamoxifen and its metabolites were measured by liquid chromatography tandem mass spectrometry (LC-MS/MS) in 134 breast cancer patient from Isfahan province of Iran. Then, the differences of the tamoxifen and its metabolites between different genotypes were evaluated using Kruskal-Wallis test. Steady-state plasma concentrations of tamoxifen and its metabolites was measured using LC-MS/MS technique. In addition to (Z) and (E)-endoxifen concentration, as the most important metabolites of tamoxifen, the concentration of some other metabolites were also showed significant differences between different genotypic groups.
Taken together, our data demonstrated the relationship between CYP2D6 genotypes and plasma concentrations of tamoxifen and its metabolites; therefore it's important to detect these patients to prevent adverse drug reactions through individualization therapy.

Keywords:
concentration, CYP2D6, endoxifen, metabolites, tamoxifen

O133

Posttraumatic stress and posttraumatic growth Simultaneously in patients with breast cancer

Dr. Manijeh Firoozi

Manijeh Firoozi
Assistant Professor in Psycho-oncology, University of Tehran, Iran, mfiroozy@ut.ac.ir

Abstract:
introduction: The posttraumatic stress and Posttraumatic Growth are experienced following a traumatic event such as cancer diagnosis. But there is not clear which them can win in the competition. The aim of this study was to test the association between posttraumatic stress disorder (PTSD), posttraumatic growth (PTG), exploring the roles of challenges to core beliefs and types of rumination among patients with breast cancer.
Method:161 women previously treated for early stage breast cancer were participated. In this study, we tested a comprehensive model of PTG, PTSD, and satisfaction with life.
Results: Results showed that challenge to core beliefs was directly associated with both deliberate and intrusive rumination. Deliberate rumination was positively related to PTG; intrusive rumination was positively related to symptoms of PTSD. PTG and PTSD, in turn, mediated the relationship between rumination styles and satisfaction with life; PTG was related to higher satisfaction with life; and PTSD was negatively related to satisfaction with life.
Conclusion: Results indicate that the intentional facilitation of PTG may be a complementary and alternative option to the reduction of PTSD symptoms for improving satisfaction with life. Findings suggest that efforts to facilitate PTG should be focused on strategies for promoting deliberate rumination in patients with cancer.

Keywords:
breast cancer, posttraumatic stress, Posttraumatic Growth, core beliefs, rumination.

O152

SOPHiA GENETICS: The AI Democratizing Data-Driven Medicine

Dr. Saeed Omidi

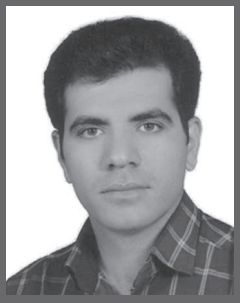
Saeed Omidi
SOPHiA GENETICS, Rue de Centre 172, 1025 Saint Sulpice, Switzerland - somidi@sophiagenetics.com

Abstract:
Reliable variants identification based on NGS technology can be challenging in routine genetic diagnosis. Sufficient coverage of target region is a well-known prerequisite of accurate variant detection. However, there are other issues that are less obvious but important to ensure correct variant identification. For example, variants exposed to the end of reads, proper trimming of the primer sequences, special care of repetitive regions, etc. Understanding the limitation of the sequencing platform, the chemistry used for enrichment, the sequence context (gene panels) is the key to ensure an accurate analysis workflows. Here I introduce SOPHiA, a powerful technology based on collective Artificial Intelligence (AI) concept that aims to achieve goals of the Data-Driven Medicine. SOPHiA universal technology continuously learns from thousands of patients' genomic profiles and experts' knowledge to improve patients' diagnostics and treatment options. Using this unique technology, all types of genomic variants are detected, annotated and pre-classified by SOPHiA, thus ensuring 99.99% specificity and sensitivity required for clinical application. Partnering with over 370 hospitals, located in 55 different countries, and diagnosing more than 150,000 patients world-wide has made SOPHiA GENETICS a pioneer in the Data-Driven Medicine.

Keywords:
NGS, AI, Machine Learning, Data-Driven Medicine, Variant Analysis, Diagnosis, Bioinformatics

O162

Prostate specific antigen in sulfur mustard exposed persons



Dr.Mohammad Rafiee

Mohammad Rafiee[1*], Yunes Panahi[2], Mohammad Yousef Alikhani[3], Hassan Rafieemehr[1], Alireza Saadat[2], Naser Shagerdi Esmaeli[4]

1) Department of Medical Laboratory Sciences, School of Para medicine, Hamadan University of Medical Sciences, Hamadan, Iran.
2) Chemical injuries research center, Baqyiatallah University of Medical Sciences, Tehran, Iran.
3) Microbiology Department and Research Center for Molecular Medicine, Hamadan University of Medical Sciences, Hamadan, Iran.
4) Department of Hematology and Blood Banking, School of Allied Medical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
*Corresponding author : Department of Hematology and Blood Banking, School of Allied Medical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran - m.rafiee911@gmail.com

Abstract:

Background

Oxidants and inflammation agents are predisposing factors for the development and progression of prostate cancer. As a chemical warfare weapon, sulfur mustard (SM) can causes cancer through various ways such as increased production of oxidants and inflammation. Due to high incidence of cancer in SM victims, concentration of prostate specific antigen (PSA) in SM victims was evaluated and compared with control group.

Materials and methods

Serum concentration of PSA in 150 male SM victims (exposed to SM in Iraq-Iran war, 30 years ago) and 150 males in control group was measured and compared by ELISA method. The data were analyzed using SPSS version 16 software.

Results

Decreasing concentration of PSA in SM victims in compare with control group was observed (0.728 vs 0.844 ng/ml, p-value: 0.103). The chemical victims group consumed N-acetylcysteine.

Conclusion

As oxidation and inflammation effects of SM, PSA concentration was likely to be increase in SM victims, but an opposite result was observed. Consumption of N-acetylcysteine (an anti-inflammatory agent), mild exposure and the short period elapsed from exposure to SM may be the reasons for this result. However, future more accurate studies on these subjects with respect to cancer seem to be necessary.

Keywords:

Prostate Specific Antigen, Sulfur mustard, Oxidant agents, N- acetylcysteine

O170

Personalized Medicine and Epidermal Growth Factor Receptor Mutation in Non-Small Cell Lung Cancer: A study from National Research Institute of Tuberculosis and Lung Disease

Hanifeh Mirtavoos-Mahyari

Hanifeh Mirtavoos-Mahyari[1*], Adnan Khosravi[2], Sharareh Seifi[3], Babak Salimi[3], Zahra Esfahani-Monfared[3], Mojtaba Ghaffari[4]

1) Tehran University of Medical Sciences, Tehran, Iran.
2) Tobacco Prevention and Control Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran.
3) Chronic Respiratory Diseases Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran.
4) Shahid Beheshti University of Medical Sciences, Tehran, Iran.
*Corresponding Author: Hanifeh Mirtavoos-Mahyari, M.D,PhD student of Medical Genetics, Tehran University of Medical Sciences, Tehran, Iran - hanifehmirmah@yahoo.com

Abstract:
Non-Small Cell Lung Cancer (NSCLC) comprises about 80-85% of all lung cancers. Epidermal growth factor receptor (EGFR) is a receptor tyrosine kinase and appears to play a central role in tumor genesis, and targeting this receptor may provide a unique approach for treating EGFR-expressing cancers. Successful examples of translating cancer genomics into therapeutics its potential to make possible personalized cancer medicine. 147 eligible participants were adults with NSCLC advanced disease from 2014 to 2017 whom referred to National Institute of Tuberculosis and Lung Disease (NRITLD), Masih Daneshvari Hospital. Informed written consent was obtained prior to participating patients in the study according to Shahid Beheshti Medical University's ethics. According to presence or absence of EGFR mutation and also, patient's demand and consensus, patients were treated with tyrosine kinase inhibitors(TKIs) or other standard first-line chemotherapy. The primary endpoint was progression free survival (PFS).DNA was extracted from paraffin-embedded of each tumor block. EGFR mutation study was done by polymerase chain reaction(PCR)-based direct sequencing at a central laboratory. Results: Figure 1 shows the trial profile. From EGFR mutant group, 24 (61.7%) were female and rest of them (n=15,38.5%) were male. Most common EGFR mutation was deletion in exon 19(n=18, 46.1%) and other mutations were (n=17,43.5%) in exon 21 and in exon 18 in 2 patients(5.1%). One patient had both mutations in exon 18, and 21. In 2 patients EGFR mutation exon was not determined. Progression was observed in 14patients (35.8%). It is significant statistical difference between patients with EGFR mutation who treated by TKIs and who received other chemotherapy agents in term of disease progression (P value=0.019).Our data revealed that personalized medicine is specific and selective treatment which targets oncogensis and may control tumor growth and invasiveness.

Keywords:
Personalized Medicine, Epidermal Growth Factor Receptor, Non-Small Cell Lung Cancer, Oncogenes.

O175

Non-coding RNAs miR-20a and miR-145 could differentiate between colon and rectum tumors

Abolfazl Akbari

Abolfazl Akbari*, Sara Eslamizadeh, Atefeh Talebi, Shahram Agah, Mohsen Masoodi

Colorectal Research Center, Iran University of Medical Sciences, Tehran, Iran

*Corresponding author: Dr Abolfazl Akbari, Colorectal Research Center, Rasoul-e- Akram Hospital, Sattarkhan Ave, Niyayesh St., Tehran, Iran - akbariia2006@gmail.com

Abstract:

MicroRNAs (miRNAs), as small non-coding RNAs and tissue specific regulators of gene transcription, have been shown to involve in initiation and progression of cancers. Colorectal cancer (CRC), affects both colon and rectum tumors as a common entity and whereas the clinical behavior and treatment of these two types are distinctly different. There is only limited evidence about different molecular characteristics between the colon and rectum tumors. The main purpose of this study was to evaluate the expression level of oncogenic and suppressor miRNAs whether could differentiate between colon and rectum cancers.

A total of 74 CRC samples (37 rectal tumor tissues and 37 colon tumor tissues) and 74 matched adjacent normal tissues were collected. The differential expression of 10 selected miRNAs (miR-20a, 22, 34a, 133b,135b, 21,145,18a, 200c and let-7g) was evaluated using quantitative Real-time PCR (qPCR). MiRNA expression levels were adjusted for multiple comparisons and tumor tissues was compared with noncancerous tissues from the same site.

The significant elevated levels of miR-21, miR-22, miR-18a, miR-20a, miR-135b, and decreased levels of miR-34a, miR-200c, miR-145, and let-7g were detected in both colon and rectal tumor samples compared to the normal groups ($P<0.05$). A difference in expression level for miR-20a and miR-145 was found ($P<0.001$). Further analysis revealed that these miRNAs were associated with tumor type and cancer localization ($P<0.05$). We identified that miR-20a and miR-145 differentially expressed between rectal and colon cancer and may be as tissue-specific biomarkers for distinguishing between these two cancers. This finding improves understanding the molecular differences between colon and rectal cancer, suggesting microRNAs as tools for better understanding personalized cancer biogenesis, evolution, diagnosis and treatment.

Keywords:

Cancer, Colon, MiRNA, Rectum

O185

New gene manipulation strategies against cancer stem cells

Dr.Raheleh Halabian

Raheleh Halabian[1*], Zohreh Norouzi[2]

1) Applied Microbiology Research Center, Systems biology and poisonings institute, Baqiyatallah University of Medical Sciences, Tehran, Iran, Personalized Medicine Research Center of BUMS

2) Department Of Molecular And Celluar Sciences,Faculty Of Advance Sciences & Technology,Pharamaceutical Science Branch,Islamic Azad University Tehran,Iran

* Corresponding author - r.halabian@yahoo.com

Abstract:

Cancer stem cells derived from a single cell that is transformed in to cancer initiating cell. Cancer stem cells have been reported in wide range of human tumour. It has capacity to proliferate and form in vivo. Cancers are responsible for overexpress cyclins. Thus, cell cycle arrest, represents a survival mechanism. There are some strategies for treatment of cancer stem cells, such as function of aldehyde dehydrogenase that focus on the role of retinoic acid and suppression of cell proliferation. In the other way, polyphenol structures and classifications are involved in the anti-cancer activities by interplay between autophagy and apoptosis. Polyphenols will target cancer stem cells. In addition, Hyaluronic acid could have coated in to the nanoparticles for targeting CD44 receptors on cancer stem cells. In other survey have been showed that, developing novel strategies against ErbB family which classified as a cancer stem cells to be responsible for tumour initiation and maintenance. In other strategies shows that Monoclonal antibody Cetuximab, in combination with ixabepilone has been eliminating cancer stem cell through inhibition of autophagy. MicroRNAs technology focused on preventing tumour recurrence and metastasis cancer stem cells. miR-34a is a key negative regulator of CD44+ as a novel therapeutic agent against CSCs. Also, infected cancer stem cell with lentiviral encoding pre-miR-34a inhibited tumour regeneration. In conclusion, new strategy such as monoclonal antibody, aptamers, microRNA could be targeted for stem cell cancer.

Keywords:

Cancer stem cells, monoclonal antibody, microRNA, targeted therapy.

O188

Familial Osteosarcoma in a large pedigree: A case report

Dr.Mehrdad Zeinalian

Zahra Sadri[1], Mahdi Hadian[1], Nafiseh Heidarzadeh Isfahani[1], Mehrdad Zeinalian[2*]

1) Ala Cancer Prevention and Control Center, Isfahan, Iran
2) Department of Genetics and Molecular biology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
* Corresponding author - zeinalianmehrdad@gmail.com

Abstract:
Osteosarcoma is a primary cancer of bones characterized by the direct development of immature bone or osteoid tissue by the tumor cells. A high malignancy with a rare prevalence (0.2% of all cancers) has been reported for the classic osteosarcoma. The age within 10-25 is the most possible time for onset the disease.
We report a large family in which 16 of 33 members, over three generations, presented 17 malignancies. Seven cases were osteosarcoma, with the average age of presentation at 23 years (range within 45-12 years. The tumors had been located in pelvis (3 cases), jaw (2 cases), tibia and shoulder (both one case). Moreover, 6 and 3 patients had been affected with brain and larynx tumors, respectively. Importantly, osteogenic sarcomas had been appeared in successive generations. It could imply to hereditable predisposition to living or nonliving carcinogens. An awareness of this entity could lead to early detection of cancer in at-risk family members.
Familial osteosarcoma could be attributed to Li-Fraumeni syndrome (germline TP53 inactivation), hereditary retinoblastoma (germline RB1 inactivation), Rothmund-Thomson syndrome (germline RECQL4 inactivation), or Bloom or Werner syndrome (germline BLM or WRN inactivation, resp.). All these familial syndromes are related to the heritable pathogenic gene variants leading to the genomic instability. A comprehensive genetic counseling and testing should be offered to the at-risk individuals for identification of the likely carriers. A complete Next Generation Sequencing panel including TP53, RECQL4, BLM, and WRN genes are suggested on genomic DNA of the patients.

Keywords:
Familial, Osteosarcoma, pedigree, case report

O193

Application of mesenchymal stem cell-based gene therapy in personalized treatment of gastrointestinal cancers

Bahareh Rahimi

Bahareh Rahimi[1], Mohammad Panahi[2], Neda Saraygord-Afshari[3*]

1) MSc. student of medical biotechnology; Student Research Committee, Iran University of Medical Sciences, Tehran, Iran
2) M.Sc. student; Department of Medical Biotechnology, Faculty of Allied Medical Sciences, Tabriz University of Medical Sciences, Tabriz, Iran
3) Assistant professor; Department of Medical Biotechnology, Faculty of Allied Medical Sciences, Iran University of Medical Sciences, Tehran, Iran
*Corresponding author - afshari.edu@gmail.com

Abstract:
Many pieces of evidence have been shown that mesenchymal stem cells (MSCs) can selectively home tumor sites and take part in tumor stroma formation, the ability which has been recently implemented in the use of MSCs as specialized vectors for gene therapy of cancer which significantly has enhanced the selectivity and sensitivity of tumor gene therapy systems compared with the application of other commonly used vectors (viral and nanoparticles for e.g.) Furthermore, MSCs have the potency to be engineered not only for transferring anti-tumor agents but also to increase their homing efficacy in a personalized manner which hinders the immunological problems associated the autologous vectors. Herein, we will focus on the recent advances in engineered stem cells, to personally treat gastrointestinal tumors.
A verity of approaches has been implemented for MSC-based treatment of gastrointestinal malignancies. Different genetic engineering techniques have been implemented for inserting anti-cancer agents (IFγ as an apoptosis inducer, IL7 as an immunostimulant, and/or NK4 as an angiogenesis inhibitor) in MSCs derived from patients' autologous tissues and/or enrichment of tumor-specific chemokines and cytokines receptors such as CCR1 (ligand of CCL3) to reduce therapeutics side effects on healthy tissues.
The use of engineered MSCs as personalized vectors of prodrug gene therapy of cancer has opened up new windows for treatment of malignancies. Today's many researchers are working hard to fit the method for targeting cancer-initiating cells and combining it with a suitable chemotherapy approach to increases its therapeutic efficacy for gastrointestinal malignancies as well as other types of cancer.

Keywords:
Mesenchymal stem cell; cancer cell therapy; personalized Medicine

O202

Identification of expressional signature of Iranian Gastric cancer patients by next generation sequencing

Dr. Kaveh Baghaei

Kaveh Baghaei[1], Nazanin Hosseinkhan[1], Habib Malekpour[2],
Hamid Asadzadeh aghdaei[2], Manijeh Habibi[1], Mohammad Reza Zali[2]

1) Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
2) Gastroenterology and Liver Diseases Research Center, Research Institute for Gastroenterologyand Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
kavehbaghai@gmail.com

Abstract:
Background: Incidence rates of Gastric cancer (GC) is significantly varied in different geographical regions. Iran is categorized as a country with high age-standardized mortality rates (ASR> 15) and crude rate of 12.8 for GC. Late stage diagnosis beside the lack of proper treatments which is due to the heterogeneous nature of GC could be the two most important reasons for the high crude rate of this cancer in Iran. In recent years, the heterogeneous molecular mechanisms involved in gastric cancer has been extensively studied over the past few years significant attention has been devoted to the field of cancer therapy with the focus on personalized medicine. The identification of expressional signature of cancer indistinct geographical regions can be very effective in cancer risk determination, as well as in the detection of the novel therapeutic targets suitably fitted to the patients of that area.
Material and Methods: By using NGS technologies we demonstrate a detailed, accurate and complete view of gene expression patterns of different medical conditions and diseases.
Result: In the present study several molecular alterations implicated in several pathways has been identified. These pathways which are involved in the GC development or are associated with the different stages of GC include metabolic, MAPK, RAS, WNT, Estrogen, Jack-STAT, Hippo, PI3K-AKT and several other pathways.
Conclusion: Investigation of molecular interactions between these pathways and mechanistic association of the genes involved in these pathways to GC progression can illustrate their potential usage as diagnostic markers and also considering them as new therapeutic targets.

Keywords:
Gastric Cancer, Next Generation sequencing, Transcriptome, Biomarker

The International Personalized Medicine Congress of Iran

Poster Presenters

P007

AKT2, miRNA and Tumorogenesis

Maryam Honardoost

Maryam Honardoost

Endocrine Research Center, Institute of Endocrinology and Metabolism, Iran University of Medical Sciences, Tehran, Iran - honardoost.m@iums.ac.ir

Abstract:

AKT (AK mouse plus Transforming or Thymoma) is a frequent oncogene expressed in most tissues which is fundamental protein mediating signals from receptor tyrosine kinases family to phosphatidylinositol 3-kinase (PI3K). Hyper activation of AKT signaling is a central key in many human cancer progression, through modulating angiogenesis, tumor growth, and cell migration, invasion, metastasis and chemo resistance. The rising data is linking deregulated AKT signaling with sporadic and inherited cancer human cancers. Numerous of studies have given a prognostic and/or predictive role for AKT2. Earlier studies provided evidences that AKT2 is required for hypoxia-stimulated angiogenesis and protects tumor cells from hypoxia condition. Tumor induction and growth depends on the regulatory networks of AKT2 signalling pathway.

MicroRNAs, short non-coding RNAs, have captured the spotlight in molecular biology with highlights like their involvement in DNA translational control, their impression on mRNA and protein expression levels, and their ability to reprogram molecular signalling pathways . MiRNAs, like other genes, undergo altered expression in cancer and depending on their function and targets classified as oncomiRs and tumor suppressor-miRs. There are a lot of examples of oncomiRs and tumor suppressor-miRs which their numbers are raising .Growing evidence represents a potential role of miRNAs participates in cancer carcinogenesis by activating or suppressing AKT2 expression (Table 1).

The miRNA mimic and miRNA silencing molecules has allowed to modulate miRNA expression in tumors, showing that miRNAs can be effectively used as therapeutic agents. Furthermore , realizing miRNA/Akt2 pivotal roles in drug resistance, they emerged as diagnostic targets orchestrating drug response in individualized therapy examples.

Conclusion: Collectively, given the widespread interest in the AKT kinases, it is reasonable to expect that there will continue to be many important mechanistic and medical insights regarding the AKT pathway, which could lead to novel therapeutic strategies of potential benefit to many cancer patients.

Keywords:

miRNA, AKT2, Tumorogenesis, Cancer

miRNA	Target	Cancer type
miR-203	AKT2/Src	Bladder cancer
miR-608	AKT/FOXO3a	Bladder cancer
miR-615	Akt2	Breast cancer
miR-2861	EGFR/AKT2/CCND1	cervical cancer
miR-194	Akt2	Colon cancer
miR-612	Akt2	Colon cancer
miR-7	AKT2/EGFR	Glioma
miRNA-641	Akt2	Glioblastoma
miR-29 family	Akt2	Gastric/AML
miR-137	Akt2	Gastric cancer
Let7 b/g	AKT2/p-AKT	Gastric cancer
miR-143-3p	Akt2	Gastric cancer
miR-302b	EGFR	Liver
miR-612	AKT2	Liver
miR-150	AKT2/p-AKT	Leukemia
miR-184	-	Neuroblastoma
miR-21	PDCD4 /Spry1	Ovarian cancer
miR-615-5p	Akt2	Pancreases cancer
miR-200	Akt2	Prostate /Breast cancer
miR-708	Akt2	Prostate cancer

Table 1. List of miRNAs that target AKT2 in cancer cells.

P008

Tumor associated macrophages (TAMs) target for cancer treatment: new promising route in cancer immunotherapy

Saeed Farajzadeh Valilou

Saeed Farajzadeh Valilou, Farkhondeh Behjati*

Genetics Research Center, University of Social Welfare and Rehabilitation Sciences
Kodakyar Ave., Daneshjo Blvd., Evin, Tehran, Iran
*Corresponding author - fbehjati@gmail.com

Abstract:

Introduction: Tumor-associated macrophages (TAM) especially M2 types play a critical role in cancer invasion and metastasis. Cancer- and host cell-derived signals generally drive the functions of TAMs towards an M2-like polarized, tumor-propelling mode; however, when appropriately re-educated. TAMs also have the potential to elicit tumor destructive reactions. Thus, targeting TAMs would impede the implicated mechanisms and enhance survival rate of patients.

Methods: We utilized PubMed database and we used cancer therapy, inflammatory microenvironment, macrophages, macrophage recruitment, chemokines, and tumour associated macrophage as keywords. Finally, we included 20 literatures which related to our topic.

Results: Experimental investigations indicate that TAMs contribute to drug-resistance and radio-protective effects, and clinical evidence shows that an elevated number of TAMs and their M2 profile are correlated with therapy failure and poor prognosis in cancer patients. Several studies on TAM-targeted strategies have led to significant progress and some pilot works have achieved encouraging results. Among these, connections between some anti-tumour drugs such as inhibitors of CCL2/CCR2 (e.g. Yondeli and RS102895), inhibitors of M-CSF/M-CSFR (e.g. anti-M-CSF mAb,JNJ-28312141 and GW2580), agonists of STAT1 (e.g. interferon), agonists of other M1 pathways (e.g. SHIP), and Inhibitors of STAT6 and their influence on TAMs have been suggested. Strategies of targeting TAMs are grouped into four categories based on the proposed mechanisms: (i) inhibiting macrophage recruitment; (ii) suppressing TAM survival; (iii) enhancing M1-like tumoricidal activity of TAMs; (iv) blocking M2-like tumour-promoting activity of TAMs.

Conclusion: In sum, targeting TAMs in different types of cancer would be promising and providing desirable results in cancer treatment and open a novel effective cancer treatment strategy in the future.

Keywords:

cancer therapy; recruitment; survival; Chemokines; Inflammation; Macrophages; tumour associated macrophage

P011

Apoptosis assessment of the essential oil from the fruits of Pycnocycla bashagardiana Mozaff. in HT-29 cells: Association with expression Bcl-2 and Bax

Zahra Ghazazani

Zahra Ghazazani[1] ,Jinous Asgarpanah[2] , Masoumeh Heshmati[3]*

1) Pharmacy student, Pharmaceutical Sciences Research Center, Pharmaceutical Sciences Branch ,Islamic Azad university , Tehran - Iran (IAUPS)

2) Assistant Professor, Department of Molecular and Cellular Sciences, Faculty of Advanced Sciences & Technology , Pharmaceutical Sciences Branch, Islamic Azad University ,Tehran -Iran (IAUPS)

3) Assistant Professor, Department of Pharmacognosy, Faculty of Pharmacy, Pharmaceutical Sciences Branch, Islamic Azad University, (IAUPS), Tehran, Iran

Heshmati.cmb@gmail.com

Abstract:

Pycnocycla bashagardiana mozaff is a rare endemic species that has been used in folk medicine in South of Iran. It is commonly distributed in Jask County, Hormozgan Province. Due to the presence of myristicin as the major component (more than 65 % of oils)cytotoxicity and anti-cancer properties of P. bashagardiana essential oil are proposed.

Colorectal cancer is the third most lethal cancer in men and fourth in women. So far, various drugs have been used to treat the disease, but because of the emergence of drug resistance to chemical drugs, the need to achieve the new natural compounds of medicinal plant derivatives is felt more active. Due to the presence of other substances, the herbal substance has a balanced biological state, so it does not accumulate in the body and has no side effects and can play an important role in the treatment of cancer. The aim of this study was to investigate the effect of Pycnocycla Bashagardiana'fruits cytotoxicity and anti-cancer on HT29 cells and L929 mouse fibroblast cells in vitro.

In this study, the cytotoxicity effects of Pycnocycla Bashagardiana'fruits at different concentrations on HT29 and normal L929 cells were monitored at 48 h by MTT assay and trypan blue exclusion and Flow Cytometric Analysis of Apoptosis(Annexin-V-FITC). The expression levels of Bax and Bcl2 in HT29 cells and normal L929 cells were detected using quantitative Real- time PCR (qRT-PCR)

Pycnocycla Bashagardiana'fruits has cytotoxic effects depending on concentration and time. IC50 values were observed at a concentration of 430 µg / ml in the HT29 and 450µg / ml in L929 cell line and the essential oils induced apoptotic cell death 77.3 % for the HT29 cells in IC50 and 3.4% for normal cells (L929) in IC50.The relative expression levels of Bax and Bcl2 were significantly higher in HT29 cells than in the normal cells ($p < 0.01$).

Comparison of IC50 values suggests that the Pycnocycla Bashagardiana'fruits has toxicity in cancerous cells and normal cells,but can induced apoptotic cell death in cancerous cell more than normal cells.

Keywords:

colon cancer- apoptos –bax -bcl_2 -Pycnocycla bashagardiana

P014

Progress in human tumour immunology and cancer immunotherapy

Elham Shojaeinia

Elham Shojaeinia*, Najmeh Shojaei
Baqiyatallah University of Medical Sciences - Personalized Medicine Research Center, Italia Street, Tehran, Iran

Abstract:
In the last few decades immunotherapy has become an important part of treating some types of cancer. Newer types of immune treatments are now being studied, and they'll impact how we treat cancer. In one method they can boost the body's immune system in a very general way and in the other method they help train the immune system to attack cancer cells specifically. Because the immune system itself doesn't see the cancer cells as foreign because the cells aren't different enough from normal cells. Sometimes the immune system recognizes the cancer cells, but the response might not be strong enough to destroy the cancer.
Among various types of cancer immunotherapy the main ones are: Monoclonal antibodies as the man-made versions of immune system proteins, immune checkpoint inhibitors as the drugs which basically take the 'brakes' off the immune system, and help it recognize and attack cancer cells, cancer vaccines which are substances put into the body to start an immune response against certain diseases, and other, non-specific immunotherapies which boost the immune system in a general way, but this can still help the immune system attack cancer cells.
Recent immunotherapy research illustrates that even bulky invasive tumours can undergo complete regression. Under appropriate immune stimulation by IL-2 has shown that it is indeed possible to treat cancer successfully by immune manipulation. Also Adoptive Cell Therapy (ACT) using autologous tumour-infiltrating lymphocytes has emerged as the most effective treatment for patients with metastatic melanoma and can mediate objective cancer regression in approximately 50% of patients. The recent discoveries of tumour antigens, and of successful means for raising anti-tumour T-cell numbers in humans by immunization, have solved some of the problems confronting the successful application of immunotherapy to the treatment of human cancer. Current studies are aimed at optimizing immunization and understanding the mechanisms used by the tumour to escape destruction.

Keywords:
Cancer, immunotherapy, immune system, tumour

P015

The Effect of Thymoquinone on Level of FOXM1 mRNA in Glioblastoma

Elahe Faezi

Elahe Faezi[1], Seyed Mohammad Moshtaghioun[1], Raheleh Masoudi[2], Mohammad Reza Sarafraz ardakani[1], Laleh Ranjbaran[2]

1) Department of Biology, Faculty of Science, Yazd University, Yazd 89195-741, Iran
2) Department of Biology, Faculty of Science, Shiraz University, Iran
*Corresponding author - faezielahe@gmail.com

Abstract:
Introduction and Objective: Glioblastoma is the most common type of malignant brain tumor. Since the tumors contain different types of cells, the treatment of glioblastoma is difficult. Thymoquinone (TQ), the main active constituent of Nigella sativa's seeds, is one of the drugs that exhibits anticancer characteristics. The aim of this study was to investigate the effect of thymoquinone on the levels of foxm1 mRNA in U87MG glioblastoma cell line.
Material/Method: U87MG cells were treated with or without thymoquinone (50µM).The effect of thymoquinone on the expression of foxm1 was analysed by semi-quantitative polymerase chain reaction (Semiq-PCR). TBP was used as housekeeping gene.
Results: TQ (50µM) is able to significantly reduce the mRNA levels of foxm1 after 20 hrs treatment.
Discussion and result: According our results, TQ can affect the expression of foxm1 gene that involved in tumorigenesis and cancer progression. Therefore, TQ can be suggested as an effective drug for glioblastoma treatment.

Keywords:
Thymoquinone, glioblastoma, foxm1, anticancer drug

P016

Topology of personalized opsonization: revealing a pattern of cancerous differential geometry

Babak Daneshfard

Reza Sanaye[1], Babak Daneshfard[2*]

1) Essence of Parsiyan Wisdom Institute, Phytopharmaceutical Technology and Traditional Medicine Incubator, Shiraz University of Medical Sciences, Shiraz, Iran
2) Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran
*Corresponding author - babakdaneshfard@gmail.com

Abstract:
To ratchet up natural body's immune response towards cancer, subtypes of opsonizing reagents have been infused through injection [before getting into the metastasis stage] into the micro-environment of the cancerous tumor.
This, of course, to a large extent, demands the "topological" onhooking of the opsonizing (re-)agents to the peripheral micro-mileu of the tumor: something which has largely been ignored, maybe due to its interdisiplinary design complications. This is to the purpose of gauging the stereometric parameters of proper molecular onslaught as metricized to the best possible precision, thus leading to nearly fully successful act of opsonization. Accordingly, the induction has been made that: the Atiyah-Hirzebruch spectral sequence does have its application in predicting the topological properties of tumor micro-environments.
The whole process revolves around the idea that the cohomology either through K-theory or by means of C-algebra not only differentiates in between normal and abnormal growth, but also brings about the likelihood of discerning those sub-spaces in which stem cell structuration could be manipulated. This even goes to the extent of molally/molecularly designing for culturing those tissues which are mostly regarded to be entelechially non-regenerable, though our success has not been --at least experimentally-- as remarkable in this latter field as it has been in early cancer diagnosis.
Differential identities are either repetitive or quazi-repetitive (not going into the details of finding quazi-repetitiveness on the same modes). We have managed to procreatively define spaces of (any) n-dimensions whereby co-planarity is not at all specified by the property of orthogonality or mirror orthogonality.
These could be copied out multifariously [in two or three stages] following high energy consumption from biochips as the medium in between the simulation In Silico and the actual In Vitro.
This is accomplishable as a result of porosity grading matrix inserted by boundary-atom schemes, which most probably acts in response to adjuvant radiation therapy when from 100 to 1000 molecules come out of their relatively stable biomolecular structure. One cannot arrive at any brand of precise constructivist image identity and/or fairly contextual essentialist identity if one --according to what was mentioned above-- does not bring about the non-orthogonality of co-planar spaces.

Keywords:
Opsonisation, Immunity, Tumor, Micro-Environment, Topology

P017

Study of BMI-1 gene expression in breast cancer tumor tissue and its relationship with cilinopathological markers

BanafshehAfkari eidehlo

BanafshehAfkari eidehlo[1*], Fourozandeh Mahjoobi[2], Mohammadhossein Sanati[3]

1) Department of biology, faculty of science, NourDanesh institute of higher education, Meymeh, Isfahan, Iran
2) Department of Medical Genetics, National Institute for Genetic Engineering and Biotechnology, Tehran, Iran
3) Department of Medical Genetics, National Institute for Genetic Engineering and Biotechnology, Tehran, Iran
*b.afkari.1992@gmail.com

Abstract:

Background:breast cancer is the most common cancer among women still is that in case of early diagnosis and timely treatment measures, the chances of survival and recovery is very high. therefore, find possible biomarkers comparing diagnostic, prognosis and response to treatment, particularly ones that have a significant impact, it can be a very important role in the physician's decision to start treatment and select the best treatment path is.. Bmi-1 is transcript inhibitor protein of polycamb family which is inhibitor of genes that induce apoptosis.BMI-1 gene as a strong inhibitor of both pathways of Retinoblastoma (pRB) and p53 is known and so the role of this gene in the process of becoming cancer cells is important. So if there is an increase in the expression of this gene in pathological examples compared to adjacent healthy examples of pathological as control is the gene can be viewed as a potential biomarker in predicting the path of the disease.

Material and Methods: 70 samples of fresh tissue samples of typical pathological which conclude 45 healthy adjacent pathological samples and 70 turmeric samples, after the surgery of the breast cancer patients was collected and immediately freeze in -70C. Being healthy and pathological specimens collected by a medical practitioner approved by the pathologist.After the extraction of RNA and cDNA synthesis, the method of Real Time PCR gene expression-gene BMI1 and B-actin genes as internal control review housewife.

Result:Bmi-1 gene expression changes in breast cancer, in healthy and pathological tissues adjacent tumor comes about. RT-PCR is a product of the expected size of the 210bp matches for pieces of Bmi-1 designed the production. Incremental changes in Bmi-1 expression of tumoraltissue in comparison with the non-tumoraltexture in 80 percent of the surveyed sample view that if reviews of significant statistical relationship can show the likelihood of the introduction of the biomarker gene as a highly anticipated increase. Statistical reviews and definitive results after the completion of tests.

Conclusion:BMI-1 gene expression as significant increase in the oncogene genes of pathological tissue than in healthy tissues, various studies have shown. A study on the Iranian population on the bladder tissue, increase the meaningful expression of this gene in the tissues of the bladder tumor comes towards the non-pathological tissue has been reported to Western-blot and Immunohistochemistry techniques also were approved. The increase far higher this gene in pathological tissues in colorectal cancer, lung and larynx is also so far has been reported in other population

Due to being The higher the expression of gene in view of pathological samples relative to adjacent healthy is important so sometimes pathological view of adjacent healthy tissue in such genes expression of the tumor may become cancer stage and perhaps for this reason that this tissue oncogenic genetic changes affect the epinephrine and breast cancer. According to these points is very likely that these could be functional genes such as candidate for bio marker suitable for the prognosis and prediction of stages of the progression of breast cancer. The aim of the present study.

Keywords:

breast cancer, BMI-1 oncogene, Biomarker, gene expression

P018

Investigation of rs 515135 and rs 639 varation in APOB gen in Familial hypercholesterolemia patients with comparison to the healthy controls

Parvin Pishva

Parvin Pishva[1], Masoumeh Dehghan Manshadi[1], Vadieh Ghodsinezhad[1], Arash Kadivari[1], Fatemeh Karami[2]

1) Medical Genetic Center, Endocrinology and Metabolism Research Institute (EMRI), Tehran University of Medical Sciences (TUMS), Tehran-Iran

2) Department of Biology, Science faculty, Science and research branch, Islamic Azad University, Tehran, Iran

Abstract:

Familial hypercholesterolemia (FH) is the most common an autosomal dominant disorder. APoB gene is one of important gene that is related to susceptibility FH. APOB is a large glycoprotein that plays an important role in metabolism of lipoprotein in human's body. APOB100 is essential in liver for produce Very Low Density Lipoprotein(VLDL) and also APOB100 is a ligand for LDLR that mediate LDL endocytosis. Rs515135 is a single nucleotide polymorphisms that happened at the 5 'end of APOB and rs693 is occur in the Exon of this gene.

In this study rs693 and rs515135 in gene APOB analyzed in 120 cases with familial hypercholesterolemia and 120 control. Polymorphism was identified by the RFLP-PCR method. The PCR product was digested with specific restriction enzyme for recongnation of each single nucleotide polymorphism. In rs515135 the pattern of enzyme digestion showed that genotype frequency of GG in case group were 68.33%, GA 29.17% and AA 2.5% and 70.83%,27.5% and 1.67% for the controls respectively. In rs693 the genotype frequency of CC in case group were 70%, CT 26.67% and TT 3.33% and the percentage of genotype pattern in control group were 85.83%, 13.33% and 0.83% respectively.For confirmation of the results digestion, some samples were sent for sequencing.

According to this study,there was no significant relationship with the occurrence of rs515135 and familiar hypercholesterolemia. Furthermore, It seems the dominant model of T allele occurrence has a protective role in emergence of disease.

Keywords:

Familial hypercholestrerolemia (FH) ,APOLIPOPROTEINB ,gene,Single nucleotide polymorphism

P019

Investigating the concomitant expression alteration of long non-coding RNAs GNAS-AS1 and BLACAT1 of breast cancer specimen

Hesam Motaleb Zade

Motaleb zade Hesam[1*], Mowla Seyed Javad[2], Irani Shiva[3]

1) Master of Science, Department of Biology, Science and Research Branch, Islamic Azad University
2) Professor, Department of Molecular Genetics, Faculty of Biological Sciences, Tarbiat Modares University
3) Associate Professor, Department of Biology, Science and Research Branch, Islamic Azad University
*Corresponding author - hes_motaleb@yahoo.com

Abstract:
Breast cancer is the most common cancer in women, and due to high rates of invasion and metastasis in these patients, the first cause of death is in women aged 40-44 years. The latest biomarkers and prognostic factors in a variety of cancers, including breast cancer, can be found in the form of Long Non-coding RNAs with a variety of oncogenic function or tumorigenic function (TSG), a marked change in the expression of this cancer showing normal breast tissue. The aim of this study was to simultaneously investigate changes in the expression of GNAS-AS1 and BLACAT1 non-coding gene expression in tumor tissue of breast cancer.
Materials and Methods: MCF7 and MCF10A cancer cell lines were used to optimize the experiments. Then with the method qRT-PCR the expression of two non-coding RNA genes, GNAS-AS1 and BLACAT1, was investigated in 45 pairs of tumor and adjacent tumor fresh samples.
Conclusion: According to the results of the study, 90 tumor samples of breast cancer were compared to the normal tumor margin of the same person, Non-coding RNAs of GNAS-AS1 and BLACAT1 have a pronounced increase in tumor tissue expression relative to the tumor margin (P = 0.0453 GNAS-AS1) (P = 0.0443 BLACAT1).
Discussion: Considering the review of previous articles and micro array studies in human specimens, the existence of a possible hypothesis about the oncogenesis of two selected genes in the present study has been found Based on real-time PCR results and comparison of data, GNAS-AS1 and BLACAT1 genes increased significantly in the cancer cell line compared to the normal cell line and in the cancerous tissue compared to normal tissue which resulted in the probability of pro-oncogenesis of these genes.

Keywords:
Gene-Breast Cancer-Oncogene- Long Non-coding RNAs - real-time PCR

P030

Investigation of DLEC1 gene methylation pattern in the human colorectal cancer cell line HT29 engineered by E- cadherin stable down regulation

Sahar Mohammadi fateh

Sahar Mohammadi fateh[1,3], Mohammad Amin Moosavi[2], Masoumeh Heshmati[3], Mehdi Kadivar[1*]

1) Department of Biochemistry, Pasteur Institute of Iran, Tehran, Iran
2) Department of Molecular Medicine, National Institute of Genetic Engineering and Biotechnology, P.O Box: 14965/161, Tehran Iran.
3) Department of Molecular and Cellular Sciences, Faculty of Advanced Sciences & Technology, Pharmaceutical Sciences Branch, Islamic Azad University, Tehran -Iran (IAUPS)
* Corresponding author - kadivar@pasteur.ac.ir

Abstract:
Methylation of high-density CpG regions known as CpG Islands (CGIs) has been widely described as a mechanism associated with gene expression regulation. Changes in promoter methylation are considered as a hallmark of some cancers or cancer stem cells. DLEC1 (Deleted in Lung and Esophageal Cancer 1) is a protein coding gene and acts as a tumor suppressor gene by inhibiting cell proliferation. DLEC1 mediates tumor-suppressive activities through NF-κB signaling. Down regulation of this gene has been observed in several human cancers. In our previous study, we derived a cancer stem cell like population from HT29 (human colorectal adenocarcinoma cell line) by lentivirus mediated down regulation of E-cadherin gene. It has been shown that dysregulation of E-cadherin promotes dysfunctions of some signaling pathways such as Wnt signaling, Rho GTPases, and NF-κB pathway and influences cell survival, invasion, and migration in carcinogenesis The aim of this study was to investigate the DLEC1 gene methylation pattern in HT29 cell line and its derived cancer stem cell like population by MSP (Methylated Specific PCR) method. Our results demonstrated that DLEC1 gene has a hyper methylated state in HT29 cell line engineered by E- cadherin stable down regulation in comparison with intact HT29 cell line. These findings may imply that how epigenetic deregulation of NF-κB pathway can contribute to form a cancer stem cell like phenotype.

Keywords:
Methylation, HT29, stem cell, DLEC1, E-cadherin

P032

The role of personal medicine in the diagnostic and treatment of cancer

Atefeh Zamani

Atefeh Zamani[1*], Massoud Houshmand[2], Hamidreza Raeespour[3]

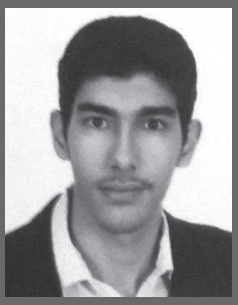
1) Mcs of Genetics and member of Zistfanavari biotechnology institute,Isfahan,Iran.
2) Faculty member of Genetic Engineering of National Research Institute of Iran, Scientific Collection, Research, Laboratory, Gene Pajoohan Ebnesina 3, Tehran, Iran
*Corresponding Author - atefeh.zamani20@gmail.com

Abstract:
In spite of large study about diagnostic and treatment in field of cancer, this is one of main cause of death. The current treatment of cancer are surgery, chemotherapy and radiotherapy may which cause side effect and also have partial effect. In the recent years, with development in the field of technology, microarray, computer sciences, mathematics and statics the possibility of the studying about GWAS (Genome Wide Association Study) is available.
With genetics info and simplicity of genome sequence determination in any person, the possibility of make genetic profile is possible now. The existence and development of these genetic profiles become basic for personal medicine, which will be new version of medicine in future. study and search in relevant article in the Google scholar, pubmed and science direct. Information of persons genetic profiles make it possible to recommend a drug with minimum side effect and proper dosage for person with cancer and also use most targeted treatment for cancer such as oncoDEEP and Monoclonal antibody.
Today personal medicine with use of genetic science, bioinformatics, biotechnology and relevant establish a new field in the medicine that with use of molecular analysis of cancer mass contribute in diagnostic and treatment of cancer. The Purpose of Personalized medicine is providing the most appropriate treatment in the best time for Suitable patient.

Keywords:
Personal medicine, Cancer, oncoDEEP, GWAS

P033

Association of Genetic polymorphism in estrogen metabolism and susceptibility to Breast cancer



Abbas Ghasemzadeh

Abbas Ghasemzadeh[1], Mohammadreza Shiri[2], Zahra Tahmasebi Fard[3]

1) Department of Cellular & Molecular Biology, Medical Science Branch, Islamic Azad University, Tehran, IRAN.
2) Department of Biology, Islamic Azad University, Shahr-e-Qods Branch, Islamic Azad University, Tehran, IRAN.
3) Assistant Professor of Molecular Biology, Roudehen Branch, Islamic Azad University, Roudehen, IRAN.
Ghasemzadeh313@gmail.com

Abstract:

Background:Genome wide association studies have identified single nucleotide polymorphisms (SNP) can affect in development of breast cancer. CYP1A1 gene is a member of the cytochrome P450 superfamily of enzymes which catalyze many reactions involved in drug metabolism and synthesis of estrogen. One of the putative functional polymorphisms in the CYP1A1 gene is CYP1A1*2A or rs 4646903. Many studies have also investigated associations between single nucleotide polymorphisms (SNPs) related to estrogen metabolism and Breast cancer risk.

Methods:We used case-control study, including 100 cases and 100 controls to genetic analysis. DNA was extracted by salting out method and genotyping was performed using the PCR-RFLP method. Deviation from the Hardy-Weinberg equilibrium was evaluated by chi-square test with 1 degree of freedom. Statistical significance P-value was less than 0.05. Statistical analyses were carried out using IBM SPSS 23.

Results:After counting the genotypes, their percentages in the cancerous specimens were TT (68%), CC (32%), and in control group were TT (86%), CC (14%), respectively. The adjusted ORs (95% CI) for women with the CC genotype were 2.89 (1.43–5.84) and 0.35 (0.17-0.71) for TT genotype. We found a decreased risk of breast cancer among TT genotype in comparison with CC genotype. So, CYP1A1*2A was significantly associated with breast cancer risk.

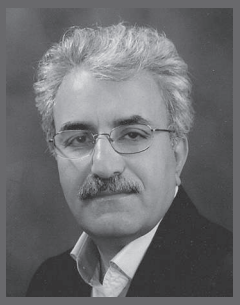
Conclusion:In conclusion, Our findings add further evidence to the idea that genetic polymorphisms related to estrogen metabolism may play a role in the development of breast cancer.

Keywords:

Breast cancer, Polymorphism CYP1A1, rs 4646903

P034

Cervical cancer, HPV and personalized medicine



Dr.Mohammad Mehdi Ejtehadi

Mohammad Mehdi Ejtehadi, Ali Masoudi kazemabad*
Dr. Ejtehadi Medical Lab.center, Rahnamaei 3, Ahmadabad Ave., Mashhad, Iran
*Corresponding author - Alimk31@yahoo.com

Abstract:
Cervical cancer is an important cause of early loss of life as it affects relatively young women. Iran has a population of 30.13 million women ages 15 years and older who are at risk of developing cervical cancer. It's with an age-standardized incidence rate of 2.2 per 100,000 women per year. Current estimates indicate that every year 947 women are diagnosed with cervical cancer and 370 die from the disease.
Human papilloma virus (HPV) infection is very common worldwide and its prevalence was 76% in cervical cancer patients. Recent evidence also suggests that a primary high risk HPV screening test could provide better protection against cancer risk than cytology. It has been found that genes encoded by oncogenic HPV synthesize proteins which can interact with host epigenetic machinery leading to its deregulation. Also numerous studies have shown the positive association between methylation of the L1 region and CIN2+ stage. Methylation of human genes also increase with length of HPV persistence, and elevated methylation may be detected up to 7 years before discovery of a cancer.
Therefore measuring DNA methylation at specific CpG sites in HPV or human genes has shown promise for the accurate detection of CIN2+ and prevention of cervical cancer and its treatment. So genetic differences in HPV positive and negative tumors (cervical, head and neck cancers) can be used to personalized cancer treatment.

Keywords:
Personalized medicine, cervical cancer, HPV, DNA methylation

P036

New challenges in cancer personalized medicine: from identifying mutation to precise modification

Shima Mohammadi

Shima Mohammadi[1], Farbod Taghavi Rad[1,2*], Rasoul Beheshtifar[1], Mehdi Moheimani[1], Mahdieh Shojaei[1,3]

1) Molecular R&D section, Masir-e-Sabz clinic, Tehran, Iran.
2) Biology department, Islamic Azad University – Ahar branch, Ahar, East Azerbaijan province, Iran.
3) Agriculture science department, Agriculture engineering faculty, payame noor university of Alborz, Alborz, Iran
*Corresponding author - farbod1990@gmail.com

Abstract:
Nowadays the genomic characterization of each tumor is a hopeful strategy for targeted therapies based on person-specific information, gain advances in precision medicine were made in human oncology. The combined efforts of specialists reveal significant progress in cancer genetic testing panels, now identified as Next Generation Sequencing (NGS) technology. NGS technology offers the ability to sequencing tumor causative mutations that allowing for more accurate targeting therapies. Moreover, development of CRISPR-Cas9 edition system to correct disease-related mutations and to activate or suppress involved genes, can be applied for therapeutic purposes. To date, preliminary evidence introduce adenine base editors (ABEs) system to correct point mutations more professional than Cas9 nuclease-based method in human cells and without double-stranded DNA cleavage. In this Progress article, we reviewed the linkage between using NGS as DNA sequencing technology and ABEs as advance genome editing with particular emphasis on the field of cancer. In conclusion, it may lead to development of individualized approaches that enable to precise medicine target.

Keywords:
NGS, CRISPR-Cas9, Cancer, ABE, personalized medicine

P039

Study expression balance of miRNA-196a-2 tumor marker in ovarian cancer patients by Real Time PCR

Fahimeh Ezzatizadeh

Fahimeh Ezzatizadeh[1], Soyar Sari[1], Ardeshir Hesampour[2*]

1) Department of molcular and cellular sciences, Faculty of advanced sciences & Technology, Pharmaceutical Sciences Branch, Islamic Azad university, Tehran-Iran

2) *-correspond: Department of Biology, Tehran Central Branch, Islamic Azad University, Tehran, Iran - a.hesampour@gmail.com

Abstract:

Background and aims: Ovarian epithelial malignancy is one of the most prevalent and crucial causes of cancer death in women. Recent studies emphasize the critical role of several noncoding RNAs (including microRNAs) in modulating disease severity and early detection of different cancer types. In this regards, it has been demonstrated that microRNA-196a-2 (miR-196a-2) plays an important role in tumorigenesis of many cancer types. However, the impact of miR-196a-2 on generation and progression of ovarian epithelial cancer is yet unclear. The objective of this study was to investigate relationship of ovarian epithelial cancer and miR-196a-2.

Materials and methods: In this study, expression level of miR-196a-2 was evaluated in ovarian epithelial tissue obtained from 50 patients, in comparison with similar quantity of normal individuals. Upon extraction of total RNA from frozen tissue samples, cDNA was generated. By designing specific primers, expression level of miR-196a-2 was relatively assessed using qRT-PCR. In this experiment, GAPDH was utilized as housekeeping gene.

Results: We determined that miR-196a-2 was significantly up-regulated in ovarian cancer, compared to normal tissue. Further investigations revealed that this overexpression is elevated by increasing the malignancy stage.

Conclusion: Our findings indicate the crucial role of miR-196a-2 in progression of ovarian epithelial cancer, suggesting the inhibitory effect of this microRNA on tumor suppressor genes. In future, further investigations are required to validate current data and navigate mechanism underlying this procedure. This could potentially lead us to find a tumor marker in early diagnosis of ovarian epithelial cancer.

Keywords:

Ovarian epithelial cancer, miR-196a-2, Tumor marker, qRT-PCR

P040

Compare the Effectiveness of Group Logo therapy and Solution- Focused Brief Therapy in the Quality Life of women with Breast Cancer

leila Heydari

Asiie Olfatbakhsh[1] ,Arya Hamedanchi[2], leila Heydari[3*]

1) Breast Disease Department, Breast Cancer Research Center, Motamed Cancer Institute, ACECR, Tehran, Iran
2) Iranian Research Center on Aging, Department of Aging, Universityof Social Welfare and Rehabilitation Sciences, Tehran, Iran
3) Breast Disease Department, Breast Cancer Research Center, Motamed Cancer Institute, ACECR, Tehran, Iran
* Corresponding author - Leila Heydari,heydaril1388@gmail.com

Abstract:
Introduction: According to statistical reports, breast cancer is the most common cancer and the second leading cause of death in Iranian women.Significant consequences of breast cancer, such as physical problems (pain and fatigue), psychological problems (anxiety and depression), and other psychosocial problems, lead to poor quality of life. The most important aspect of care for these patients is the attention, evaluation and improvement of their quality of life Purpose: To compare the effectiveness of group-based logo therapy and Solution-focused brief therapy on the quality of life of women with breast cancer in order to help improve the quality of life of these patients.Methods: This study was a semi-experimental design with pre-test and post-test. The statistical population of this study was breast cancer women who referred to breast cancer research center, of the age range of 23-65 years old.Participants in the study included 45 individuals who were randomly divided into three groups (15 control group and 30 subjects in two experimental groups). The experimental group under the treatment of Solution- focused brief therapy, intervention strategies, post-modern and group-oriented approaches, were subjected to existential treatments, and no intervention was performed in the control group. To measure the variables of the research, the EORTCQLQ-C30 (QOL) questionnaire was used to analyze the obtained data using the covariance method.Conclusion: Findings showed that there is a significant difference between the control group and the two groups in terms of overall health, function and symptoms of breast cancer women. Based on the results of intervention, logo therapy treatment had better outcomes than the solution's focused brief therapy, but these differences were not significant.

Keywords:
Solution- focused brief group therapy, logo therapy, quality of life, breast cancer

P046

Gynecomastia, as an extremely rare presentation of chest wall lymphoma, a case report and review the articles

Mohammad Javad Behzadnia

Soleyman Heydari[1], Fatemeh Saboori[2], Mohammad Javad Behzadnia[3*]

1) Department of surgery, Faculty of Medicine, Baqiyatallah University of Medical Sciences, Tehran, IR Iran
2) Cancer Institute, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, IR Iran
3) Department of Emergency Medicine, Faculty of Medicine, Baqiyatallah University of Medical Sciences, Tehran, Iran
*Corresponding author - Behzadnia@bmsu.ac.ir

Abstract:
Primary tumors of the chest wall are not so prevalent, and the incidence of malignancy is reported approximately 50% in some studies. Chest wall masses are usually metastatic or invasive tumors derived from the other organs like breast and lung tumors. Male breast enlargement as gynecomastia may be due to drug effects or even a sign of underlying systemic diseases. Male breast malignancy must also be considered in the differential diagnosis. We present a young man with primary chest wall lymphoma as gynecomastia, without pre-existing problem or other disease. The mass resolved successfully and he treated properly with six cycles of R –CHOP regimen chemotherapy followed by local radiotherapy. We present his clinical manifestation, management, and his early outcome. Chest wall lymphoma as an Initial presentation of isolated chest wall mass in males is a rare clinical entity and its presentation as gynecomastia is even extremely unusual.

Keywords:
chest wall tumor, gynecomastia, B – cell lymphoma; male, primary breast lymphoma

P047

Exosome based Technology in Personalized Cancer Medicine

Mohammad Hasan Soheilifar

Mohammad Hasan Soheilifar[1], Abdolvahab Moshtaghian[2], Razieh Amini[1], Masoud Saidijam[1*]

1) Research centre for molecular medicine and genetics, School of Medicine, Hamedan University of Medical Sciences, Hamedan, Iran
2) Deputy of Research and Technology, Semnan University of Medical Sciences, Semnan, Iran
*Corresponding author - sjam110@yahoo.com

Abstract:
Introduction: Exosomes are 50-150 nm membrane bound vesicles that act as shuttles between cells and can enter the body fluids and protect their cargoes from degradation. In recent years, exosomes have been emerged as an important player in tumor development. The present mini review article aimed to exploring exosome applications in cancer.
Method: This mini review gathered from research and review studies published in valid databases including PubMed, Science Direct, Medline, Google scholar and Scopus using the following keywords: exosomes, cancer and personalized medicine. Result: Expression Changes in miRNA, lncRNA and other biomolecules in several type of cancer influenced by genetic and environmental factors that will be reflected by exosomes harvested from cancer patients, so making them promising tools in personalized medicine era. Since exosomes are transferred from their origin cells to target cells mostly through the circulation they can be harvested non-invasively from blood as potential biomarker for cancer diagnosis. Exosomes could serve as natural therapeutic nanovectors that are capable of carrying drug or small molecules for inhibition of tumor growth. Furthermore immunostimulatory and immunoinhibitory properties of some types of exosomes like dexosomes could be a choice for cancer immunotherapy. Nowadays the microfluidic technologies are introduced for exosome extraction which has some advantages including high purity and low cost rather than the routine isolation techniques like ultracentrifugation that make them ideal for clinical setting.
Conclusion: In cancer patients, the contents of isolated exosomes would be different from healthy control which could be used as a potential biomarker in cancer diagnosis and therapy. Altogether exosomes investigations highlight a promising therapeutic strategy in personalized cancer medicine.

Keywords:
Exosome, Cancer, Biomarker, Personalized Medicine

P051

MicroRNAs expression signatures as a novel approach in cancer detection

Mohammad Yahya Vahidi Mehrjardi

Seyed Mohsen Aghaei Zarch[1], Mohammad Yahya Vahidi Mehrjardi[1*]

1) Department of Medical Genetics, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

* Corresponding author - mmvahidi@gmail.com

Abstract:

Cancer is a genetic disease and currently become one of threatening life factor and yearly many health expenditures devoted to its treatment. Mortality rate due to cancer is linked with its progression into advanced stage so its detection in early stages is the most promising approach to enhance long-term survival of individuals with cancer. MicroRNAs (miRNA) are type of single strand RNA which are involved in post-transcription regulation. These molecules by direct targeting mRNAs play crucial role in cellular process. Due to their stability and ease of detection, they are usable as a powerful biomarker in different disease especially cancer. Recently it was disclosed that aberrant expression levels of miRNAs occur in different cancer compare to normal controls. It also has been found that miR expression signatures also known as precision medicine are linked with specific stage in cancer progression so miRNA as a biomarker enable us to detect cancer before the onset of metastasis.Percision medicine is also being used to characterized tumors at the molecular level, and several clinical successes have shown that such information can guide the design of drugs targeted to a relevant molecule. In this review, we introduce some major biomarker involved in cancer and their application in cancer detection.

Keywords:

Cancer, miRNA, Biomarker, precision medicine

P053

Personalized forensic toxicology: the promises of pharmacogenomics in the interpretation of drug poisonings

Maryam Akhgari

Akhgari Maryam[1*], Etemadi-Aleagha Afshar[2]

1) Legal Medicine Research Center, Legal Medicine Organization, Tehran, Iran
2) Tehran University of Medical Sciences, Amir Alam Hospital, Tehran, Iran
*Corresponding author - akhgari1349@yahoo.com

Abstract:

Objectives: Pharmacogenomics involves the assement of personalized contributions in response to drugs, adverse drug reactions and also drug poisoning. Pharmacogenomics is a useful area in the prediction of responses to drugs and poisons in different subjects. Some aspects of forensic toxicology importance of pharmacogenomics are the interpretation of forensic toxicology analysis results in alive and postmortem cases and their role in inducing life threatening outcomes and even death.

Methods: To perform the present study many databases such as PubMed, Google scholar, … were searched to find the role of personalized and interindividual variations in drug induced poisoning.

Results: Results showed that genetic and environmental factors cause interindividual differences in response to drugs and poisons. For example fluoxetine induces death in poor CYP2D6 metabolizer genotype subjects due to the accumulation of parent drug. There is a high prevalence in CYP family variation. Decedents intoxicated with methadone and oxycodone had shown decreased CYP2D6 enzyme activity. Warfarin has a narrow therapeutic index with a large interindividual variation. Overconversion of codeine in ultrarapid metabolizers with greater CYP2D6 activity results in high morphine amount and therefore toxicity and death.

Conclusion: Pharmacogenomics might aid in dose adjustment of drugs in different individuals. Also pharmacogenomics helps the interpretation of the side effects of many drugs in different populations and drug poisoning related deaths.

Keywords:

personalized medicine, drug metabolism, interindividual variation, drug toxicity, forensic toxicology

P054

Association Micro-RNA 125 and Micro-RNA 152 Polymorphisms with Long Cancer Risk in Iranian Patients

Maryam Akhgari

Masoumeh Dehghan Manshadi[1], Vadieh Ghodsinezhad[1], Parvin Pishva[1], Arash Kadivari[1], Babak Arjmand[2], Hossein Adibi[2]

1) Medical Genetic Center, Endocrinology and Metabolism Research Institute (EMRI), Tehran University of Medical Sciences (TUMS), Tehran-Iran

2) Metabolomics and Genomics Research Center, Endocrinology and Metabolism Research Institute (EMRI), Tehran University of Medical Sciences (TUMS), Tehran-Iran

Abstract:

Lung cancer is the leading cause of cancer-related deaths worldwide, and about 80% of patients have non–small cell lung cancer (NSCLC).Both environmental and genetic factors contribute to the mortality of patients with NSCLC. Recent evidence indicates that small noncoding RNA molecules known as microRNAs (miRNAs) can function as tumor suppressors and oncogenes. The loss and gain of function of specific miRNAs were also thought to be key events in the genesis of diverse cancers .In lung cancer, miRNA expression profiles and specific miRNAs have been shown to be correlated with survival of lung adenocarcinomas. Single nucleotide polymorphisms (SNPs) or mutations occurring in the miRNA gene region may have effects on the function of miRNAs through altering miRNAs expression and/or maturation, consequently contributing to cancer susceptibility.

In this case–control study, we genotyped two SNPs [rs12976445 (mir-152) and rs12940701 (mir-125a)] in Iranian patients with late-stage NSCLC and healthy control by PCR-RFLP methods. Our result provides evidence for the application of miRNA SNPs as predictive biomarkers in future personalized medicine for patients with NSCLC

P055

Cell-based drug delivery; a new trend in personalized medicine

Moein Amoupour

MoeinAmoupour[1], ParastooTarighi[1]*, Reza Nekouian[1]

1) Department of Medical Biotechnology, Faculty of Allied Medicine, Iran University of Medical Sciences, Tehran, Iran.
*Corresponding author - tarighi.p@iums.ac.ir

Abstract:
Personalized medicine is an emerging approach to patient care based on individual characteristics that guide clinical decisions for the right treatment for the right patient at the right time. In most approaches, personalized medicine requires time and cost severity to find out individual characteristics such as genetic profiling to achieve successful treatment. However, cell-based drug delivery offers a promising alternative; especially the use of synthetic biology in reprogramming cells and production of therapeutic products. Cell-based drug delivery is one of the approaches to the drug delivery system which includes encapsulation of drugs inside the cells or attached to the cell surface and genetic engineering of cells to secrete therapeutic molecules.Various cells could be involved including; RBC, dendritic cells, tumor cells and stem cells. RBC drug acceptability in the form of encapsulation of drugs into RBC or attached to the surface. in fact, provide an elegant means of personalized medicine; using a patient's own RBC for drug delivery. Patient's own DCs can be used for development of cancer treatments. In fact DCs are loaded with tumor-associated antigens ex vivo or genetically engineered. An alternative cell-based drug delivery involves transduction of cells with genes to achieve a constant production of therapeutic products including; tumor cells and stem cells. Advantage of this approaches include biocompatible, targeting properties and reduced immunogenicity using the patient's own cells to improve treatment. Advances in personalized medicine to engineer patient's own cells could lead to maximize therapeutic efficacy and minimize side effects.

Keywords:
Drug delivery, Personalized medicine, Synthetic biology, RBC, Dendritic cells, Tumor cells, Stem cells, Cancer treatment

P059

Majority of TP53 signaling pathway related genes are up-regulated in Tamoxifen-treated MCF-7 human Breast adenocarcinoma cell line

Milad Rouhimoghadam

Milad Rouhimoghadam[1*], Shahrokh Safarian[2]

1) Department of Cell and Molecular Biology, School of Biology, College of Science, University of Tehran
2) Department of Cell and Molecular Biology, School of Biology, College of Science, University of Tehran
*Corresponding author - milad.rouhi@ut.ac.ir

Abstract:
Introduction:Worldwide, breast cancer is the most common cancer in women, with an estimated 1.38 million new cases diagnosed per year. Tamoxifen has been widely used to treat breast cancer as an endocrine therapy. Apoptosis, or programmed cell death, is critical for embryogenesis and for normal tissue homeostasis. The ability of p53 to control passage through the cell cycle (in G1 and in G2) and to control apoptosis in response to abnormal proliferative signals and stress including DNA damage is considered to be important for its tumor suppression function. The ability of tamoxifen to inhibit proliferation has been extensively studied. However, the molecular mechanism by which tamoxifen initiates apoptosis is poorly understood.
Methods: MCF-7 cells were treated with 250µM Tamoxifen for 48 hours and cultivated at 37 °C in a 5% (vol/vol) CO2 environment. RNA was extracted and samples were prepared according to standardized protocols before being sequenced on an Illumina HiSeq 4000 sequencing system. We apply Cuffdiff 2, an algorithm that estimates expression at transcript-level resolution and controls for variability evident across replicate libraries.
Results: Our data from differential expression studies and pathway enrichment analysis display that in Tamoxifen-treated sample group (in comparison to control group) 19 genes related to p53 signaling axis (CDKN1A; GADD45B; GADD45A; GORAB; TNFRSF10B; RCHY1; PPM1D; GADD45G; CASP8; ZMAT3; CASP3; SESN1; SESN2; FAS; CYCS; PMAIP1; MDM4; SFN; TP53) are over-expressed by the adjusted p.value of 0.00715.
Discussion: In addition to its role in suppressing tumorigenesis, p53-dependent apoptosis contributes to chemotherapy-induced cell death. These findings indicated that Tamoxifen as a potent chemopreventive drug can effectively trigger apoptotic cell death through activation of TP53 signaling axis.

Keywords:
TP53, Breast cancer, Tamoxifen, Apoptosis

P060

Interaction between obesity-related MC4R (Rs17782313) gene, associated to an increase of Breast Cancer risk.

Mina Mozafarizadeh

Mina Mozafarizadeh[1], Massoud Houshmand[2*]

1) Department of Cellular and Molecular Biology, Nour Danesh Institute of Higher Education, Isfahan, Iran
2) National Institute for Genetic Engineering
*Corresponding author Massoud Houshmand

Abstract:
Background: Breast cancer (BC) is a complex disease and obesity is a well-known risk factor for its development, especially after menopause. Several studies have shown singe nucleotide polymorphism (SNP) linked to overweight and obesity, such as: rs17782313 (T/C) in Melanocortin 4 Receptor gene (MC4R). Thus, we aimed to investigate the association between these obesity-related SNP and BC risk. Methods: Genomic DNA was extracted from peripheral blood of 63 breast cancer patients and 83 normal controls. Height and weight were measured to calculate body mass index (BMI). All were genotyped for the SNPs rs17782313 using a Tetra-primer ARMS-PCR method. For statistical analysis P-value test and SPSS software were used. Results: In this study, two Odds Ratio and P-value factors were investigated. Our research has shown those who have cancer and are overweight cause a significant increase in breast cancer (P-value>0.005).but those who are obese are the result of a reverse. Conclusion: To our knowledge, the present meta-analysis suggested that only there might be a significant association of the MC4R Rs17782313 polymorphism with breast cancer risk. The basis of our research we suggest that further functional may elucidate the role of genomic variation in breast cancer development.

Keywords:
Breast Cancer, MC4R, Obesity, Polymorphism

P061

Evaluate of influential factors affecting survival of patients with Leukemia cancer using Logistic Regression model

Nazanin Ramezani

Nazanin Ramezani[1], Mahsa Moosavi[2], Ahmadreza Baghestani[3*], Sina Salari[4]

1) Department of Biostatistics/Faculty of Paramedicalsciences, Shahid Beheshti University of medical sciences, Tehran, Iran
2) Department of Biostatistics/Faculty of Paramedicalsciences, Bu Ali University of medical sciences, Hamedan, Iran
3) Department of Biostatistics/Faculty of Paramedicalsciences, Shahid Beheshti University of medical sciences, Tehran, Iran
nazaninramezani69@gmail.com

Abstract:
Leukemia is one of the disease which is a burden of severe disease. Its mortality rate is 2.8%. Therefore it is necessery to study corelation between affecting factors of this disease.
Logistic regression model is the most common statistical method in data analysis that have a random response variable in this paper, with using a logistic regresion model we examined the corelation between patient's life after receiving transplant with the gender of patient and the level of hemoglobin in the blood.
Data used in this research extracted from the records of patients in the bone marrow transplant departement related to the Taleghani Hospital affiliated of Shahid Beheshti University of Medical Sciences. The patient's record were formed during 2007 to 2015 years. And their review was carried out between 2015 and 2016 years.
Taking into account the condition of life as a response variable. We have fitted the data binary logistic regression model, and the meaningful explanatory variable of gender and blood hemoglobin level were assessed.
After estimated a binary logistic regression model, the explanatory variable of gender didn't have any statistically significant correlation with the patient's life status in this study.
Estimated odds ratio survival for a unit of increase in blood hemoglobin level is 1.2 time and 95% confidence interval is obtained for odds ratio of the hemoglobin level of the blood (0.53 , 1.42).
Blood hemoglobin level has a significant effect on patient's life status. (P-value=0.048)
This study showed that, there is a significant correlation between variables hemoglobin level and the life of patients with Leukemia.

Keywords:
logistic regression, leukemia, survival analysis, bone marrow transplant, odds ratio

P062

Expression evaluation of cell cycle regulatory genes (P27, P21, P14) in AML patient

Naser Shagerdi Esmaeli

Naser Shagerdi Esmaeli[1],Atousa Homafar[2],Mohyedin Barzegar[1],
Mohammad Rafiee[1], Mohammad Hossein Mohammadi[1], Mehdi Allahbakhshian Farsani[1*]

1) Department of Hematology and Blood bankingShahid Beheshti University of Medical Sciences,Tehran,Iran
2) Department of nutrition science,Tabriz Branch,Islamic Azad university,Tabriz,Iran
Allahbakhshian@SBMU.ac.ir

Abstract:

INTRODUCTION: Cell cycle control has a critical role in normal hematopoiesis, leukomogenesis can affect key cell cycle regulators such as CDI gene family.P27, P21 and P14 in CKI family are frequently involved in AML.Their defects disrupt the balance between proliferation and apoptosis which can be led to cancer formation.

OBJECTIVES: The present study aimed at expression investigation of such essential cell cycle proteins (P21, P27, P14) in bone marrow biopsies and peripheral blood obtained from newly diagnosed acute myeloid leukemia patients.

METHODS: The results of present study obtained from bone marrow and peripheral blood sample of 93 newly diagnosed AML patients (39 males and 54 female classified in 3 age group ;< 35, 35-60 and >60 years old) obtained from Taleghani hospital. We have 45 APL patient and 48 Non M3 patient. In addition expression of target genes was detected compared with ABL as housekeeping gene using the ΔΔCT method.

RESULTS: P21 and P27 had 1.44 and 4.10 higher expression respectively in comparison with normal control group (PV>0.05), and average expression fold change of P14 compared with the control group was 3.69 that shown significant reduction (Pv>0.05). We found no correlation between expression level of the mentioned genes and common AML prognostic factors including: age, gender, blast cell type and even sample type.

CONCLUSION: We hypothesized that at the first step they get rid from their anti-tumor function and at the second step the malignant cells employ these proteins at their service.

Keywords:

AML, Regulatory cell cycle proteins, P27, P21, P14, Expression evaluation

P063

Melanoma and microRNAs; remarkable relationship

Negin Afrang

Negin Afrang, Maryam Honardoost*

Endocrine Research Center/ Institute of Endocrinology and Metabolism/Iran University of Medical Sciences, Tehran/Iran
*Corresponding author - marymail79@gmail.com

Abstract:
Recently, skin cancers are becoming as common cancers amongst white societies. Melanoma is one of the prevalent and aggressive types of skin cancer which occurs in specific cell types called melanocytes, producing melanin pigment that is responsible for color skin. Mentioned pigments are condensed in an organelle called melanosome responsible for ultra-violet protection (UV) of skin cells. Since youth are more in danger and treatment methods are not accessible it became a serious subject in novel researches. MicroRNAs have documented as a pioneer biomolecule in cancer therapy, specifically in melanoma. Several molecular modifications in abnormal cells are accomplished by micro-RNAs. MiRNAs are small non-coding RNAs (18-22 nucleotides) regulating gene expression by binding to 3'UTR of target mRNA and inhibit translation or degrade it. As a result of this progression in molecular studies, small non-coding RNAs are investigated in foresaid topics. Regulating function of micro-RNAs in melanoma have reported in many studies. As an example, miR-221 and miR-222 could target various molecules such as tyrosin protein kinase kit (c-KIT) which modulates microphthalmia-associated transcription factor (MITF), an important mutated factor in melanoma. This targeting process is carried out by up-regulation of miR-221 and miR-222. Another over-expressed micro-RNA, miR-34a/c, attached to ULBP2 and facilitated evading process from natural killer cells (NKCs). However, there are some over-expressed micro-RNAs in melanoma; multiple down-regulated miRNAs have distinguished, too. MiR-let7-b, an essential micro-RNA, is reduced in melanoma. Therefore, protein levels of cyclin-dependent kinases D1 (CDK), basigin (BSG) and extracellular matrix metalloproteinase (MMP) is increased responsible for progression and metastasis in melanoma.
Discussion: While melanoma is known for recent years, there are no accurate treatments for this prevalent cancer, yet. Application of micro-RNAs in various studies have documented in recent decade. Moreover, scientists have slightly declared these non-coding biomolecules' function in cancers including melanoma. As a result of this, there are multiple researches around their precise role in prognosis, diagnosis and therapeutic processes. In addition, different investigations have reported aberrant expression of responsible and chief proteins due to up/down-regulation of micro-RNAs. Our endeavor in this review is to mention tasks of miRNAs in various, remarkable basis researches of melanoma.

Keywords:
Non-coding RNAs, Micro-RNAs, Melanoma, Molecular therapy

P065

Can seasonal Variations affect breast cancer? (Review)

Vajihe Nayebzade

Vajihe Nayebzade[1*], Hengameh Dortaj[2]

1) MsC student, Faculty of Medicine, Shahid Sadoughi University of Medical Sciences and Health Servicesi, Yazd, Iran
2) MsC, Faculty of Medicine, Shahid Sadoughi University of Medical Sciences and Health Servicesi, Yazd, Iran
vajihenayebzade16@gmail.com

Abstract:

Introduction: Breast cancer is the most common female cancer. A seasonal variation in the initial detection of breast cancer has been previously observed in pre-menopausal women. The aim of this review was to investigate the Seasonal effects on Mechanisms associated with cancer .

Methods: A search was conducted in the google scholar, Pubmed, Science Direct electronic databases. Articles were relevant for seasonal variations in cancer mechanisms specialized breast cancer rates and detection of breast. Variables were compared using one-way parametric analysis, SPSS (version18) and SAS version 9.3.

Result: Female breast cancer patients exhibited an improved survival in the summer as compared to the winter at all latitudes. There was no significant association between later stage of breast cancer and travel. Seasonal changes in detection of breast cancer may in part relate to seasonal changes in hormone responsiveness within tumor tissue. The abnormal reduction of serum melatonin and promote tumor growth and contribute to the decreased survival seen in wintertime in winter detectors of breast cancer observed compared with summer detectors.

Conclusions: The relatively normal seasonal profile of melatonin observed in summer detectors could allow increased ovarian steroidogenesis in spring/summer with a resulting increase in tumor growth and consequent rise in tumor detection rate at this time. Cyclic changes in tumor growth mediated by the effects of melatonin on ovarian function and vitamin D have a protective role in cancer survival. As a result, seasonal Variations can be effective in breast cancer.

Keywords:

Seasonal Variation, vitamin D, Hormone, breast cancer

P067

Personalize medicine: New epigenetic mechanisms of differentiation umbilical cord mesenchymal stem cells to neural stem-like cells

Yadallah Dalvand

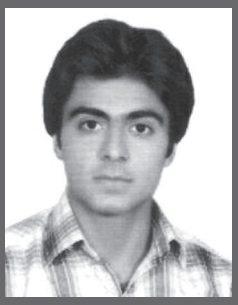
Yadallah Dalvand
Department of Medical Genetics in MOM center, Tehran Iran - dalvandyadola@yahoo.com

Abstract:
Neurodegenerative disorders are great threats to human health, and transplantation of healthy functioning neurons to replace dead neurons is considered to be a viable therapeutic method. Neural progenitor cells (NPCs) can proliferate and more attractive candidate also subsequently differentiate into almost all neural cell lineages, but limited by the number of brain tissue donors other cell sources that can transdifferentiate into neural cells, such as umbilical cord mesenchymal stem cells (UMSCs), are potentially ideal alternative cell sources. UMSCs is sources of multipotent stem cells can transdifferentiate to neural stem-like cells (uNSCL) under natural or experimentally induced conditions.
In this review we assess Epigenetics can be described as a bridge between genotype and phenotype, more important, it provides a powerful tool for regulating key of stem cell development features such cell fate determination, commitment, and differentiation. In new study E1A-like inhibitor of differentiation3 (EID3) directly associates with DNMT3A during transdifferentiation of human umbilical cord mesenchymal stem cells to NPC-like cells. These findings indicated a novel mechanism by which EID3 could directly affect DNMT3A; this enzyme possesses dual methylation and demethylation abilities in cells, as well as protein expression of EID3 is high while DNMT3A is very low in UMSCs; and EID3 is low while DNMT3A is high in uNSCL.
In conclusion we can say there is a relationship between EID3 and DNMT3A during the process of UMSC to uNSCL transdifferentiation. Furthermore, indicating the need to take multiple factors into account as one seeks to understand transdifferentiation mechanism.

Keywords:
Neurodegenerative, Neural progenitor cells, Epigenetics, umbilical cord mesenchymal stem cells

P074

Association of body mass index and waist circumference with bone metabolism markers in Iranian elderly



Hamed Kord-Varkaneh

Hamed Kord-Varkaneh[1*], Sakineh Shab-Bidar[2]

1) Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences (TUMS), Tehran, Iran

* Corresponding author - email: hkord@razi.tums.ac.ir

Abstract:

Objective: There is no agreement on the role of obesity as a protection factor or unfavorable factor on bone. In the present study, the association of body mass index (BMI) and waist circumference (WC) with osteocalcin, C-terminal telopeptide of type 1 collagen (CTX-I), hs-CRP, parathormone (PTH) and 25-hydroxyvitamin D (25(OH)) in elderly was investigated.

Methods: This cross-sectional study was conducted on 178 elderly residents in Tehran, with a mean age of 67.04 (60-83). Serum osteocalcin, hsCRP, 25(OH) D, PTH and urine CTX-I, were measured for all participants. Waist circumference, weight and height were measured and BMI was calculated. Linear regression and Pearson Correlation were performed to evaluate the relation of BMI and waist circumference with other variables.

Results: A significant inverse association was found between BMI with osteocalcin ((Beta = -.171, p= 0.027)) after control for covariates. In addition, there were a statistically significant relation of BMI and WC with hs-CRP (Beta =0.246, p= 0.002 and Beta =0.219, p= 0.006, respectively), and PTH (Beta = 0.1169, p= 0.040 and Beta = 0.200, p= 0.018), respectively). The present study didn't show a statistically significant relation of BMI and WC with urine CTX-I after adjustment for potential confounders (Beta =-0.143, p= 0.065 and Beta = -0.104, p= 0.183, respectively).

Conclusion: The present study has concluded that obesity is an undesirable factor in bone by reduced serum osteocalcin and increasing hs-crp and PTH which contribute to bone resorption, beauty of this region.

Keywords:

obesity, bone marker, elderly, osteocalcin, CTX-I

P076

CRISPR/Cas9-mediated Genome Editing

Elahe Kamali

Elahe Kamali[1], Zohreh Hojati[1*], Fatemeh Rahbarizadeh[2], Mehdi Shamsara[3]

1) Division of Genetics, Department of Biology, Faculty of Science, Isfahan University, Isfahan, Iran
2) Department of Medical Biotechnology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran
3) Department of Animal, Avian and Marine Biotechnology, National Institute of Genetic Engineering and Biotechnology, Tehran, Iran
* Corresponding author - z.hojati@sci.ui.ac.ir

Abstract:
Adoptive immunotherapy with genetically-engineered T-cells, specially CAR-T cell therapy, has shown promise in clinical trials. However, this approach is limited by the requirement of generating autologous, patient-derived, T-cells, which is costly, labor-intensive, and time-consuming. To create CAR-T therapy more attainable, a methodology which allow the generation of allogeneic universal T-cells would be highly recommended. When allogeneic CAR T cell infusion is considered, host versus graft and graft versus host reactions must be avoided to elicit successful antitumor activity. In this project, we exploit the CRISPR/Cas9-mediated editing system to develop a process for manufacturing of T cells deficient in expression of some alloreactive antigens. gRNAs design using the available online tools, cloning of the gRNAs oligo inserts into the pSpCas9(BB)-2A-GFP and pSpCas9(BB)-2A-Puro plasmids by Golden Gate Assembly cloning strategy, Sequence validation of CRISPR plasmids, Transfection of sequence verified plasmids into HEK293 Cell line (functional validation), Selection of transfected Cells, Screening of CRISPR/Cas9-Mediated Deletions.
gRNAs were designed and cloned to recognize and cleave the coding sequences of human TRAC and CD52 genes. Two or three colonies were picked to check for the correct insertion of gRNAs. The sequence of each colony was verified by sequencing to check the insertion of guide sequence between the U6 promoter and the remainder of the gRNA scaffold. The sequence verified clones were selected to transfect the HEK293 cell line to validate the efficiency of gRNAs. Transfected cells were selected by FACS or antibiotic selection to validate the functional efficiency at genomic level.

Keywords:
Adoptive Immunotherapy, Gene editing, Universal T Cell, CRISPR/Cas9

P077

Mir-21 is a New Biomarker for Personalized Oncology

Alina Abdolahi

Alina Abdolahi[1,2], Mohammad Abdi[2], Shima Rahmati[1,2]

1) Student Research Committee, Kurdistan University of Medical Science, Sanandaj, Iran
2) Cellular & Molecular Research Center, Kurdistan University of Medical Sciences, Sanandaj, Iran
*Corresponding author - alina.abdolahi@yahoo.com

Abstract:
Lung cancer is the most common cause of death among all cancers and despite advances in combination chemotherapies, the prognosis of lung cancer is still dismal. miRNAs are a class of endogenous non-coding RNAs, that are inhibit gene expression at the post-transcriptional level. The levels of individual miRNAs vary significantly between tissues, developmental stages and physiological processes. The tissue- and disease-specific expression patterns of miRNAs indicate their potential as diagnostic and prognostic cancer biomarkers and therapeutic tools and helpful in matching targeted therapies with patients.
A total of 40 newly diagnosed primary lung cancer patients and 40 cancer-free subjects were enrolled in this study. All the patients were classified according to the 7th International Union Against Cancer tumor, lymph node, and metastasis staging system. Total RNA was extracted from blood using TRIzol reagent according to the manufacturer's protocol. Quantitative real-time PCR (qRT-PCR) was performed. The special primer was used to synthesize miR-21 cDNA. The relative expression of genes was calculated using the $2^{-\Delta\Delta Ct}$ method from an independent experiment, and HGPRT was used to normalize mRNA.
In the present study, we found that miR-21P was frequently up-regulated in lung cancer patients than control group and also the increasing miR-21p expression was closely related to advanced stage and lymph node metastasis of NSCLC.

Keywords:
Biomarker, Personalized Oncology, Lung Cancer, MicroRNA.

P078

A meta-analysis on vitamin D level and vitamin D deficiency with risk of preeclampsia: an approach to individualized therapy

Babak Khodadadi

Babak Khodadadi[1*], Seyyed Amir Yasin Ahmadi[2]

1) Young Reserchers and Elite Club,Khorramabad Branch,Islamic Azad University,Khorramabad,Iran
2) Scientific Society of Evidence-based Knowledge, Lorestan University of Medical Sciences, Khorramabad, Iran
*Corresponding Author - Khodadadi_babak@yahoo.com

Abstract:
Introduction: Vitamin D level can be a good serum manifestation of FOXP3, VDR and IL-10 genes polymorphism and expression. Because of the immune modulatory effects of vitamin D3 in preeclampsia via affecting such genes, we intend to have a meta-analysis on association of both 25-hydroxy vitamin D (25-OHD) level (parametric approach) and 25-OHD deficiency (non-parametric approach) with preeclampsia. As well, for the parametric part, we used receiver operating characteristic (ROC) curve model.
Methods: We used Web of Science, PubMed and Science Direct data bases through searching in titles. Google Scholar search engine was used in order to find missing papers. Finally 23 studies were imported. Both random and fixed models were reported. This meta-analysis is a part of a thesis entitled "Association of FOXP3 gene polymorphisms with risk of preeclampsia". The registration number is LUMS: A-10-1869-1.
Results: Based on the forest plot, lower levels of 25-OHD were significantly associated with risk of preeclampsia (fixed and random P<0.001). Based on the forest plot, vitamin D deficiency (25-OHD <20 ng/ml) was significantly associated with risk of preeclampsia (fixed P<0.0001; random P =0.0029; fixed OR=1.33; random OR=1.54). Based on ROC curve results, we found 2 cutoffs of 10.60 and 20.05 ng/ml.
Conclusion: Women with vitamin D deficiency at cutoff 20 ng/ml are more at risk of preeclampsia. This association can be specific up to 90% at 10.60 ng/ml cutoff. Treatment of vitamin D deficiency is necessary before pregnancy.

Keywords:
vitamin D, immune modulation, preeclampsia, meta-analysis

P079

Limitations and solutions in precision medicine for Breast cancer

Behnoosh Tasharrofi

Behnoosh Tasharrofi
Department of Medical Genetics, Shahid Beheshti University of Medical Sciences, Tehran, Iran - Zeynab.imanisaber@gmail.com

Abstract:
Introduction and aim: Breast cancer has caused many questions for researchers on the metastasis feature due to its diverse genetic and histologic molecular profiles and metastatic aspects of this cancer are one of the big challenges that every patient and doctor faces to find the best treatment. It is necessary to apply the drug development regarding this type of diversity so that both the patient will suffer the least physical and mental damage and incur the least cost as well as the doctor will be able to treat effectively and purposefully; this will not be possible except by examining the individual profile of each cancer.
Method: Identification of driver mutations, for example, has also remained as the biggest challenge and Development of a bioinformatics tools can help solve this problem along with evaluating the pathway activation and dependency. The occurrence of the secondary resistance, such as ESR1 mutations following Endocrine Therapy raises further challenges. Ultra Deep sequencing and the examination of circulating tumor DNA can cause early detection of the genetic events, including the resistance and awareness of the combination therapy. The practical issues also create the main limitations for the personal medicine progress like the low incidence of most genomic alterations and the number of the screened.
Conclusion: We discuss these limitations and their solutions, including increasing the number of the patients who are examined to detect their genomic variations, categorizing the genomic variations in different pathways and developing the experiments in the field of personalized medicine.

Keywords:
personalized medicine, Breast cancer, molecular profile, drug development

P081

Personalized medicine in treatment of prostate cancer

Samane Eftekhari

Samane Eftekhari, Parastoo Tarighi*, Reza Nekouian
Department of Medical Biotechnology, Faculty of Allied Medicine, Iran University of Medical Science, Tehran, Iran
*Corresponding author - Tarighi.p@iums.ac.ir

Abstract:
Advancements in tumor profiling technologies like next Generation Sequencing have improved our understanding of prostate cancer(PCa) biology, guiding precision medicine in the near future. Personalized medicine is a considerable approach for matching patients with the best treatments regarding to their drawbacks. PCa, the second leading cause of cancer related death in men, has heterogeneity in onset, progression and drug responses. However, the only available biomarker for its early diagnosis is PSA (prostate Specific Antigen) test. This serum based biomarker has low specificity, which has led to over-screening, over-biopsy and even over-treatment in men with average or low cancer risk. To overcome these obstacles, many studies are looking for new biomarkers for precised diagnosis and prognosis. In this field, some specific biomarkers have been introduced, including: LncRNAs(Long Non-Coding RNAs); such as PCAT-14 and PCA-3, and also cell free miRNAs;etc. Furthermore, genetic analysis are also considerable and some variations, such as ERG-TMPRSS2 gene fusion, mutation of Spop, FoxA1;etc are being reported as specific genetic markers for PCa. For evaluating these mutations individually, two operative techniques should be done continuously; isolating single circulating tumor cells(CTCs) from bloodstream and whole-exome sequencing on CTCs genetic material. Following these procedures, we would be able to analyse mutations, and guide therapy choices, trace the genomic evolution and even monitor drug resistances.
Personalized medicine has opened new horizon for proper diagnosis and treatment. Therefore, we could step beyond the implementing just a serum-based test and pay more attention to genetic variations of individuals.

Keywords:
Personalized medicine, Prostate cancer, Biomarker, Sequencing

P083

Biomarkers for the management of Prostate cancer

Fatemeh Mansouri

Fatemeh Mansouri[1,2*]

1) Department of Genetics and Immunology, Faculty of Medicine, Urmia University of Medical Sciences, Urmia, Iran
2) Cellular and Molecular Research Center, Urmia University of Medical Sciences, Urmia, Iran
*Corresponding author - mansouri1600@hotmail.com

Abstract:
Prostate cancer can be described in several steps: benign, high-grade PIN (Prostatic intraepithelial neoplasia), primary adenocarcinoma, metastasis and therapeutic resistance. A major challenge in cancer research is to understand the underlying mechanisms of cancer. Great effort has been spent on determining genes, biomarkers and many observable morphological events associated with prostate cancer.
Biomarkers and exosomal miRNAs are potential candidate biomarkers for detection, progressive and therapeutic agent and to monitor the treatment response in prostate tissue and biofluids and more than 50 miRNA have been identified. Reduced or increased expressions profiles of biomarker correlate with clinicopathological progression of prostate cancer including high Gleason score, peri-neural invasion and lymph node metastasis. The role of individual tumor biomarkers by utilized those as drugs or drug targets may adequately reflect as diagnostic power than serum prostate specific antigen (PSA), Prostate cancer antigen 3(PCA3) and other markers. Another hallmark of pathological prostate cancer is activation of a set of molecular heredities genes such as p27/CDKN1B, MYC, GSTP1, BCL-2, ETS gene fusions and loss of PTEN. These gene analyses provide an important insight into miRNA association with disease and disease progression and miRNAs can directly regulate these genes in prostate cancer.
Unlike other markers, mirRNAs levels are stable over long periods, have no diurnal variation, can be measured inexpensively with available high-sensitivity assays and have shown specificity in terms of predicting the risk of cancer.
Biomarkers are very informative at each tumor stages (low-stage or high-stage) and help eliminate invasive biopsies or unwanted surgery. Personalized biomarkers therapies are considered as new methods of targeted drug delivery and clinical trials for a good response to therapy to each patient's requirements.

Keywords:
Prostate cancer, Biomarkers, Exosomal miRNAs

P084

MicroRNA-based therapies: Small biomarkers with big clinical application

Fatemeh Mansouri

Fatemeh Mansouri[1,2*]

1) Department of Genetics and Immunology, Faculty of Medicine, Urmia University of Medical Sciences, Urmia, Iran
2) Cellular and Molecular Research Center, Urmia University of Medical Sciences, Urmia, Iran
*Corresponding author - mansouri1600@hotmail.com

Abstract:
Recent works have discovered, several microRNAs have now opened up new start in the field of medicine for new targets for further therapeutic approaches and prognostic options. The task now is to develop safe and effective tools that can deliver therapeutic genes into specific cell lines and maintain long-term regulated expression of target genes. There is growing evidence some miRNA may promote tumorigenesis and development of cancers and appear as an oncomir. MiRNAs can be roughly divided into two groups: tumor suppressor and oncogenic miRNAs. Various microRNAs can contribute to creating a suitable tissue microenvironment into a variety of cell types for bioengineered implants in patients. MicroRNAs have been demonstrated in different genomic locations: intergenic miRNA genes, intronic miRNAs, within both protein coding genes and long non-coding RNAs, and exonic miRNAs. MicroRNAs can increase the proliferation, angiogenesis and cell survival via different molecular targets. Selected miRNAs can release growth factors, drugs and cytokines into different cells and tissue.
MiRNAs are stable and present in blood circulation and rapidly growing number of reports of these molecules as biomarkers for various diseases. Approaches of miRNA-based tissue regeneration therapies including: wound healing, decreasing collagen accumulation and reducing fibrosis.
MiRNAs are stable and levels of specific miRNAs can be regulated by different strategies such as i) delivery of synthetic oligonucleotides miRNA and ii) overexpression of miRNAs transcripts to up regulate or down regulate their activity in target cells.
There are several methods for delivery of miRNAs and anti-miRs into target cells and tissues:1) direction injection systemic or subcutaneous injection of miRNAs by direction injection; 2) different viral vectors (AAV, Retrovirus, Lentivirus, Baculovirus); 3) chemically modified miRNAs (decoy-based strategies and sponges); 4) non-viral carriers (Cells as carriers, Liposomes, Cationic liposomes, Natural and synthetic polymers, hydrogels and nanoparticles). These are attractive tools for local release of growth factors and resistant to nucleases.
Therefore miRNA-based therapies will help to overcome some of the limitations intrinsic to the extracellular environment to attain the desired therapeutic efficacy into the target tissue type. As a result, attention has increasingly turned to the role of individual tumor biomarkers, to use those biomarkers for development of personalized medicine and treatment strategies.

Keywords:
MicroRNA, Therapy, Clinical application

P087

Proteoglycans and Colorectal Cancer: A review Study

Mohammad Hasan Soheilifar

Mohammad Hasan Soheilifar[1], Abdolvahab moshtaghian[2], Razieh Amini[1*]

1) Research centre for molecular medicine and genetics, School of Medicine, Hamedan University of Medical Sciences, Hamedan, Iran
2) Deputy of Research and Technology, Semnan University of Medical Sciences, Semnan, Iran
*Corresponding author e-mail - aminra14@gmail.com

Abstract:
Introduction: Understanding the molecular mechanisms underlying colorectal cancer (CRC) is a crucial point in finding novel biomarkers and treatment strategies. PGs have important roles in gastrointestinal tract cancers including CRC. The expression pattern of some PGs is deregulated in CRC. The aim of this study was to investigate the effect of PGs deregulation in CRC progression.
Method: This mini review gathered from research and review studies published in valid databases including PubMed, Science Direct, Medline, Google scholar and Scopus using the following keywords: proteoglycan, colorectal cancer, tumorigenesis and signaling pathways. Result: Proteoglycans have a dual role in colon cancer. Expression of oncogene and tumor suppressor PGs change in CRC and their related functions or signaling pathways involved in CRC have been shown in different research studies. It has been demonstrated that shed Syndecan-1, Syndecan-2, CD44, Testican, Betaglycan and Biglycan are overexpressed in CRC and have oncogenic role by activation of EGFR, FAK/ERK, Wnt, PI3K/Akt, MAP and ERK signaling pathways respectively. Lumican and Versican upregulation involved in adenoma-to-carcinoma progression. However some proteoglycans such as Decorin is downregulated in CRC and plays tumor suppressor role by stabilization of E-cadherin. Conversely, sundecan-2 promotes E-cadherin shedding by the protease MMP-7. Contradictory to shed form of syndecan-1, the transmembrane form is downregulated and involved in inflammation-driven colon tumorigenesis. Agrin is upregulated in serum of CRC patients, however, its function is not yet identified.
Conclusion: One of the most common cancers in the digestive tract is CRC. Investigation of molecular pathways in colon tumorigenesis revealed proteoglycans as important mediators in cancer cell signal transduction pathways. Expression of PGs changes in gastric cancer and can be used as potential diagnostic and prognostic biomarker in CRC.

Keywords:
Proteoglycan, Colorectal Cancer, Tumorigenesis, Signalling pathways

P088

Proteoglycans in Gastric Cancer: A review Study

Mohammad Hasan Soheilifar

Mohammad Hasan Soheilifar[1], Abdolvahab moshtaghian[2], Razieh Amini[1*]

1) Research centre for molecular medicine and genetics, School of Medicine, Hamedan University of Medical Sciences, Hamedan, Iran
2) Deputy of Research and Technology, Semnan University of Medical Sciences, Semnan, Iran
*Corresponding author e-mail - aminra14@gmail.com

Abstract:
Introduction: PGs are glycosylated proteins with context-dependent function and are expressed in the extra cellular matrix (ECM), in the cell and on the cell surface. The expression patterns of proteoglycans (PGs) change in the gastric cancer. Gastric cancer is one of the major causes of cancer related death in the world. PGs have important roles in initiation and progression of gastric cancer. The present study aimed to investigate various functions of PGs in gastric cancer
Methods: In this study we reviewed research articles published in online databases including PubMed, Science Direct, Medline, Google scholar and Scopus using relevant keywords such as: proteoglycan, gastric cancer and signaling pathways and tumorigenesis.
Results: Changes in PGs expression and their functions or signaling pathways involved in gastric cancer.
It has been shown in various research studies that more proteoglycans are upregulated in gastric cancer. Asporin, Biyglycan and Lumican overexpressed in gastric cancer and involved in EGFR, FAK and integrin β1-FAK signaling pathways respectively. SRPX2 promote cell migration and adhesion through FAK signaling. So it could be concluded, FAK signaling has major role in proteoglycans oncogenic functions in gastric cancer. Furthermore Versican and Syndecan-2 play important role in cancer cell migration, invasion and proliferation. Testican induce slug-mediated epithelial-mesenchymal transition in gastric cancer. On the other hand, some proteoglycans like Serglycin and Syndecan-1 are downregulated in gastric cancer but the exact role and signaling pathways that these proteoglycans involved in have not been identified yet. Although it seems that these molecules may play tumor suppressor role in gastric cancer.
Conclusion: PGs expression patterns altered during gastric cancer development. Although the biological role of some PGs like serglycin is still not fully understood in gastric cancer but it has been shown that PGs act as an oncogene or tumor suppressor and involved in tumor signaling pathways through mediation of ligand/receptor interaction and promote or inhibit cancer cells migration and invasion. In conclusion deregulated expression of PGs involved in carcinogenesis and can be used as potential biomarkers for gastric cancer diagnosis, prognosis and in cancer treatment.

Keywords:
Proteoglycan, Gastric Cancer, Tumorigenesis, Signalling pathways

P089

Classifying the Evolutionary and Ecological features of Neoplasms

Dr.Mohammad Mehdi Jahani

Mohammad Mehdi Jahani[1], Zeynab imanisaber[2*]

1) Islamic azad university, shahrekord branch, faculty of veterinary medicine,Shahrekord,Iran.Email:mmehdi_jahani@yahoo.com
2) Tehran university of medical science, department of medical genetics,Tehran,Iran,Email:Zeynab.imanisaber@gmail.com
*Corresponding author

Abstract:
Neoplasms undergo a process of cell-level evolution driven by genetic and epigenetic changes over time. The microenvironement's alterations of neoplastic cells and it's positive or negative effects are very significant for patient's survival or failure of treatment.
Unfortunately, there is not any proposed system for making a clinical distinction between different evolving tumors regarding their alterations and whether theses alterations benefited the patients or not. In this article, by reviewing the four relevant components, we propose a frame work for classifying tumors.
By considering indices such as evolutionary index which evaluate the changes of diversity of neoplastic cells over time; and ecologic index which is concentrated on effects of these changes neoplastic cell survival, we represent comprehensive classification of tumor heterogeneity. This classification is mentioned in some reach resources. Using this measurement for predicting the effect of alteration are very important study tools.
Finally, development of this classification system enables clinicians to do a personalized optional intervention according to the evolvability of the patient's tumor. These indices provide a common lexicon for communicating about how neoplasms change in response to interventions, with potential implications for clinical trials, personalized medicine and basic cancer research.

Keywords:
neoplasm; Eco-index; Evo-index; cancer heterogeneity; measurement model

P090

A novel stop-gain mutation in the MSH2 gene among a Persian family fulfilling classic Amsterdam criteria for Lynch syndrome

Dr.Mehrdad Zeinalian

Mehrdad Zeinalian[1,2*], Mohammad Hassan Emami[3], Mohammad Amin Tabatabaiefar[1], Morteza Hashemzadeh-Chaleshtori[4]

1) Department of Genetics and Molecular biology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
2) Ala Cancer Prevention and Control Center, Isfahan, Iran
3) Gastrointestinal and Hepatobiliary Diseases Research Center, Poursina Hakim Research Institute for Health Care Development, Isfahan, Iran
4) Cellular and Molecular Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran
*Corresponding author - zeinalianmehrdad@gmail.com

Abstract:
Lynch syndrome (LS) is the most common hereditary cancer predisposing syndrome whose molecular pathogenesis is germline mutations in at least one of the four DNA mismatch repair (MMR) genes including MLH1, MSH2, PMS2, and MSH6. We report in this article a new pathogenic variant of MSH2 gene which was found in a Persian family with LS.
We designed a case series study for clinical and molecular screening of CRC patients at risk for LS in central Iran. Using Amsterdam II criteria (AC-II), 31 families were candidate for immunohistochemically staining (IHC-MMRs) and microsatellite instability (MSI) testing. Finally, 7 probands were diagnosed as MMR deficient and harbored genetic testing through next generation sequencing (NGS) of the candidate genes. Bioinformatic analysis was performed to identify pathogenic variants according to ACMG guidelines. A co-segregation analysis of the variant was run using genomic DNA of three first degree relatives of the proband, one affected and two others healthy.
After NGS mutation analysis of MMR genes, a likely pathogenic-related variant was identified on the first exon of MSH2 gene on chromosome 2 (rs374127044) which had been caused by an A>T change on the first exon of MSH2 gene (NM_000251.2:c.364A>T). This heterogeneous mononucleotide substitution creates a stop codon-gained mutation. Sanger sequencing of an amplified genomic DNA segment including the variant revealed a similar heterogeneous variant in the proband's affected father. But, none of two healthy sisters of the proband presented this variant. Given the lack of enough molecular and clinicopathologic information about LS affected families among Iranian populations, more evaluations are recommended to explore other pathogenic variants of MMR genes among Iranian LS families.

Keywords:
mutation, MSH2 gene, Amsterdam criteria, Lynch syndrome

P093

MicroRNAs: New Powerful Weapons in Personalized Colon Cancer Treatment

Natita Tavazohi

Nazita Tavazohi[1], Mina Mirian[1,*], Hamid Mir Mohammad Sadeghi[1], Homa Talabaki[1]

1) Department of Pharmaceutical Biotechnology, School of Pharmacy, Isfahan University of Medical sciences, Isfahan, Iran.
mina.mirian@yahoo.com

Abstract:

Introduction and background: Although chemotherapy is an important therapeutic strategy in colon cancer, but resistance to chemotherapy is one of the biggest threats. Recent studies indicate that some molecules like microRNAs (miRNAs) play critical regulatory role in development of drug resistance to colon cancer. MiRNAs are single- stranded non-coding molecules that can regulate mRNA translation. The specific miRNA profile modulates distinctly resistance and sensitivity to chemotherapy drugs, affecting the expression of cancer genes. Here, we highlight the recent advancements in miRNA-associated chemoresistance researches which are the most common and serious obstacle in colon cancer treatment.

Methods: In this narrative review, a comprehensive search of PubMed database was performed with the following Mesh term search using keyword: MicroRNA along with keywords: colon cancer and drug resistance. Published data have been included since first finding until August 2017, in the study. The inclusion criteria for the study were: all studies that introduced new MicroRNA associated with chemoresistance and chemosensitivity in colon cancer treatment.

Results: The results from 83 papers provide a broad view of miRNAs involved in the response to chemotherapy in colon cancer.

Discussion and Conclusion: Numerous studies have revealed novel aspects of various cellular microRNA-regulated networks such as proliferation, cell cycle, survival and cancer-specific metabolism pathways developed chemoresistance involved in colon cancer. Moreover, recent studies have demonstrated that different microRNAs increase tumor chemosensitivity with induce apoptosis and cell cycle arrest and decrease expression of drug efflux pump genes. Thus, these molecules potentially influence the efficacy of popular chemotherapeutic agents such as 5-fluorouracil, paclitaxel, oxaliplatin, irinotecan, doxorubicin, cetuximab in colon cancer. Therefore, cancer-specific miRNAs signatures provide powerful new weapon in the battle against cancer drug resistance based on personalized cancer care. Lastly, in this review we focus on the latest advances related to miRNA that increase resistance or sensitivity to common anticancer drugs and discuss about opportunities and limitation of miRNA applications for precision colon cancer medicine.

Keywords:

Colon cancer, MicroRNAs, Chemoresistance, Chemosensitivity, Precision medicine

P095

Targeted therapy in metastatic differentiated thyroid Carcinoma (DTC)

Hamid Reza A. NAGHASH

A.Naghash H[1,4], Ansarinejad N[2,4],Abbasi B[3,4] , Ramim T[4], Fardad F[2,4], Houshmand M[3]

1) Karaj Branch, Islamic Azad University,Karaj,Iran
2) Iran University of Medical Sciences,Tehran,Iran
3) National Institute of Genetic Engineering and Biotechnology (NIGEB),Tehran,Iran
4) Cancer Pharmacogenetics Research Group (CPGRG), Iran University of Medical Sciences, Tehran, Iran
Corresponding author - hamidnaghash@yahoo.com

Abstract:
Differentiated thyroid carcinoma (DTC), is the most common endocrine malignancy, approximately 3 -- 15% DTC patients have distant metastases at presentation and recurrent disease is diagnosed during the further follow-up in up to 30% of patients, among them distant metastases in 6 -- 23%.
Some advanced cases have a poor prognosis, especially cases of radioiodine- refractory or radioiodine-resistant DTC and cases of medullary thyroid cancer (MTC) and anaplastic thyroid cancer (ATC) that are unresectable because they are locally advanced or metastatic, etc., and their prognosis is poor.
Preclinical studies have demonstrated that sorafenib inhibits tumor growth in a wide spectrum of human cancers (melanoma, renal, colon, pancreatic, hepatocellular, thyroid, ovarian, and non-small cell lung carcinomas (NSCLCs)) and in some cases induces tumor regression. In 2013, sorafenib was also approved by the FDA to be the first-line treatment option in advanced, radioiodine-refractory differentiated thyroid carcinoma (DTC).
Sorafenib inhibits tumor cell proliferation and angiogenesis via targeting numerous serine/threonine and tyrosine kinases (RAF1, BRAF, VEGFR 1, 2, 3, PDGFR, KIT, FLT3, FGFR1, and RET) in multiple oncogenic signaling pathways. Resistance to sorafenib may appear under treatment and may be associated with increased aggressiveness of the neoplasia.
In this review, we discuss the clinical pharmacology of sorafenib and highlight genetic variations that may contribute to the diverse pharmacological responses to sorafenib. Better understanding of the factors contributing to the high variability of response to sorafenib should improve the efficacy and safety of the drug, and help select patients who will benefit most from sorafenib therapy.

Keywords:
Differentiated thyroid carcinoma, Sorafenib, BRAF, RET, FGFR1

P096

Inhalation exposure of Biological barrier nanoparticle induced oxidative stress in Au

Farimah jamal navaei

Farimah jamal navaei, Dr.Parvane Naserzadeh, Dr Mehrdad Hashemi
Islamic Azad University of Medical Science Tehran,iran
Department of Pharmacology and Toxicology, Faculty of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Department of medical biotechnology Tehran Medical Science brunch Islamic azad university Tehran,iran
Farimahnavai@yahoo.com

Abstract:
1. With the ever-increasing use of biological barrier in health-related and engineering applications, the hazardous risks of this material have become a major concern. It is well known that biological barrier accumulate with cytotoxic and genotoxic levels within vital organs. It has also been shown that treating cell cultures with biological barrier resulted in cell cycle arrest and increased apoptosis/necrosis.
2. In this study, we investigated chronic exposed to biological barrier at the exposure chamber in mice. The animals were divided into two groups (control and exposed group to biological barrier at the concentration of 3 µg/m3 for 5 h/day,) in a whole-body inhalation chamber.
3. Our results showed that exposure to biological barrier induced the hematological and biochemical changes. The target organs for biological barrier were the Au in the mice, respectively. Also, NPs increased reactive oxygen species (ROS) generation, lipid peroxidation (LPO), the collapse of mitochondrial membrane potential (MMP), decreased a level of reduced glutathione (GSH) and finally increased a level of glutathione disulfide (GSSG) in Au tissues. Our results suggest that exposure to biological barrier can induce oxidative stress in the tissue mentioned.
4. These results suggest that exposure of researchers and workers with biological barrier probably increase a risk of respiratory, cardiovascular and cerebral disorders through oxidative stress. However, good ventilation, appropriate personal protective equipment and using of anti-oxidant compounds in daily diet of worker are suggested.

Keywords:
biological barrier, chronic exposure, oxidative stress, reactive oxygen spices

P099

Predictive role of genetic variants in neoadjuvant chemotherapy of breast cancer

Hamid Reza A. NAGHASH

A.Naghash H[1,4], Ansarinejad N[2,4],Abbasi B[3,4] , Ramim T[4], Fardad F[2,4], Houshmand M[3]

1) Karaj Branch, Islamic Azad University,Karaj,Iran
2) Iran University of Medical Sciences,Tehran,Iran
3) National Institute of Genetic Engineering and Biotechnology (NIGEB),Tehran,Iran
4) Cancer Pharmacogenetics Research Group (CPGRG), Iran University of Medical Sciences, Tehran, Iran
Corresponding author - hamidnaghash@yahoo.com

Abstract:

Variation in the human genome is a most important cause of variable response to drugs. Different patients respond in different ways to the same medication. There are many inter-individual differences in drug response owing to the sequence variants of genes that encode drug-metabolizing enzymes, drug transporters, or drug targets.

Many studies have shown that genetic factors greatly contribute to influence the variability in drug effects. Current advances in the biology of cancer and emergence of high-throughput sequencing for genome analysis are expected to provide new approaches for optimizing treatment and lead the future direction for personalized medicine.

Chemotherapy is an impor¬tant adjuvant systemic therapeutic approach for the successful treatment of breast cancer and, during early stage breast cancer, has been demonstrated to improve survival rate.

Most of the drug-metabolizing enzymes and transporters have a broad range of genetic polymorphisms, which may cause inter-individual variability with different concentrations of drugs. In addition, anticancer therapies are known to have a narrow therapeutic range; a high concentration in a patient's body increases the toxicity, and a low concentration decreases the effect of the drug.

Various combinations of cytotoxic chemotherapeutic drugs such as cyclophosphamide, anthracyclines, and taxanes are an integral part of the systemic treatment of breast cancer patients.

Genetic variations such as single nucleotide polymorphisms (SNPs) are present across individuals and might affect pharmacokinetics and pharmacodynamics of drugs.

In this review, we highlight obtained from recent studies on genetic variants associated to pharmacokinetics and pharmacodynamics of most of the important drugs used in neo-adjuvant chemotherapy of breast cancer like cyclophosphamide, doxorubicin, Epirubicin, paclitaxel, docetaxel and 5-fluorouracil.

Keywords:

breast cancer, genetic polymorphisms, neo-adjuvant chemotherapy, cyclophosphamide, doxorubicin, Epirubicin, paclitaxel

P101

Inhalation exposure of diamond nanoparticle induced oxidative stress in melanoma

Maryam mirzaei

Maryam mirzaei, Dr.Parvane Naserzadeh, Dr Mehrdad Hashemi
Islamic Azad University of Medical Science Tehran,iran
Department of Pharmacology and Toxicology, Faculty of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Department of medical biotechnology Tehran Medical Science brunch Islamic azad university Tehran,iran
Maryam.mirzaeiiii.1396@gmailcom

Abstract:
1. With the ever-increasing use of (Diamond) in health-related and engineering applications, the hazardous risks of this material have become a major concern. It is well known that diamond accumulate with cytotoxic and genotoxic levels within vital organs. It has also been shown that treating cell cultures with diamond resulted in cell cycle arrest and increased apoptosis/necrosis.
2. In this study, we investigated chronic exposed to diamond at the exposure chamber in mice. The animals were divided into two groups (control and exposed group to diamond at the concentration of 3 µg/m3 for 5 h/day,) in a whole-body inhalation chamber.
3. Our results showed that exposure to diamond induced the hematological and biochemical changes. The target organs for diamond were the melanoma in the mice, respectively. Also, NPs increased reactive oxygen species (ROS) generation, lipid peroxidation (LPO), the collapse of mitochondrial membrane potential (MMP), decreased a level of reduced glutathione (GSH) and finally increased a level of glutathione disulfide (GSSG) in melanoma tissues. Our results suggest that exposure to diamond can induce oxidative stress in the tissue mentioned.
4. These results suggest that exposure of researchers and workers with diamond probably increase a risk of respiratory, cardiovascular and cerebral disorders through oxidative stress. However, good ventilation, appropriate personal protective equipment and using of anti-oxidant compounds in daily diet of worker are suggested.

Keywords:
Diamond, chronic exposure, oxidative stress, reactive oxygen spices

P102

Inhalation exposure of Graphene nanoparticle induced oxidative stress in Melanoma

Rezvane Doroudian

Rezvane Doroudian, Dr.Parvane Naserzadeh, Dr Mehrdad Hashemi
Islamic Azad University of Medical Science Tehran,iran
Department of Pharmacology and Toxicology, Faculty of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Department of medical biotechnology Tehran Medical Science brunch Islamic azad university Tehran,iran
parniyan70@yahoo.com

Abstract:
1. With the ever-increasing use of Graphene nanoparticle in health-related and engineering applications, the hazardous risks of this material have become a major concern. It is well known that Graphene NPs accumulate with cytotoxic and genotoxic levels within vital organs. It has also been shown that treating cell cultures with Graphene NPs resulted in cell cycle arrest and increased apoptosis/necrosis.
2. In this study, we investigated chronic exposed to Graphene NPs at the exposure chamber in mice. The animals were divided into two groups (control and exposed group to Graphene NPs at the concentration of 3 µg/m3 for 5 h/day,) in a whole-body inhalation chamber.
3. Our results showed that exposure to Graphene NPs induced the hematological and biochemical changes. The target organs for Graphene NPs were the melanoma in the mice, respectively. Also, NPs increased reactive oxygen species (ROS) generation, lipid peroxidation (LPO), the collapse of mitochondrial membrane potential (MMP), decreased a level of reduced glutathione (GSH) and finally increased a level of glutathione disulfide (GSSG) in melanoma tissues. Our results suggest that exposure to Graphene NPs can induce oxidative stress in the tissue mentioned.
4. These results suggest that exposure of researchers and workers with Graphene NPs probably increase a risk of respiratory, cardiovascular and cerebral disorders through oxidative stress. However, good ventilation, appropriate personal protective equipment and using of anti-oxidant compounds in daily diet of worker are suggested.

Keywords:
Graphene NPs, chronic exposure, oxidative stress, reactive oxygen spices

P104

Role of radiation oncology in precision medicine

Parisa Esmaeili Kordlar

Parisa Esmaeili Kordlar[1]*, Z.Imani Saber[2], M. Taghavi Basmenj[1], M. Mehdi Jahani[3]

1) Molecular Medicine Department, Biotechnology Research Center, Pasteur Institute of Iran, Tehran, Iran
2) Department medical genetic Tehran university of medical science
3) Islamic Azad University, Shahrekord branch, faculty of veterinary medicine
*Corresponding author - Parisaesmaili64@gmail.com

Abstract:
Precision medicine is a therapeutic model in which most diagnostic tests are used to find optional therapeutic approaches based on the genetic content of a person. Such tools applied in precision medicine are molecular diagnosis and radiotherapy. Current advanced photon-based radiotherapy techniques including IGRT, IMRT and Stereotyping Radiation Therapy (SRT), are close to physical level of forming high doses to target tissue volume. However there is still to improve motion control and imaging for radiotherapy. In the past century, radiation oncology, has developed individualized treatments based on anatomical information and clinical parameters. The goal of radiotherapy is to eliminate all stem cells in primary tumor and tumor lymph nodes or oligometastatic diseases, while limiting damage to natural tissues.
Two major strategies will enable further widening of therapeutic window of radiation oncology in precision medicine. Technology based improvement of treatment conforming, including advanced guidance and particle therapy and novel concepts like biomarker-guided prescription combined adaptive treatment mediates. Biomarkers, including bio-imaging, which assess the presence and magnitude of resistance to radiation in tumors, are rapidly emerging ad leading to interventional trials. Unique radiotherapy, in addition to several valid biomarkers for dose administration and treatment planning, can enhance the degree of personalized treatment. Furthermore, radiotherapy based on bioassay tests in very effective for cancer stem cells eradication and distinctive from other methods. Therefore, radiation oncology has potential for personalized cancer treatment.

Keywords:
Precision medicine, Radiation oncology, Biomarkers, photon-based radiotherapy

P106

The role of Precision Medicine in controlling of OSCC according to ethnicity

Hamed Heidari

Hamed Heidary*[1], Ali Mardi[2]

1) Department of Pediatrics, Faculty of Medicine, Ali Asghar Children Hospital, Iran University of Medical Sciences (IUMS), Tehran, Iran.
2) Department of genetics and molecular medicine, school of medicine,zanjan University of medical sciences, zanjan,iran.
* hamedheidary1988@yahoo.com

Abstract:
In dealing with oral cancer, which has recently become one of the prevalent cancers in Asian societies, several factors have to be considered in targeting strategies.
Because of the confrontation of various communities with various environmental, nutritional, and infectious factors that play a major role in oral cancer, race and ethnicity are one of the most important factors to be considered And the expression of should be explained genes according to that particular ethnicity.For example, in the OSCC disease, ABOBEC3B deletions can Significantly be seen as a prognostic factor due to inhibition of acquired immune system in a community with Taiwanese ethnicity that is more exposed to environmental and infectious factors. In this review article, the role of this protein in suppressing acquired immunity and the response of the inherent immune system to this extinction by increasing the expression of A3A has been attempted to identify this factor in the survival of patients with OSCC.
It should be noted that for the targeted treatment of these patients (Personal Medicine), it is very important to pay attention to the type of gene expression in a particular ethnic group. That is why the information obtained from this article is different from the information available in the OSCC-TCGA data base

Keywords:
oscc, ABOBEC3B, A3A, Personal Medicine

P107

miRNA Antagonists: a new strategy to cancer and other diseases treatment

Davod Jafari

Davod Jafari[1], Arshad Hosseini[1*]

1) Department of Medical Biotechnology, School of Allied Medicine, Iran University of Medical Sciences, Tehran, Iran.
*Corresponding author - hoseini.a@iums.ac.ir

Abstract:
As more information gathered from individual miRNAs in recent years, their roles in oncogenesis, progression and suppression in some cancers as well as their involvement in some other diseases, like autoimmune and cardiovascular have been revealed. These cancers are the results of miRNA dysregulation, particularly they are upregulated and then they suppress tumor suppressor genes that leads to tumorization. In this review, we reviewed the latest studies in the miRNA Antagonist development to cancer treatment. In recent years some treatment for these disorders based on miRNA therapy was emerged like miRNA Antagonism and miRNA mimics. A miRNA antagonist is the using of modified nucleotides sequences that has a complementary region to upregulated miRNAs. These nucleotide sequences called anti-miRNA, Antagomir, miRNA sponges and miRNA masks. The first developed anti-miRs target mir-122 in the liver. Locked Nucleic Acid (LNA) anti-miR-221 recently evaluated in NOD.SCID mice. Inhibition of mir-9 with a miRNA sponge make a decrease in the breast cancer metastasis in contrast anti-miR-10b significantly decrease the metastasis but cannot effect in primary tumor growth in breast cancer. Various miRNA antagonists are now under preclinical investigations thus a LNA-anti-mir for Hepatitis C Virus (HCV) called Miravestin is now under phase I and phase IIa clinical trials. RG-101 an anti-miR for mir-122 has undergone to phase I clinical trial. A phase II trial also has performed with RG-101 in combination with real antiviral components like Harvuni that showed a 100% response to drug with no relapse after 24 weeks. These discoveries and clinical trials offer an opportunity for development of miRNA-based cancer-specific therapies. However, it is difficult to identify the best target miRNA for a specific disease.

Keywords:
miR-Antagonist, Cancer, miRNA, AntagomiR

P108

Human Cancer Modeling: effects of tumor heterogeneity on personalized medicine

Sara Boosaliki

S.Boosaliki[1*], K. Forouzanfar[2], M. Mehdi Jahani[3], Z. Imani Saber[2]

1) Medical Genetic Departments, Shahid Beheshti University of medical science, Tehran, Iran
2) Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute Tehran University of Medical Sciences, Tehran, Iran
2) Medical Genetic Department, Tehran University of medical science, Tehran, Iran
3) Islamic Azad University, Shahrekord branch, faculty of veterinary medicine, Shahrekord,Iran
saraboosaliki@sbmu.ac.ir

Abstract:
The extensive analysis of human cancers has shown that development and progression of somatic cancers is not just a simple linear phenomenon, but due to cellular, molecular, cytological and even pathological heterogeneity of cancer tissue cells, the prognosis, diagnosis and treatment of affected patients would be complicated for clinical and laboratory specialists or even patients and their families.
A wide range of studies have been done on the characteristics of the tumor, but cancerous tissues need to be removed. To be studied outside the human body.
Cancer cell lines, xenographts and etc. have significant achievements in discovering the effects of drugs,causes of initial migration of cancer cells to specific tissues and the role of stroma in the development and spread of cancer.
For example, one of the most recent findings from xenographts in the field of personalizing breast cancer treatment is Her2 positive with metastasis in the brain, which include a large number of patients in this category, and so far, the reasons for the highly effective scientific and medical justification have not been explained. Therefore it is possible to represent a personalized breast cancer treatment in a microcategorized form as a potential suppressive factor of metastasis. In this article, we will try to review the use of these models to find the answer to some questions.

Keywords:
Human Cancer Modeling, Cancer heterogeneity, Individualizing treatment

P109

Down-regulated MicroRNA 148a expression as predictive biomarker in lung cancer

Shima Rahmati

Shima Rahmati[1,2], Mohammad Abdi[2], Alina Abdolahi[1,2]

2) Student Research Committee, Kurdistan University of Medical Sciences, Sanandaj, Iran.
3) Cellular & Molecular Research Center, Kurdistan University of Medical Sciences, Sanandaj, Iran
Rahmati_may66@yahoo.com

Abstract:
Lung cancer is one of the most common invasive and lethal cancers in the world. Among the various types of lung cancer, 80% are classified as non-small cell cancers (NSCLCs) and 20% are small cell lung cancer cells (SCLCs). Despite the recent advances in diagnostic methods, such as CT scan that led to early diagnosis still more than 70% of patients are detected in metastatic phase, so finding a method for early detection seems necessary. According to recent studies, miRNAs are considered as tumor suppressors and oncogenes. Therefore, changes in the expression of miRNAs play a crucial role in tumorigenicity and cancer progression. Recently, a subset of miRNAs known as epi-miRNA, can directly or indirectly affect epigenetic processes, which confirms the relationship between miRNAs and epigenetics. The family of miR-148/152 is one of the reported miRNAs in various malignancies. In this study, 40 patients with NSCLC and 40 control samples were considered. miRNA was extracted from 2 groups. Then valuation of miRNA expression was don by using qRT-PCR (normalization whit snord). Finally, statistical analysis was used to compare miRNA expresion between cases and controls.
It has been shown that serum levels of 148a microRNA have been significantly reduced in NSCLC patients compared to control group. Onset and progression of lung cancer is the result of the genetic and epigenetic interaction. One of the most important epigenetic changes that has been studied extensively is DNA methylation. One of the epi-miRNAs that affect the expression of DNMT1 and methylation is miR-148a, so, due to the reduced expression of this miRNA in cancerous specimens, the role of this microRNA consider as a tumor suppressor. In summary miR-148a can be introduce as a new marker for early diagnosis.

Keywords:
MicroRNA 148a, diagnostic marker, lung cancer

P110

Reciprocal relationship between epi-miRNAs and Epigenetic Modifications in cancer

Shima Rahmati

Shima Rahmati[1,2], Ali shojaeian[3]

1) Student Research Committee, Kurdistan University of Medical Sciences, Sanandaj, Iran.
2) Cellular & Molecular Research Center, Kurdistan University of Medical Sciences, Sanandaj, Iran
3) Cellular & Molecular Research Center, Shahrekord University of Medical Sciences
Rahmati_may66@yahoo.com

Abstract:
Epigenetic modifiers play important roles in regulation of the cellular transcriptome. Any imbalance in these processes may lead to abnormal transcriptional activity and thus result in disease state. Distortions of the epigenome have been reported in cancer initiation and progression. Epigenetic regulation usually includes DNA methylation and histone modifications. miRNAs, a class of small noncoding RNAs, frequently deregulated in many diseases including cancer. The connection between epigenetics and miRNAs has been supported by a specific subgroup of miRNAs called ‘‘epi-miRNAs’’that can directly and indirectly modulate the activity of the epigenetic machinery. The retrieved studies were searched through the PubMed (MEDLINE), Google Scholar, Scopus, databases. Different studies have been demonstrated that Changes in DNA methylation, altered histone modifications and epi-miRNA expression are functionally associated with cancer initiation and progression. Various aspects of the epigenome have also been investigated as biomarkers for different stages of cancer detection.
Oncogenic miRNAs, can all serve as important targets in cancer therapy; knocking down of these miRNAs may stunt the cancer growth. On the other hand, restoring tumor-suppressor miRNAs can also be a powerful approach in treating cancer. The finding that epigenetic drugs 5-Aza-2′-deoxycytidine is able to lead to the up-regulation of miR-127, which can down-regulate BCL6, is especially exciting. Furthermore it demonstrates that epigenetics drugs may exert their antitumor effects on two fronts: they not only turn on have the tumor-suppressor had genes that were aberrantly silenced epigenetically, but they also turned on tumor-suppressor miRNAs that down-regulate target oncogenic mRNAs.

Keywords:
DNA methylation; histone modifications; epi-microRNA

P111

Exosomal proteins as a new approach in cancer diagnosis

Ali shojaeian

Ali shojaeian[1*], Shima Rahmati[2, 3]

1) Cellular & Molecular Research Center, Shahrekord University of Medical Sciences
2) Student Research Committee, Kurdistan University of Medical Sciences, Sanandaj, Iran.
3) Cellular & Molecular Research Center, Kurdistan University of Medical Sciences, Sanandaj, Iran
* Corresponding author

Abstract:
The term "personalized medicine" has gained widespread acceptance in field of oncology, where it most often refers to a vision of cancer treatment which is tailored to individual patients based on the molecular profile of their tumour. In addition, scientists are developing and using diagnostic tests based on genetics or other molecular mechanisms to better predict patients' responses to targeted therapy. Exosomes are small sized (30–120 nm) extracellular vesicles with endosomal origin that throw directly from the budding of the plasma membrane. Exosomes play and crucial role in cell-to-cell communication by carrying their contents, including proteins, metabolites, RNAs, DNAs and lipids. While exosomes are secreted by multiple cell types, cancer derived exosomes not only influence the invasive potentials of proximally located cells, but also affect distantly located tissues.
The retrieved studies were searched through the PubMed, Google Scholar, Scopus, databases. Different studies have been demonstrated that, cancer derived exosomes likely serves as biomarker for early detection of cancer as they carry the cargo reflective of genetic or signaling alterations in cancer cells of origin. Exosome purity is assessed by measuring exosome-specific marker antigen or protein using ELISA assay, nanoparticle tracking analysis (NTA), and flow cytometry (FACS).
Exosomes contain a variety of proteins that reflect their origin and alteration of the parental cells. Exosome-based diagnostics provide higher sensitivity and specificity over conventional biopsy or liquid biopsy biomarkers due to their stability in biofluids. Furthermore it provides the convenient and non-invasive way of diagnosis over tissue biopsy that requires surgery. Some proteins serve as exosomal cancer markers for instance: CD63 (in melanoma), CD24 and EpCAM (in breast cancer) etc.

Keywords:
Exosome, diagnostic marker, cancer

P112

The role of personalized medicine in Head and Neck cancer

Katayoon Forouzanfar

K. Forouzanfar[1], Z.Imani Saber[2], S.Boosaliki[3]

1) Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute Tehran University of Medical Sciences, Tehran, Iran
2) Medical Genetic Department, Tehran University of medical science, Tehran, Iran
3) Medical Genetic Departments, Shahid Beheshti University of medical science, Tehran, Iran
katayoonforouzanfar@yahoo.com,Zeynab.imanisaber@gmail.com,saraboosaliki@sbmu.ac.ir

Abstract:
Head and neck squamous cell carcinoma (HNSCC) is one of the most common cancers worldwide associated with one-tenth cause of mortality and morbidity in our country. In spite of the prevalence of this cancer in elderly, over use of cigarette and hookah during the past decade compare to two decades ago it has been more diagnosed in 30-40 ages.
Since oral cancer could be treated easily by early diagnosis, oral premalignant lesions (OPL) detection such as leukoplakia could be helpful as an accessible prognosis of malignant to determine diagnostic tests and targeted treatment. Poor value of pathological factors in predicts of OL transformation and high frequency of clinical heterogeneity leads us to personalize medicine and develop molecular-based strategies and biomarkers in tumor gene expression signature in 3 levels: Genome, Transcriptome and Proteome. Oral cavity is a complex anatomical site critical for speech, swallowing and appearance so surgery is pivotal in this cancer so it provides small size of margin to access large gene panel and find the correlation between molecular profile and metastasis.
In treatment field we categorize patients due to expose with microenvironment such as tobacco, alcohol and also HPV virus or not. For instance HPV positive is associated with a higher radiosensitivity thought to be linked to P16 overexpression so radiotherapy would be the targeted therapy.
As a consequence a comprehensive review from histopathology to molecular expression analyze head us to precision medicine which particularly relevant in this disease.

Keywords:
Head and neck squamous cell carcinoma, Oral premalignant lesions, Clinical heterogeneity, Gene expression signature

P113

Use of the next-generation functional diagnostics in cancer precision medicine

Maryam Taghavi Basmenj

Maryam Taghavi Basmenj[1*], Z.Imani Saber[2], P.Esmaeili Kordlar[1], M. Mehdi Jahani

1) Molecular Medicine Department, Biotechnology Research Center, Pasteur Institute of Iran, Tehran, Iran
2) Department medical genetic Tehran university of medical science
3) Islamic Azad University, Shahrekord branch, faculty of veterinary medicine
* Corresponding author - Taghavi.mtb@gmail.com

Abstract:
One of the precision medicine concepts is the allocating a specific drug to particular patient based on genetic profile and ethnicity. In cancer, there is a growing tendency to make precision medicine synonymous with genomics. In current methods, functional testing is used to remove the limitations of old therapies based on the phenotype-genotype relationship, including live tumor cells exposure to adjuvant therapy and following assessment of cells before and after treatment. One application of tumor tissue sample and chemical agent's effects on that is a target therapy of HER2 positives treated with adjuvant therapy. In this treatment, as well as switching off the HER2 pathway, other pathway is to become switched with on and resulted side effect is metastasis.
By surveying tumor tissues and their expression profiling, these pathways can be found, while applying the adjuvant and Herceptin, an approviate silencer can be used for switching on side effects of adjuvant and reduction of metastasis. Currently, there are several next generation functional diagnostic technologies, including novel methods for tumor manipulation such as conditional reprogramming (CR), circulating tumor cells (CTC) and also insitu methods based on tools. The aim of these new technologies is to integrate functional testing with next generation sequencing and immunoprofiling to precisely match combination therapies for a specific cancer patient.

Keywords:
Precision medicine, Next generation sequencing, Adjuvant therapy, HER2

P115

Personalized sequencing for Treatment of colorectal cancer, forward personalized medicine: recent advances and future challenges

Hadi Bamehr

Hadi Bamehr
Research center for molecular medicine, Hamadan University of Medical Sciences, Hamadan, Iran
hbamehr@yahoo.com

Abstract:
Colorectal cancer or (CRC) is a major health problem worldwide and the third most common cancer associated with significant mortality. Despite Considerable progress has been made in screening test, Survival rates from colorectal cancer (CRC) are still high due to delays in diagnosis of patients with CRC. On the other hand, in spite of a plethora of effective anticancer drugs, CRC treatment outcome is still poor on the basis of CRC heterogeneous nature unique to an individual's tumor. An important issue have to resolve is early detection and then customize treatment in order to better clinically management of CRC in view the heterogeneity of individual patient. One of the most significant current discussions in personalized medicine is personalized sequencing recently has gained increasing attention for its prospect to individually customize medical treatment based on unique information for its biological attributes. The developments of large-scale 'omics' technologies parallel to sophisticated computational analyses making it possible to providing integral omics platforms and new insights into the biology of CRC. These approach might allow better clinically management at the individual patient level for both early detection and development of effective cancer treatment regimens. It is possible to hypothesize that personalized sequencing are more likely to become the paradigm of future healthcare.
This review has discussed the current state of knowledge on the Personalized sequencing and new technologies such Next-generation sequencing (NGS), and challenges in CRC management, customize treatment by sequence-based platform and an insight into new approaches may help in development of personalized medicine for CRC.

Keywords:
Colorectal cancer, personalized sequencing, personalized medicine, 'omics' technologies

P116

Studying the relation of blood lead level with the thyroid hormone concentrations and blood cell count

Hanieh Babaei

Hanieh Babaei[1], Maryam Sadat Daneshpour[2*], Maryam Ghobeh[3]

1) Department of Biology, Science and Research Branch, Islamic Azad University, Tehran, Iran.
2) Cellular and Molecular Endocrine Research Center, Shahid Beheshti University of medical sciences, Tehran, Iran.
3) Department of Biology, Science and Research Branch, Islamic Azad University, Tehran, Iran.
*Corresponding author - daneshpour@endocrine.ac.ir

Abstract:
Background and Purpose: Lead has many applications in the industry but does not play a specific physiological role in the body. According to performed studies, lead has an undesirable effect on the nervous, gastrointestinal, respiratory, and endocrine systems. People who are highly exposed to this element, due to their occupation or living place, are affected by its harmful effects. The aim of this study was to evaluate the level of thyroid hormones and blood cells in people highly exposed to lead.
Analysis method: This cross-sectional study was carried out on 37 patients with high exposure level to lead in Tehran. After filling out the consent form and questionnaire, the blood samples were collected from them and their levels of blood lead, thyroid hormones and blood parameters were evaluated in a laboratory. Normal distribution of data was assessed by Kolmogorov Smirnov test by Med Calc 14.8.1.
Results: Obtained results demonstrated that there was no significant association between blood lead levels and levels of thyroid hormones, number of blood cells and related blood cells parameters (HCT, HGB, MCV, MCH and MCHC) in this study. However, according to Kolmogorov Smirnov test by Med Calc 14.8.1, there was a weak link between blood lead levels and age ($r = 0.25$).
Conclusion: High lead levels did not affect the level of the thyroid hormones, the number of blood cells and the levels of the red blood cells parameters in this cross-sectional study.

Keywords:
Lead, Thyroid hormones, Red blood cells, White blood cells, Platelets, Hemoglobin, Hematocrit.

P117

Personalized medicine in breast cancer

Anahita Ahmadsina

Anahita Ahmadsina[1*] , Kamran Ghaedi[2], Mansoureh Azadeh[3], Atefeh Zamani[4]

1) NourDanesh Institute of Higher Education, Meymeh, Isfahan, Iran
2) Cellular and Molecular Biology Division, Biology Department, Faculty of Sciences, University of Isfahan, Isfahan, Iran
3) Zistfanavari biotechnology institute, Isfahan, Iran
4) Zistfanavari biotechnology institute, Isfahan, Iran
*Corresponding Author - anahita.6060@gmail.com

Abstract:
Breast cancer is a complex disease caused by the progressive accumulation of multiple gene mutations combined with epigenetic dysregulation of critical genes and protein pathways. The discovery that mutations in the BRCA1 and BRCA2 genes increase the risk of breast cancers has radically transformed our understanding of the genetic basis of breast cancer, leading to improved management of high-risk women. Genomic changes differentiate tumors from normal tissues, permitting targeted treatments for several types of tumor and thereby extending survival and improving patients' quality of life. According to the U.S. National Institutes of Health (NIH), personalized medicine is "an emerging practice of medicine that uses an individual's genetic profile to guide decisions made in regard to the prevention, diagnosis, and treatment of disease". The immediate challenge is to learn how to use the molecular characteristics of an individual and their tumor to improve detection and treatment, and ultimately to prevent the development of breast cancer. Personalized medicine builds on the Human Genome Project, which was forecasted to revolutionize disease risk prediction, with projected relative risks. The ultimate goal of personalized medicine is to furnish the proper treatment to the right person at the right time. Based on articles by google scholar, pubmed and science direct, we got these results. Personalized medicine is receiving a large amount of growing attention for its tremendous potential with myriad new opportunities. The ultimate promise of personalized medicine depends on the discovery of the personal genetic causes of disease.

Keywords:
Personalized medicine; Breast cancer; BRCA1; BRCA2; Treatment; Human Genome Project

P119

The effect of personal medicine with analysis epigenetics biomarkers and changes of miRNA expression profile in diagnosis and treatment of prostate cancer

Hamidreza Raeespour

Hamidreza Raeespour[1], Nafise Taromi[2]

1) Pajoohane Ebne Sina genetic research Laboratory, Keshavarz Boulevard, Tehran, Iran
2) Department of Medical Biotechnology, Faculty of Allied Medical Sciences, Iran University of Medical Sciences, Tehran, Iran
hraeespour@yahoo.com

Abstract:
One of the incident cancer in men is prostate cancer, which in spite of large study about diagnosis and treatment of this cancer, this is one of main reason of death in the men. Prostate cancer like other cancer, have different environmental and genetic reasons that the analysis of genetic reason available the field of study about personal medicine diagnosis and treatment of this cancer. Personal medicine is advanced branch of medicine that with use of the most appropriate diagnostic biomarkers, determine the kind and the best treatment for person with cancer. The study of expression changes of biomarkers such as microRNAs (miRNAs), is one of the method in targeted diagnostic and treatment. In this study a table of microRNAs expression changes and genes that have effect in diagnosis and treatment of prostate cancer, with study in relevant article and search in science direct, PubMed and google scholar get available. In addition of genetic changes, mechanism of epigenetics such as DNA methylation, Histone modifications and change in miRNAs expression, have effect in the diagnosis and treatment of prostate cancer. MicroRNAs after the transcription play their regulatory role, and because of stability and specificity expression in any tissue, they are used as the best biomarkers for prognosis factor and treatment of cancers, also prostate cancer.

Keywords:
Personal medicine, Prostate cancer, microRNA, Epigenetics biomarkers

P120

Genetic polymorphism of CENP-E and susceptibility colorectal cancer in Ahvaz

Mahdi Bijanzadeh

Rahim Alidadi[1], Alihossein Saberi[2], Mohammad Hossein Modarressi[3], Abdolhossein Talaiezadeh[4], Mahdi Bijanzadeh[5*]

1) MSc Student in Human Genetics, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
2) Department of Medical Genetics, Faculty of Medicine, Ahvaz Jundishapour University of Medical Sciences, Ahvaz, Iran
3) Department of Medical Genetics, Tehran University of Medical Sciences, Tehran, Iran
4) Cancer, Environmental and Petroleum Pollutants Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
5) Department of Medical Genetics, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
mbijanz@yahoo.com

Abstract:
BACKGROND AND PURPOSE: Colorectal cancer (CRC) is the third most common cancer across the world. At least 3 pathways have been identified in the colorectal cancer pathogenesis: chromosomal instability (CIN) or microsatellite instability (MIN) and CpG island methylator phenotype (CIMP) pathways. Mutations in the genes encoding centromere proteins have been identified as a stimulating factor in the formation of aneuploidy and tumorigenesis. Centromere-associated protein-E (CENP-E) is a kinesin-like centromere protein that required for efficient capture of spindle microtubules by kinetochores and for efficient chromosome segregation. Therefore, defect in this protein causes an aneuploidy (CIN) and CIN is a hallmark of most solid tumors. We have analyzed an important polymorphism in CENP-E gene which have been implicated in the development of CRC.
MATERIAL AND METHOD: In this case-control study, 100 patients with colorectal cancer and 100 healthy controls participated (from hospitals in Ahvaz). We used from polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) analysis for CENP-E Tyr63His detection. Finally, 70 samples (35 case and 35 healthy control) were sequenced by Sanger method for validation of the RFLP results. Frequency were constructed using the SPSS (24.0 version) and threshold for significance was $p< 0.05$.
RESULT: Cases and controls were matched on age, sex and ethnic characteristics, and no significant difference were between them (P = 0.34, 0.77 and 0.61, respectively). There was no significant difference between patients and healthy controls. Also, there was no significant association between genotypes and susceptibility colorectal cancer. The allele frequency was similar between patients and healthy controls, and there was no significant difference between the two groups.
CONCLUSION: This polymorphism was studied in Ahwaz, southwest of Iran, The CENP-E Tyr63His (A/G) polymorphism may be associated with colorectal cancer in other Asians, but it appears to have no such effect in Southwest of Iran. The study also highlights the importance of conducting genetic association studies in different ethnic populations.

Keywords:
Colorectal Cancer, Polymorphism, CENP-E, susceptibility, Ahvaz

P121

Frequencies of common CYP2D6 alleles and genotypes within Isfahan population of Iran

Dr.Mansoor Salehi

Mansoor Salehi[1,2,3*], Zahra Khalaj[1,2], Zohreh Baratieh[1], Parvaneh Nikpour[1,3], Fariborz Mokarian[4], Hossein Khanahmad[1], Rasoul Salehi[1,3]

1) Department of Genetics and Molecular Biology, Faculty of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
2) Medical Genetic Center of Genome, Isfahan, Iran
3) Child Growth and Development Research Center, Research Institute for Primordial Prevention of Non-communicable Disease, Isfahan University of Medical Sciences, Isfahan, Iran
4) Cancer Prevention Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
*Corresponding author - m_salehi@med.mui.ac.ir

Abstract:
Cytochrome P450 2D6 (CYP2D6) is an important drug metabolizing enzyme involved in the pharmacokinetic metabolism of drugs. The CYP2D6 gene is highly polymorphic and the combination of different alleles yields different phenotypes such as: extensive metabolizer (EM), intermediate metabolizer (IM) and poor metabolizer (PM). Genotyping of the important alleles in the population for assessing the efficacy of drug is of particular importance. In Iranian population, the abundance of CYP2D6 gene alleles is not well known. So in this study, the frequency of CYP2D6 *1, *2, *4, *5, *6, *10, *17 and *41 alleles as well as the frequency of different genotypes related to these alleles were studied in Isfahan province of Iran.
Using TaqMan® assays common alleles of CYP2D6 were identified in 134 breast cancer patient from Isfahan province of Iran. According to our study, the frequencies of CYP2D6 *1, *2, *4, *6, *10, *17 and *41 alleles were 42.5%, 34%, 10.4%, 0.4%, 3.0%, 0.4% and 9.3% respectively. In the present study EM/EM, EM/IM, EM/PM, IM/IM and PM/PM genotypes were reported with the frequencies of 59.7%, 17.91%, 15.67%, 3.73% and 2.99%, respectively.
Taken together, our findings illustrated that the frequency of PM or IM alleles and different genotypes harboring this alleles were relatively high in Iranian population. Therefore it's important to detect these patients to prevent adverse drug reactions through individualization therapy.

Keywords:
allele, CYP2D6, frequency, genotype

P125

Bioinformatics study in personal medicine of medulloblastoma

Dr.Fateme Shaabanpour Aghamaleki

Fateme shaabanpour aghamaleki[1], Shirin farivar[2*]

1) Department of cellular and molecular biology, Shahid beheshtiUniversity, Tehran, Iran
2) Department of cellular and molecular biology, Shahid Beheshti University, Tehran, Iran
*s_farivar@sbu.ac.ir

Abstract:

Introduction: Medulloblastoma is the most common malignant brain tumor in children. Dysregulation of signaling pathways that regulate normal stem cell development, may contribute to medulloblastoma pathogenesis. Correction of the dysregulation in these signaling pathways may target medulloblastoma and eliminate tumor cells completely. One of the important gene that play role in medulloblastoma is MINA or RIOX2 (Ribosomal Oxygenase 2) is a c-Myc target gene that may play a role in cell proliferation or regulation of cell growth. Since it is SNPs that are responsible for over 80% of the variation between two individuals, they are ideal for the task of hunting for correlations between genotype and phenotype. As some SNPs predispose individuals to have a certain disease or trait or react to a drug in a different way, they will be highly useful in personal medicine and drug development.

Material and method: genes expression profiling by array of 19 human primary medulloblastoma and 3 human neural stem cells were extracted from NCBI Geo datasets. Genes are compared with logfc for their expression, and sorted by their p-value. Finally gene with most modification in medulloblastoma is selected for further analysis. Its most important SNPs are selected from NCBI database. Also its most related pathways and gene function are identified by Gene Card database. It's normal and affected RNA structure (with SNP) is determined by genebee database, and its normal and affected protein structure are identified through soft berry and ExPASy database.

Results: RIOX2 has hyperexpression in medulloblastoma patients. It plays an important roles in targets of C-MYC transcriptional activation and interact with MYC and SP9 that establish its function in medulloblastoma pathogenesis. RIOX2 protein has multiple α-helix, β-sheet and β-turn in its protein structure. Its RNA structure has several hairpin and stem loop, especially at the both end of the RNA. There are a differences between its natural RNA and protein structures and its structures with SNP through analysis.

Conclusion: according to RIOX2 function and pathways, this point is stated that RIOX2 has potential activity in medulloblastoma pathogenesis. The structures differences that make through SNP can be used for medulloblastoma therapy through drug designing against its affected structures in chemotherapy, because each individuals have especial SNPs in this gene that affect its RNA and protein structures.

Keywords:

Medulloblastoma, RIOX2 gene, RNA and protein structure, SNP, Personal medicine

P127

study of prostate cancer metastasis in bone

Kamelia Mobasheri

Kamelia Mobasheri
phD student, Islamic Azad University Branch, Tehran - Mobasherikamelia@gmail.com

Abstract:
Metastasis to bone is common in prostate cancer. in this cancer, the bone is often the only clinically detectable site of metastasis, and the resulting tumours tend to be osteoblastic (bone forming) rather than osteolytic (bone lysing). The interaction between host cells and metastatic cancer cells is an important component of organ-specific cancer progression.
Western blot analysis and RT-PCR was used to determine BMP receptor expression on osteoblastic prostate cancer cell lines LAPC-4 and LAPC-9. Migration, invasion, and cellular proliferation assays were used to quantify the effects of BMP-2, −4, and −7 on LAPC-4 cells in vitro. LAPC-9 cells alone or transfected with a retrovirus overexpressing noggin were injected into the tibias of SCID mice, and the animals were followed for 12 weeks.
We determined that BMP receptor mRNA and protein was expressed on osteoblastic prostate cancer cell lines LAPC-4 and LAPC-9. In vitro studies showed that BMP-2 and −7 stimulated cellular migration and invasion of prostate cancer cells in a dose-dependent fashion, although BMP-4 had no effect. Noggin inhibited cellular migration and invasion of BMP-2- and −7-stimulated LAPC-4 cells. LAPC-9 cells implanted into immunodeficient mouse tibias formed an osteoblastic lesion with sclerotic bone at 12 weeks.
These findings suggest that BMPs are critical in the formation of the osteoblastic lesions associated with prostate cancer metastases, and the progression of osteoblastic metastases induced by human prostate cancer cells may be limited by BMP inhibitors.

Keywords:
Metastasis, prostate cancer, osteolytic

P128

The exosomal microRNA as reliable biomarker to early detection of pancreatic cancer

Mohammad Amin Mahmanzar

Mohammad Amin Mahmanzar[1,2*], Pegah Larki[2], Binazir khanabadi[1,2], Ali Tafti[1], Ehsan Nazemalhosseini-Mojarad[3], Amir Sadeghi[2]

1) Department of Cellular and Molecular Biology, Tehran Medical Sciences Branch, Islamic Azad University
2) Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3) Gastroenterology and Liver Diseases Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
* Mahmanzar74@gmail.com

Abstract:
Pancreatic ductal adenocarcinoma(PDAC) is the most common lethal type of pancreatic cancers.PDAC include 80%–90% of all pancreatic solid tumours and unfortunately these patients have the best up to five-year survival if surgery, chemotherapy, and radiation are Prescribed in the first or second pre-metastatic stage of development. Because of the absence of early symptoms and the lack of early detection, this disease has become one of the most lethal cancers because more than 50% of PDA patients are diagnosed in stage IV.So early detection of this cancer has significant effects on patients survival and treatment methods.Today, microRNAs (miRNA), the subjects of transcriptional and post-transcriptional regulation, are introduced as novel biomarkers because they are stable in a body fluid, inexpensive, Noninvasive and more specific.
In this study, refer to bioinformatic technics, we aimed to review novel miRNA that can be used as a reliable biomarker for early detection of pancreatic cancer.
we collected the newest and relevant article by searched Pancreatic ductal adenocarcinoma, biomarker, microRNA and early detection as keywords in a valid data base such as NCBI and Scopus.
The number of articles detected in our study was 48 that screened 12 of them. Afterward, check out the miRNAs in miRBase and miRCancer data base.Notably selected 23 reliable microRNAs such as miR221, miRLET7A1 and miR155 as miRNA panel for PDAC early detection.
Based on results, we collected valuable microRNAs as a biomarker to detect pancreatic cancer at the early stage that causes selected accurate treatment methods.

Keywords:
Pancreatic ductal adenocarcinoma, biomarker, microRNA and early detection

P128

Genetic Variations of CHRNA5 Gene Correlated to High Risk of Lung Cancer in Iranian Patients

Maryam Majidzadeh

Maryam Majidzadeh[1], Seyed Mohammad Moshtaghioun[1*], Ali Falahati[1]
1) Department of Biology, Faculty of Science, Yazd University, Yazd, Iran
*Corresponding author - moshtaghiun@yazd.ac.ir

Abstract:
Lung cancer is one of the most common malignant tumors and leading cause of cancer death that become a major public health problem worldwide. It appears to result from interactions between genetic susceptibility of the individual and risk factors in the environment. Genome wide studies have reported an association between the chromosome 15 region (15q25) and lung cancer risk and smoking habit. The region, spanning 203 kb, contains six genes including acetylcholine nicotinic receptor subunit α5 gene (CHRNA5) that might be good candidates for lung cancer risk. The strong linkage disequilibrium in this region has led to the identification of several single nucleotide polymorphisms (SNP) showing significant association with lung cancer risk. A particularly interesting variant in this locus is the single nucleotide polymorphism that lies in the fifth exon of CHRNA5 (rs16969968). This variant encodes a change from an aspartic acid to an asparagine residue at amino acid position 398 (D398N).
In this case-control study, 89 patients with lung cancer and 90 control individuals to examine the association between polymorphism (rs16969968) and the risk of lung cancer, using PCR- RFLP and sequencing were studied. The results of this study indicated no significant association between this polymorphism and lung cancer risk in the population studied (OR = 1.26, 95% CI = 0.68-4.1, P > 0.05).
Unlike previous studies, by examining the results of this study, no relationship between polymorphism (rs16969968) and risk of lung cancer was observed, probably due to small sample size or different spread of polymorphisms in different populations.

Keywords:
lung cancer, polymorphism, CHRNA5, nicotine

P132

Multi-dimensional model of hospital and healthcare environment for patients with cancer and their family

Dr. Manijeh Firoozi

Manijeh Firoozi
Assistant Professor in Psycho-oncology, University of Tehran, Iran - mfiroozy@ut.ac.ir

Abstract:
Aims: A renewed interest in hospital design provides an opportunity to consider hospitals and health care center as 'therapeutic environments' for patients with cancer and their family. Noting that the therapeutic value of hospitals is related to their physical, social and symbolic design.
Results: In this research was introduced a multi-dimensional model of healing spaces that meet patients with cancer, their family and staff's needs. The first axis allocated to special needs: hospitals should be clinically efficient, be integrated within the community, be accessible to consumers and the public, and encourage patient and staff well-being. Second axis related to Healing Spaces (Elements of Environmental Design That Make an Impact on Health such as healing gardens): attempt to reduce stress and anxiety, increase patient satisfaction, and promote health and healing, safety and well communicated to the staff. The third axis improves psychosocial environment where they were seen as a unique person: the patients wanted to support a good physical environment. The fourth axis concluded reinforcement of self-control or self-management in patients (special who resident for long-term in hospitals), appearance and beatification.
Conclusion: In this model is emphasized on being meaningful, healing hospital environment feet to patients with cancer' requests and enhance co-designing (inviting patients and caregivers to contribute to decision-making and discussions about their needs and perception to design health environment).

Keywords:
Hospital, Healing environment, Patients with cancer.

P137

A novel mutation in pkhd1 gene in an Iranian family with an abortion affected with Autosomal Recessive polycystic kidney disease

Fatemeh Ghadyani

Fatemeh Ghadyani[1], Saeid Morovvati[2*]

1) Department of Cellular and Molecular , Faculty of Biology Sciences, Islamic Azad University of Tehran-North,Tehran, Iran
2) Human Genetics Research Center, Baqiyatallah University of Medial Sciences, Tehran, Iran

Abstract:
Polycystic kidney disease (PKD) is a genetic disorder in which abnormal cysts develop and grow in the kidneys. Cystic disorders can express themselves at any point, infancy, childhood, or adulthood. PKD is characterized by the presence of multiple cysts typically in both kidneys; however, 17% of cases initially present with observable disease in one kidney, with most cases progressing to bilateral disease in adulthood. The two types of PKD are autosomal dominant polycystic kidney disease (ADPKD) and autosomal recessive polycystic kidney disease (ARPKD). ARPKD is the lesser common type and the incidence of ARPKD is estimated at 1:10,000 to 1:40,000. The majority of individuals with autosomal recessive polycystic kidney disease (ARPKD) present in the neonatal period with enlarged echogenic kidneys. Mutations in the PKHD1 on chromosome 6p12.2 cause ARPKD. Symptoms and signs include abdominal discomfort, polyuria, polydipsia, incidental discovery of hypertension, and abdominal mass. At initial presentation, approximately 45% of infants have liver abnormalities. With neonatal respiratory support and renal replacement therapies, the ten-year survival of those who live beyond the first year of life has improved to 82%. A minority present in older childhood or young adulthood with hepatosplenomegaly and evidence of portal hypertension. The classic presentation for ARPKD is systemic hypertension with progression to end-stage renal disease (ESRD) by the age of 15. : This study includes a couple who their child was aborted due to PKD. PKHD1 gene was analyzed in father by NGS method, and the mutation found in the father was analyzed in the mother by Sanger sequencing.A possible pathogenic mutation, c.6469C>T (p.Gln2157Ter), on PKHD1 (NM_138694) gene was detected in parents both Although there is no report that this mutation is ever identified in PKHD1 gene in ARPKD patients, the early termination of amino acid production is expected to affect the protein's function as a possible pathogenic mutation in a heterozygous state.
Although there is no report that this mutation is ever identified in PKHD1 gene in ARPKD patients, the early termination of amino acid production is expected to affect the protein's function as a possible pathogenic mutation.

Keywords:
polycystic Kidney disease ,PKHD1 ,cystic disorder, ARPKD

P139

The anticancer activity of metformin through microRNAs modulation

Fatemeh Mansouri

Fatemeh Mansouri
Department of Genetics and Immunology, Faculty of Medicine, Urmia University of Medical Sciences, Urmia, Iran
Cellular and Molecular Research Center, Urmia University of Medical Sciences, Urmia, Iran
mansouri1600@hotmail.com

Abstract:
Metformin is considered one of the common anti-hyperglycemic and cost-benefit drugs to treat patients with type II diabetes and polycystic ovary syndrome in women. Metformin has important role by enhancing glucose uptake into the skeletal muscle and inhibiting hepatic gluconeogenesis and cellular energy homeostasis. The availability of glucose for glycolytic ATP generation, lipid and cholesterol synthesis plays a pivotal role in cancer development and progression. Metformin impacts on cell proliferation through the modulation of microRNAs deregulation and their mRNA targets in both cancer and diabetic cell systems and low expression of DICER is correlated with cancer development.
The current state and application of metformin in clinical practice including:
a) The increase of insulin- like growth factor binding protein 1 (IGFBP1), to limit the binding between IGF1 and their receptors and consequently the production of androgen. b) Inhibition of IGF1R sensitized and circulating growth factors to the cytotoxic effects of chemotherapy treatment. c) Inhibiting the tumor necrosis factor alpha (TNFα) production in human lymphocytes. d) Modulation the activity of checkpoints, which results in an increased sensitivity of cancer cells against DNA damage and inhibited the growth of carcinoma by inducing G1 cell cycle arrest. e) Modulation of insulin signalling and lipid homeostasis by mir-33b and cholesterol homeostasis by mir-33b regulation. f) Up-regulation of miR-26a, miR-192 and let-7c to inhibit cell proliferation, invasion, migration and increased cell apoptosis. g) Down-regulation of miR-222 to inhibit cell growth and cell cycle progression via direct of p27, p57 and PTEN. h) Modulation of miR-140, miR-222, miR-142 and miR-192 in plasma samples collected from type 2diabetes.
Therefore, metformin can perform anti anticancer effects and reprogram cancer metabolism through miRNA modulation and expression of DICER.

Keywords:
Metformin, anticancer, microRNAs

P142

Breast Cancer During Pregnancy

Maryam al-Sadat Marashi

Maryam al-Sadat Marashi
Midwifery expert at Khatam-al-Anbia Hospital (pbuh)

Abstract:
Breasts have lymph vessels and lymph nodes. Cancerous cells, if released, are usually found in these lymph nodes.
The main cause of this illness is unknown. But factors such as race, obesity, lack of physical activity, alcohol consumption, smoking, age, family history, gene changes do not affect its incidence. Breast inflammation, breast asymmetry, stretch of the breast skin into the inside, deformation of the nipple, changes in breast color to redness and discharge from duct of a breast are very important to us and have to be investigated. Monthly examinations in 5-7 days of menstrual cycle by a woman, especially those with a hereditary history in this area, have a significant effect on early detection and prevention of the disease in women. In pregnant women, a precise periodic examination by the midwife and training women to differentiate the mammary glands from the cancerous glands is very effective. The least benefits of these actions are the identification of small tumors which can be treated with brief surgical proceedings. More than 65% of the breast tumors are discovered by patients themselves.
Breast self-examination can be done in two ways. In the first method, in front of the mirror, the breasts should be examined in terms of symmetry and the adhesion of the breast after raising the hands has to be paid attention. In the second method, while bathing, breasts should be examined to be same in size and weight and nipples should be checked for no bloody discharge.
If needed, the sonography is used for better diagnosis of the disease. When a tumor is observed, it is usually biopsied. Surgery is usually the first method of treating breast cancer. Even if all visible cancerous tissue is removed during surgery, the patient may undergo radiation therapy, chemotherapy or hormone therapy after surgery to eliminate remaining cancerous cells.
It is interesting to note that after breast cancer treatment and discontinuation of medications, gestation and breastfeeding is possible even in the affected breast, but since the most likely recurrence of breast cancer is two to three years after treatment, it is advisable to delay pregnancy.

Keywords:
Cancer, Breast Cancer, Pregnancy and Breast Cancer, Breast Examination

P145

A genetic polymorphism in rs1801133 in MTHFR, rs10811661 in CDKN2A/B genes associated with breast cancer

AmirReza Hesari

AmirReza Hesari, Faezeh Ghasemi*

Department of Biotechnology, Faculty of Medicine, Arak University of Medical Sciences, Arak, Iran.
*Corresponding author - Ghasemi_f@arakmu.ac.ir & Ghasemi_808@yahoo.com

Abstract:
Methylenetetrahydrofolate reductase (MTHFR) is the rate-limiting enzyme in the methyl cycle, encoded by the MTHFR gene. MTHFR plays a key role in homocysteine plasma level and is associated with the risk of breast cancer. The CDKN2A/B is the tumour suppressor in cell cycle regulation. The single nucleotide polymorphism (SNP) is thought to be associated with the predisposition of breast cancer and subsequent immune response in the different populations. The aim of present study is the evaluation of rs10811661and rs 1801133 SNPs in CDKN2A/B and MTHFR with the risk of breast cancer in patients with carcinoma of breast and controls. The TaqMan real time PCR technique was applied for genotyping of participants. The correlation of both variants and demographic data were investigated with the risk of breast cancer. Our data showed that the MTHFR allele T and TT genotype had the higher prevalent in patients (p value=0.0001) and (p value=0.003) than control group. Also, the CDKN2A/B allele CC genotype had the higher prevalent in patients (p value=0.003) than control group. Indeed, the correlations of menarche and underlying hormonal disorder with the risk of breast cancer were evaluated, also our result confirm the correlation of breast cancer with CDKN2A/B rs10811661. Our investigations demonstrated that the MTHFR rs180113 could be used as prognostic factor.

Keywords:
Breast cancer, MTHFR gene, CDKN2A/B gene, Polymorphism

P150

Circulating miRNA-containing Exosomes as potential biomarkers for diagnosis and monitoring of breast cancer

Davod Jafari

Davod Jafari, Arshad Hosseini*
Department of Medical Biotechnology, School of Allied Medicine, Iran University of Medical Sciences, Tehran, Iran.
* Corresponding author - hoseini.a@iums.ac.ir

Abstract:
Breast cancer is most prevalent cancer in women and responsible for a great number of cancer related deaths in women around the world. Traditional diagnosis methods for breast cancer like mammography limited to require a minimum size of tumor cells. Therefore, not all of breast cancers can be detect in their early stages, when they are amendable to treatment. specific molecular biomarkers can be used to detection of early stages cancers. Exosomes are extracellular vesicles that secreted by a variety of cells and they are contain some components like miRNAs. Exosomes from different type of cells contain parent-specific component. Application of exosomal miRNAs for breast cancer may be differ in diagnostic, subtype prediction and drug resistances. Mir-101, mir-372, mir-21 and mir-1246 increase in the serum of breast cancer patients. mir-210 upregulated and mir-19a and mir-29c downregulated in breast cancer that metastases to brain. mir-10b, mir-9 and mir-939 began to upregulation in tumor cells and increasing in patient's serum when the cancer change to metastasis form. mir-231 that secreted by TAMs promote cell invasion in breast cancer. mir-273 related to ER and PR negative subtype of breast cancer. Mir-210 contained exosomes that secreted from tumor cells in hypoxia condition led to angiogenesis in tumor site. Mir- 222 make drug resistance in tumor cells for Adriamycin and mir-221/mir-222 make resistance to tamoxifen. Therefore, these researches reveals that exosomal miRNAs has this potential to become biomarkers of different condition of breast cancer. Some clinical trial in this field is underway to assess these molecules. Some challenges should be resolved in this field, for example, source of miRNA as well as a universal and repetitive simple method for purification of exosomal miRNAs is need.

Keywords:
Breast cancer, Exosomes, miRNA, Biomarker

P156

Organoids transplantation, the new model to speed up personalized medicine researches in Colon cancer and metastasis

Fatemeh Sanjabi

Fatemeh Sanjabi[1], Reza Nekouian[2*]

1) Iran University of Medical Sciences , Tehran, Iran

2) *Institute of endocrinology and metabolism, Tehran, Iran - nekouian.r@iums.ac.ir

Abstract:

Organoids are three dimensional in vitro culture systems derived from self-organizing stem cells. They can recapitulate the in vivo architecture functionality and genetic signature of original tissues. Researchers used CRISPR (which is consisting of a DNA-cutting enzyme called Cas9 and short RNA guide strands that target specific sequences of the genome, telling Cas9 where to make its cuts) to introduce cancer-causing mutations into the organoids and then delivered them via colonoscopy to the colon, where they attached to the lining and formed tumors. Once the tumors are established in the mice, the researchers can introduce additional mutations at any time, allowing them to study the influence of each mutation on tumor initiation, progression and metastasis. In human patients, mutations never occur all at once. Mutations are acquired over time as the tumor progresses and becomes more aggressive, invasive and metastatic. Now we can model these mutations in mice by using the organoid transplantation model. To demonstrate this ability, researchers delivered organoids with a mutated form of the APC gene, which is the cancer-initiating mutation in 80 percent of colon cancer patients. Once the tumors were established, they introduced a mutated form of KRAS, which is commonly found in colon and many other cancers. Furthermore, they delivered components of the CRISPR system directly into the colon wall to not only quickly model colon cancer by editing the APC gene, but also to edit the gene for P53, which is frequently mutated in colon and other types of cancers. The researchers' further investigations showed that they could grow tumor cells from patients into organoids that could be transplanted into mice. This could give doctors a way to perform "personalized medicine" in which they test various treatment options against a patient's own tumor cells. Thus, this approach provides a fast and flexible means to produce tailored CRC mouse models for genetic studies and pre-clinical investigation.

Keywords:

Organoid, CRISPR, Colorectal cancer, Personalized medicine

P157

miRNAs in pathogenesis, prognosis, and directed therapies of chronic lymphocytic leukemia (CLL)

Fatemeh Moghbeli

Fatemeh Moghbeli, Reza Nekouian*
Iran University of Medical Sciences - rnekouian@gmail.com

Abstract:
MicroRNAs (miRNAs), are new class of conserved small non-coding RNA that containing about 22 nucleotides and found in eukaryotes. They regulate the expression and can silence RNAs by hybridizing to them. They bind to their complementary sequence in mRNA that leads to a short-ened half-life of mRNA and reduces translational activity so the outcome is less protein. miRNAs play a role in differentiation of hematopoietic stem cells and tumorigenesis. miRNAs act in diverse biological processes including development, cell growth, apoptosis, and hematopoiesis , suggesting their association with cancer. The finding of biomarkers in various levels including genomics, transcriptomics and proteomics levels could provide better treatment for various cancers such as chronic lymphocytic leukemia (CLL). It has been shown that expression of miRNAs could lead to the activation of B cells and BCR. Moreover, exosomes containing miRNAs are one of the other molecules which could contribute to BCR stimulation and progression of CLL cells. Hence, miRNAs and exosomes released from CLL cells could be used as potential diagnostic and therapeutic biomarkers for CLL. we review the roles of emerging miRNAs and the miRNAs regulatory networks in CLL pathogenesis, prognosis, and miRNA-directed therapies.

Keywords:
leukemia, blood cancer, genetic engineering, hematopoietic, non-coding RNA, biomarker

P159

Tissue Engineered Cells in Breast Cancer

Leila Rezakhani

Leila Rezakhani*, Akram Alizadeh, Morteza Alizadeh

Cellular and molecular research center, basic health sciences institute, shahrekord university of medical sciences, shahrekord. iran
Leila_rezakhani_yahoo.com

Abstract:
The incidence of breast cancer in the world is high, and this disease often causes metastasis and death. The treatment of breast cancer should be taken seriously. Chemotherapy today is widely used and due to its systemic effects, it has many side effects. So the new tissue engineering science is trying to help cure this disease with engineered methods. In recent years, as a result of advances in the tissue engineering and biomaterials fields, a small number of researchers have moved beyond simple gel culture systems and have started utilizing more tunable and mechanically superior polymer matrices as substrates for 3D cancer growth to provide a more well-defined architecture for tumor cell growth. Advances in tissue engineering have traditionally led to the design of scaffold- or matrix-based culture systems that better reflect the biological, physical and biochemical environment of the natural extracellular matrix. Healthy cells of the patient are used such as mesenchymal cells and by manipulating their cell cycle, they reduce the life of these cells. The drugs are loaded to these cells and injected directly into the cancerous tissue. Because the life of these cells has been reduced by manipulation, after multiple fractions in the cancerous tissue, they develop apoptosis. After mesenchymal apoptosis, the drug is released in the tumor tissue and plays its role.
Conclusion: Tissue engineering can help prevent side effects and anticancer drug is used topically.

Keywords:
Breast Cancer, Tissue Engineering, Apoptosis

P161

Concentration of CEA, CA-125 and CA19-9 tumor markers in sulfur mustard exposed veterans

Mohammad Rafiee

Mohammad Rafiee[1*], Naser Shagerdi Esmaeli[1], Mohammad Yousef Alikhani[2], Yunes Panahi[3]

1) Department of Hematology and Blood Banking, School of Allied Medical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
2) Microbiology Department and Research Center for Molecular Medicine, Hamadan University of Medical Sciences, Hamadan, Iran.
3) Chemical injuries research center, Baqyiatallah University of Medical Sciences, Tehran, Iran.
*Corresponding Author - m.rafiee911@gmail.com

Abstract:

Background

Sulfur mustard (SM) is a chemical warfare weapon that leads to alkylation, epigenetic changes, and increased production of oxidants in the cells and also known as a carcinogen. Carcinoembryonic antigen (CEA), cancerantigen125 (CA-125), and cancerantigen19-9 (CA19-9) are tumor markers applicable in diagnosis and follow-up of gastrointestinal, pancreas and lung cancers. Given the carcinogenic effect of SM and the importance of tumor markers, aim of this study is compare of the tumor markers in chemical victims and control group.

Method

150 Iranian chemical victims of SM during Iraq-Iran war and 150 healthy controls that had no exposure to SM were studied. Serum concentration of CEA, CA-125, and CA19-9 were measured by ELISA and compared between the two groups.

Results

Mean concentration of tumor markers in chemical victims group compared with control was 2.72 vs 1.88 ng/ml; ($p < 0.01$) for CEA, 9.06 vs 4.44 U/ml; ($p < 0.01$) for CA-125, and 22.35 vs 11.33 U/ml; ($p < 0.01$), for CA19-9. Weakly positive correlation was found between CEA and CA-125 (p: 0.018, r: 0.193), as well as between CEA and CA19-9 (p: 0.047, r: 0.184) in control and chemical victims group, respectively.

Conclusion

Significant increased levels of CEA, CA-125 and CA19-9 in SM victims are consistent with the results of other studies on carcinogenic property of SM. In addition, as weakly positive correlation between CEA and CA19-9 in exposure to SM in this study and confirmation of this association by other researches, more precise experiments are suggested in the future concerning colorectal and pancreatic cancers in SM victims.

Keywords:

Sulfur mustard, CEA, CA125, CA19-9, cancer

P163

Can sulfur mustard effects on Alpha fetoprotein and β-human chorionic gonadotropin tumor markers in exposed veterans?

Mohammad Rafiee

Mohammad Rafiee[1*], Mohammad Yousef Alikhani[2], Hassan Rafieemehr[3], Yunes Panahi[4]

1) Department of Hematology and Blood Banking, School of Allied Medical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
2) Microbiology Department and Research Center for Molecular Medicine, Hamadan University of Medical Sciences, Hamadan, Iran.
3) Department of Medical Laboratory Sciences, School of Para medicine, Hamadan University of Medical Sciences, Hamadan, Iran.
4) Chemical injuries research center, Baqyiatallah University of Medical Sciences, Tehran, Iran.
* Corresponding author - m.rafiee911@gmail.com

Abstract:

Introduction

Sulfur mustard (SM) is a blistering agent that was typically used on Iran. SM has been known as a carcinogen. Chromosomal breakage and aneuploidies have also been reported from exposure to SM, which are potential carcinogenic factors. Alpha-fetoprotein (AFP) and human chorionic gonadotropin (hCG) are tumor markers used for diagnosis and follow-up of some cancers. Given the importance of tumor markers and carcinogenicity of SM, aim of study was the comparison of serum levels of these tumor markers in SM victims and healthy subjects.

Method

150 Iranian chemical victims exposed to SM, as well as 150 healthy subjects (as control group) were studied. Serum levels of AFP and β-hCG were measured by ELISA in both groups.

Results

The mean concentrations of AFP and β-hCG tumor markers in SM victims in compare with controls were 6.16 vs 3.89 ng/ml (P-value<0.01) and 0.452 vs 0.393 mIU/ml (P-value=0.266) respectively. There was no correlation between age-tumor marker and tumor markers in the two groups.

Conclusion

Increase in the main liver-related tumor marker (AFP) can be due to the role of liver as the main scavenger of oxidants, as well as the involvement of SM in the increase of oxidant in cells. Increased AFP levels in the chemical victims are indicative of the occurrence of unfavorable processes. Because of the clinical value of tumor markers, this significant increase should be taken seriously. However, the importance of increased AFP levels in exposed victims suggests the requirement of precise specific tests in future.

Keywords:

AFP; β-hCG; sulfur mustard; cancer

P164

Diagnosis of Circular Cancer Stem Cell by Microfluidic System

Morteza Alizadeh

Morteza Alizadeh*, Leila Rezakhani, Saleh Hadidi

Cellular and Molecular Research Center, Basic Health Sciences Institute, Shahrekord University of Medical Sciences, Shahrekord, Iran
mor1361@gmail.com

Abstract:
Cancer is a disease that is spreading day by day around the world and taking lives of thousands of people every day. Detection of late cancer leads to the death of many cancer patients, so it is very important to detect it at an earlier stage. Investigating cell-cell interaction, cell-Nano composite, stem cell and cancer cell migration, studying the interaction of cell-scaffold, drug-cell and the effect of mechanical factors on microfluidic systems of perfusion can be checked. The Labyrinth system, is one of the newest techniques that are available to isolate cancer cells from thousands of blood cells, and this can be used to isolate cancer stem cells from blood cells in this system we could labeled desired cells and isolate circulating tumor cells (CTCs) by using the combination of long loops and sharp corners to focus both CTCs and white blood cells (WBCs) . Using these systems, like these, cancers can be detected at much lower levels. one or two cells circulating in the bloodstream. Multiple single-cell techniques have emerged in recent years, making the genome, transcriptome, and proteome of single cells. Designing this kind of device is inspired by the Labyrinth in Greek mythology, an elaborate structure with numerous turns and corners built to hold the Minotaur. This method can be the key to the development of new cancer treatments. If you can isolate invasive cancer cells (from other cells), you have a better chance of developing a cancer treatment.

Keywords:
Microfluidic, Cancer, Stem Cell

P165

challenges and opportunities of Breast cancer personalized medicine

Neda bafandeh

Neda bafandeh
medical University, Department of GeneticsTehran - nedabafandeh@yahoo.com

Abstract:
In fact, we have know
the complexity of molecular pathogenesis of breast cancer the reasons could be related to diversity of populations in term of age, ethnicity and environment risk factors.Risk factors related to cancer progression include genetic reproduction,nutrition,Obesity and exposure to environment Emerging landscape of molecular biology of Breast cancer,represent afew dominant driver mutations reflecting special genes or pathway,Reavired for tumoorgenesis.for daily clinical management of cancer affected patients,personalized medicine is highly valuable goal Although we stiu.Need to expand our knowledge about molecular aspect of disease and its variety. Applied sciences use achieved information from bereast cancer biology to select genes and preventive targeted therapy methods, aswell as applying imovative drug designs and virtual biomarkers for clinical management of patient.The emerging picture of the molecular biology of breast cancer suggests that there are some predominant driver mutations that reflect specific genes or pathways as an event required for tumorigenicity.Personalized medicine for the routine clinical management of breast cancer patients is a lofty goal that will require expansion of our knowledge of the molecular underpinnings of this disease and its various subtypes,Applied science will harness the information generated related to the biology of breast cancer to select genes and pathways for development of targeted therapies and innovative drug designs and to investigate practical biomarkers for clinical management.

Keywords:
Breast cancer,personalized medicine,molecular pathogenesis, mutations,clinical management

P166

Circulating tumor cells in individualized cancer treatment

Nafise Taromi

Nafise Taromi[1], Hamidreza Raeespour[2], Sonia Daraei[3], Behnaz Motahari[4*]

1) Personalized Medicine Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran
2) Gene Pajoohane Ebne Sina genetic research Laboratory, Keshavarz Boulevard, Tehran, Iran
3) Personalized Medicine Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran
4*) Gene Pajoohane Ebne Sina genetic research Laboratory, Keshavarz Boulevard, Tehran, Iran
* Corresponding author - motahari1982@gmail.com

Abstract:
Circulating tumor cells (CTCs), shed from solid tumors, are new biomarkers originating from primary and/or metastatic tumors. CTCs represent a key to understand the biology of non-hematological cancer metastasis and provide non-invasive diagnostic and prognostic tool to pursue therapeutic responses and also the status of the tumor progression.CTCs assessment provides promises for early diagnosis, finding new personalized therapeutic targets, handing more powerful personalized treatments, detecting of relapses and extending life expectancy as one of the most medical purposes. Accordingly, novel technologies have been developed to efficiently isolate CTCs from patient peripheral blood and enumerate them. Most popular and applied methods of CTC assay are based on the genomic or protein content of the cells, which are thoroughly associated with genetic modulation and changes of affected cells in cancer progression. minute abundance and heterogeneity of CTCs in blood samples hinder effective identification and isolation of these promising biomarkers in each individual person, however considering the importance and reliable feature of these individualized biomarkers as diagnostic and prognostic tools, more efficient and suitable procedures have to be developed to determine CTCs properties and use them as personalized cancerous biomarkers in order to increase the chance of successful personalized treatment.

Keywords:
Circulating tumor cells, biomarker, early diagnosis, personalized treatment

P167

Oxidative stress and mitochondrial dysfunctions in personalized cancerous signalling pathway

Nafise Taromi

Nafise Taromi[1], Neda Saray-Gord Afshari[2*]

1) Department of Medical Biotechnology, Faculty of Allied Medical Sciences, Iran University of Medical Sciences, Tehran, Iran
2*) Department of Medical Biotechnology, Faculty of Allied Medical Sciences, Iran University of Medical Sciences, Tehran, Iran
*Corresponding author - afshari.edu@gmail.com

Abstract:
Extracellular/intracellular oxidative stress and mitochondrial dysfunctions are known to play important roles in onset and the progression of the long-term complications in late-stage of numerous cancers. In cancer patients, according to it genetic differences, oxidative stress can be caused by many mechanisms including increased protein glycation and glucose autoxidation, activation of protein kinase C isoforms, and overproduction of superoxide. Down regulation and disruption in function of components of mitochondrial respiratory chain have been implicated as a key factor in the development of most of all cancer complications. Oxidative damages, which caused by increase in mitochondrial reactive oxygen species (ROS) production due to overproduction of free radical and reduction in antioxidant defences, are increased under cancerous conditions. Moreover, alterations in structure and function of mitochondrial DNA (mtDNA), which may be result from increase in rate of mutations, reduction in content and number of mitochondrial DNA and also decreased mitochondrial fusion have been linked to the pathogenesis of almost all cancers. In addition, abnormal mitochondrial reactive oxygen species production may be the main cause of mitochondrial DNA alterations and hyperglycaemic damages, which themselves, can induce the generation of reactive oxygen species. Hence cancer complications and increase in reactive oxygen species levels have direct association with each other and also patient genome structure, inhibition of ROS production or modulation of mitochondrial biogenesis will be one of the next personalized therapeutic target for cancerous patients.

Keywords:
cancer, personalized therapy, oxidative stress, mitochondria, reactive oxygen species, mitochondrial DNA

P168

Cancer Stem Cell

Vahidreza Esfehani

Vahidreza Esfehani, Mahsa Alikarami, Fatemeh Zahra Esfehani, Fatemeh Poureghbal
Islamic Azad University Medical Sciences of Tehran / Personalized Medicine Research Center of BUMS
Islamic Azad University Tehran Medical Branch / Personalized Medicine Research Center of BUMS
Payame Noor University of Tehran East, Iran / Personalized Medicine Research Center of BUMS
Islamic Azad University-Dezful Bbranch,iran / Personalized Medicine Research Center of BUMS
vahidstar26@gmail.com

Abstract:
Cancer is a class of diseases caused by uncontrollable cell growth in parts of the body.
Based on the available evidence, the underlying cause of cancer is a group of stem cells called cancer stem cells. Cancer stem cells secrete many substances such as protease enzymes which are the main reason of causing tumors.
Based on studies of signaling pathways in cancers such as BMI1 / Wnt or beta-cat which have similar effects on self-renewal process of normal and cancerous stem cells, each population is sorted based on common pathways. Cancer stem cells are found in hematologic and Solid tumors including breast, brain, prostate, lung and liver cancer. The various strategies which have been expressed in Personalized Medicine led to provision a suitable treatment for each person.

This includes:
1. targeted pharmacy (using of such substances as Liposomes, Nanotubes, and Nano gels).
2. Targeting the drug resistant genes and making the proper treatment for each person.
3. Destruction of stem cell niche.

Keywords:
Stem cell, cancer stem cell, tumors, cancer

P169

Effects of Vasectomy on Prostate Cancer Rate

Vajihe Nayebzade

Vajihe Nayebzade[1*], Hengameh Dortaj[2]
MsC student, Faculty of Medicine, Shahid Sadoughi University of Medical Sciences and Health Servicesi, Yazd, Iran
MsC, Faculty of Medicine, Shahid Sadoughi University of Medical Sciences and Health Servicesi, Yazd, Iran
vajihenayebzade16@gmail.com

Abstract:
Vasectomy is a male contraceptive method involving only one small operation of vasal ligation. However, There is a hypothesis vasectomy is associated with the increased risk of prostate cancer. The aim of this study was to investigate between relationship vasectomy and prostate cancer risk.
Method: For this study, we used Peer reviewed articles published in pubmed within 2014-2016 of 6 articles which had most citations. Articles were relevant to the association of vasectomy with prostate cancer. Variables were compared using one-way parametric analysis SPSS (version18) and cohort studies.
Result: The results of the review were very different, but more of the articles showed that vasectomy was associated with an increased risk of prostate cancer overall and associations were not driven by differences in sex hormone levels, Sexually transmitted infections or cancer treatment.
Conclusion: This study support an association between vasectomy and prostate cancer and need more studies about this between different nations of the world.

Keywords:
male, prostate cancer, vasectomy, hormone levels.

P172

Methodology of paradigm shift towards personalized medicine

Babak Daneshfard

Babak Daneshfard[1*], Reza Sanaye[2], Majid Nimrouzi[3]

1) Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran
2) Essence of Parsiyan Wisdom Institute, Traditional Medicine and Medicinal Plant Incubator, Shiraz University of Medical Sciences, Shiraz, Iran
3) Department of Persian Medicine, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
* Corresponding author - babakdaneshfard@gmail.com

Abstract:
Since evidence-based medicine scarcely considers the preferences of patients in intricate situations, the mis-interpretation(s) coming from the sheer Heterogeneity of Treatment Effects-misappropriation (or, say, -mal-adjustment) acts as a barrier to the personalized medicine that is badly needed whenever the heterogeneity of treatment crops up even more grossly. It is for this reason that the evidence that Evidence Based Medicine harms the patients less than interventions based on other philosophical schools seems scant.
Person-Centered Care (PCC) is a new entity, concerned about patient as a person not as a medical case. In PCC, the person substituting the patient has to be adapted to imposed conditions by medical settings, but he/she has the right to participate in the medical decisions by bringing up his/her own preferences to the clinician. It must not be confused with the term of personalized medicine that concerns genotypic or phenotypic characteristics of the patients in designing a medical plan. PCC cares about the person who is a human being with own feelings, needs and values, all earned throughout the lifetime. For instance, Ekman et al found that using a full PCC program could shorten the duration of hospitalization in the patients with congestive heart failure. Along with other causes prompting patients to intentionally prefer Complementary and Alternative Medicine could be the fairly famous three Ts that a complementary therapist has the capacity to offer: Time, Talk, and Touch.

Keywords:
Personalized Medicine, Paradigm Shift, Person-Centered Care, Complementary and Alternative Medicine

P173

A novel approach to personalized cancer treatment withelectric-induced field emission materials

Babak Daneshfard

Reza Sanaye[1], Alireza Jangjoo[1], Babak Daneshfard[2*]

1) Essence of Parsiyan Wisdom Institute, Phytopharmaceutical Technology and Traditional Medicine Incubator, Shiraz University of Medical Sciences, Shiraz, Iran

2) Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran

*Corresponding author - babakdaneshfard@gmail.com

Abstract:

The approach of electron therapy to tumors has, up to now, been restricted to "superficial" tumors, and: superficial tumors lying over bone and cartilage tissues at that. We are, to the best of our knowledge, hereby introducing –for the first time– the application of electron therapy to cancerous tumors not necessarily superficial. Moreover, we are doing this in such a manner as to bring about the most probable PRECISION TARGETING whereby the minimal level of non-cancerous cell/tissue damage would be incurred. The effective treatment of relatively in-depth solid cancer tumors is thus carried out not by sudden stoppage of electron currents to produce and/or apply X-ray, but rather: by fine-tunedly applying electron beams into the tumors themselves. We have not been unaware of seeing into various effects of the field-procreating materials. Nor that we have neglected the very intricacies of how the electron currents [and electron plumes thereof] have been brought into existence.

Our electron field(s) has been given birth to both by external induction and internal induction. The controlling of the whole process has been carried out by means of transporting the field-effective materials towards the "receiver", where the field effect producers are under the execution of our fine-tuned time-dependant field(s). In its totality, this procedure has the maximum concentration onto the intended tumor cells. The minutiae of the techniques applied and the continuous vs pulsed electron field exertion, are of course on the record to be peer-reviewed.

Not only that we have created precision beams [and at differing levels of dosage] but also that we have been able to –not randomly– procreate veins of quasi-clustered electron beams to statistically significantly boost the effect of electrons (plumes) on both the topological center of solid cancer tumors and the whole micro-environment thereof.

Keywords:

Cancer, Electron Field, Topology

P174

Evaluation and comparison of the effect of anti-SALL4 siRNA on growth and sensitivity of the colorectal cancer cell line

AmirReza Hesari

AmirReza Hesari, Faezeh Ghasemi*

Department of Biotechnology, Faculty of Medicine, Arak University of Medical Sciences, Arak, Iran.
*Corresponding author - Ghasemi_f@arakmu.ac.ir & Ghasemi_808@yahoo.com

Abstract:

Colorectal cancer is the third most common cancer in men and women, and is the second leading cause of cancer deaths in many countries. Spalt like transcription factor 4 is a transcription factor that plays a major role in the proliferation of cancerous cells. SiRNA is a short-chain molecule of 20 to 25 nucleotides that protrude on two sides of the 3 ‘, two nucleotides. In this study, using a specific sequence of SiRNA against the sequence of this gene, its activity is investigated in the cell line of colorectal cancer (sw742). The colorectal cancer cells (sw742) were cultured and then, using a specific anti-SALL4 SiRNA, their toxic doses were determined. Then, the gene is introduced into the cell using lipofectam, and the expression of the gene is measured using the Real Time-PCR method. The specific concentration of SiRNA IC50 of the SALL 4 gene was 62.5 nmole. The results of the gene expression test showed that the expression of SALL4 gene in the SiRNA group was significant (2 fold). Apoptosis gene expression results showed that expression of Bcl-2 gene in the siRNA group was significantly reduced (5 fold). Cell cycle results in the group treated with SiRNA and the cell control group showed that the treated group had a higher percentage of SubG1 (23.08%) compared with the control group of cells (0.66%). SubG1 percent represents apoptosis in the cell ($P < 0.05$). SiRNA can increase the standard drug effect in colorectal cancer cells by reducing the gene expression of SALL4, it can be used as a combination drug. This strategy, in addition to increasing the sensitivity of cancer cells to the standard drug, also reduces the dose of it.

Keywords:

Colorectal cancer, SALL4, siRNA, Bcl-2

P176

Cancerous Women Personal Health Record

Kobra Aligolbandi

Kobra Aligolbandi
Faculty member of Mazandaran University of Medical Sciences - k.golbandi@gmail.com

Abstract:
Introduction: Cancer is one of the health problems in whole the world. Breast cancer disease has become the most common illness among women at recently decade in Iran. When individual health record can effect of facilitating communication between doctor and patient and support of self care way. So we decided check out PHR of cancerous women.
Objective and research importance: PHR often are as a source of data and as subcategory of patient medical records. Individual health record woman that suffering of cancer can include: Detection related note, treatment, laboratory results, mammography, chemotherapy, radio Therapy, Doctors advice.
Methods: This cross –sectional research occurred on 123 random sample of hospitalized patients at educational hospitals of Mazandaran University of medical sciences in 1394 and 1395 year. Data collection accrued with interview by questionnaire to 4 part consist of; lab information, treatment, diagnostic procedures and consultation. Data was presented with SPSS software and descriptive statistics.
Results: Close to %56/3 of patients they can keep their medical information & %91 they cannot keep medical record because they do not enough have time & they are bored.
Discussion: In attention to lack of awareness of patients is suggested that keep the individual health records is very important, so necessary educations to be given a bout creation personal health record in paper form and computerized form.

Keywords:
personal health record, patient care, women cancer

P177

The impact of health information technology in promotion of personalized medicine

Mohamad Jebraeily

Mohamad Jebraeily
Department of Health Information Technology, Urmia University of Medical Sciences, Urmia, Iran

Abstract:
Since each patient is unique, in recent years the health care industry has developed provide personalized medicine. In fact, personalized medicine is a therapeutic approach that healthcare services based on the specific characteristics of each patient such as individual's needs, values and preferences. Health information technology (HIT) has the potential to support the delivery of personalized medicine. The purpose of this study was identified impact of HIT in promotion of personalized medicine.
We conducted a literature search of databases including PubMed, Web of Sciences, Science Direct, EMBASE, Cochrane Library, Scopus and CINAHL which were investigated from 2007 through 2017. The search was performed using a combination of the following terms: personalized medicine, patient-centered care, health information technology and information technology. Finally, 11 reviewed articles met the inclusion criteria.
The results showed that most researches emphasized that HIT can be used to promote personalized medicine by providing better access to information and health services, improved patient care and safety, integration of care and empowered patients. Effective use of HIT can be having a helpful role in enhancing the patient-clinician relationship and active participation patient in the decision-making process.
The HIT tools are critical to support the delivery of personalized medicine. Therefore, it seems necessary to establish IT infrastructures required and develop privacy rules for ensure protection of data. It is very important to train skills required to work with HIT tools for healthcare providers and patients.

Keywords:
personalized medicine, patient-centered care, health information technology, information technology

P179

Microfluidic approaches for separation of Mouse Tumoral Cells from Neonate Spermatogonial Cells Suspensions

Kadijeh Ashtari

Khadijeh Ashtari[1,2], Narges Esmaeilzadeh[1], Ehteram Hossenzadeh[1], Sara Tanbakoei[2], Mehdi Mehdizadeh[2,3], Majid Ebrahimi Warkiani[4*], Ronak Shabani[2,3*]

1) Department of Medical Nanotechnology, Faculty of advanced technology in Medicine, Iran University of Medical Sciences, Tehran, Iran.
2) Cellular and Molecular Research Center, Iran University of Medical Sciences, Tehran, Iran.
3) Department of Anatomical Sciences, School of Medicine, Iran University of Medical Sciences, Tehran, Iran.
4) School of Mechanical and Manufacturing Engineering, University of New South Wales, Sydney, New South Wales 2052, Australia.
* Corresponding author - Shabani.r@iums.ac.ir

Abstract:
Some male survivors of childhood cancer are in distress from azoospermia. Conventional cancer cell sorting techniques, which have been reviewed elsewhere, are not effective. The aim of this study was to separating the mouse malignant cell line (EL-4) and spermatogonial stem cells in vitro.
Spermatogonial cells were co-cultured with mouse malignant cell line (EL-4) cells and divided into 3 culture groups: 1) Control (co-culture in culture medium), 2) Co-culture were sorted by FACS, 3) Co-cultured cells were separated by microfluidic chip. The percent of cells were assayed after treatment using flow cytometry and the identity of cultured cells were confirmed by RT-PCR and immunocytochemistry. The present work demonstrates the use of electrophoretic lab-on-a-chip device in effectively separating cancer cells from spermatogonial cells (42.14 EL4, 0.12 SSC) and (0.32 EL4, 80.38 SSC,) compare with FACS technique.

Keywords:
Microfluidic device, Spermatogonial Cells, Cancer cells, cell sorting

P182

Role of Micro-RNAs in Growth Hormone Deficiency: the Current Evidence

Seyyed Amir Yasin Ahmadi

Seyyed Amir Yasin Ahmadi, Reza Nekouian*
Pediatric Growth and Development Research Center, Institute of Endocrinology and Metabolism, Iran University of Medical Sciences, Tehran, Iran
*Corresponding author - rnekouian@gmail.com

Abstract:
Introduction: Micro-RNAs (miR) are small RNAs encoded by downstream sequences of different genes. They play their roles through regulation of gene expression. Hence we intend to have a review on the recent evidence about the role of miRs in growth hormone deficiency.
Methods: Scientific search engines were used in order to find papers. NCBI and miRDB database was used to assess to miR and genetic information.
Results: Among the miRs, miR-15a, -26b, -29a, and -29b found to be associated with growth process. Most of them where in-vitro and animal studies. MiR-29a had a stronger evidence which was a human cohort study. This miR is down regulated by growth hormone replacement therapy and IGF-I. In addition it plays its role in myotubes and also insulin resistance level. The other miRs had similar functions but with lower evidence.
Conclusion: Levels of the related miRs should be assessed in growth hormone deficiency children. As well these levels should be compared in responsive and resistant groups of replacement therapies. The evidence should be completed further because current drugs can be carcinogen.

Keywords:
Micro-RNA, child growth, growth hormone deficiency, personalized medicine

Micro RNA	Effect direction	Target in human	Study design	Setting or stage
miR-15a	Negative*	GHR	In vitro (bovin mammary gland)	At GHR level
miR-26b	Down regulated by GH	adipoQ family	In vitro (human adipocytes)	Related to obesity and insulin resistance
miR-29a	Down regulated by GHRT# and IGF1	PTEN, COL3A1, FSTL1, SERPINH1, and SPARC	Cohort	In myotubes and Insulin resistance
miR-29b	Down regulated by GH and up regulated by starvation	INSIG1, IGF1 and IGF2	In vitro (rat liver)	At liver level

*Its role is against growth
Growth hormone replacement therapy

P183

Most used microRNA in inflammatory bowel disease

Samira Shajari

Samira Shajari, Zahra Mahmoodi, Reza Nekouian*
Iran university of medical science, Tehran, Iran
*corresponding author - rnekouian@gmail.com

Abstract:
MicroRNAs (miRNAs) have recently emerged as important mediators of immune development and responses. miRNAs are short (21–25 nucleotide), non-coding RNA molecules that are most commonly transcribed by RNA polymerase II and processed by proteins such as Drosha and Dicer. MicroRNAs play important roles within the complex intestinal immune system. They can be expressed within hematopoietic cells in response to inflammatory signals from pattern recognition receptors (PRR) and antigen receptors (AR). In this way, miRNAs can regulate immune responses, including secretion of cytokines, chemokines, and antibodies, all of which affect intestinal homeostasis. Within intestinal epithelial cells (IECs) and other non-hematopoietic intestinal cells, miRNAs are expressed in and regulate pathways involved in secretion of antimicrobial peptides, cell renewal, and barrier permeability, among others. These noncoding RNAs function as rheostats to the immune response as opposed to binary switches as they act to adjust the magnitude of gene expression. miRNAs also work in feedback loops, ensuring that the immune system does not produce inappropriately strong responses while also promoting protective immunity when needed. In this way, miRNAs themselves can be considered mediators of homeostasis within the immune system as they act to buffer inflammation.
IBD is a chronic relapsing disorder of the gastrointestinal tract that is due to intestinal inflammation and epithelial injury and includes Crohn's disease and ulcerative colitis. Although IBD is thought to arise through interactions among genetic, immunologic, and environmental factors, the etiology underlying the pathophysiology of IBD remains largely unknown.
Studies to date have identified unique miRNA expression profile signatures in IBD and preliminary functional analyses associate these deregulated miRNAs to canonical pathways associated with IBD pathogenesis.
UC-associated peripheral blood miRNAs were found to be differentially expressed (increased: miRs-28-5p, -151-5p, -103-2, -199a-5p, -340,-362-3p, -532-3p; decreased: miR-505) miRs-199a-5p, -362-3p, -532-3p, -16, -106a, -195, -340 and miRplusE1271 were increased and miR-149 was decreased in the peripheral blood of patients with CD.
In this review, we summarize and discuss the miRNA expression signatures associated with IBD in peripheral blood, highlight miRNAs with potential future clinical applications as diagnostic and therapeutic targets, and provide an outlook on how to develop miRNA based therapies.

Keywords:
inflammatory bowel disease, microRNA, Crohn disease, ulcerative colitis

P184

Groth hormone and cancer risk

Zahra Mahmoudi

Zahra Mahmoudi[1], Faeazeh Mousavi[2], Reza Nekooian[3*]

1) Iran university of medical science, Above Vanak Sq, Valiasr Ave.,Tehran, Iran
2) National Institute of Genetic Engineering and Biotehnology, Shahrak-e Pajoohesh, km 15, Tehran - Karaj Highway, Tehran, Ira
3*) Iran university of medical science, Above Vanak Sq, Valiasr Ave.,Tehran, Iran
*Corresponding author - rnekouian@gmail.com

Abstract:
Growth hormone (GH) via its mediator, insulin-like growth factor-I (IGF-I) do have mitogenic and anti-apoptotic activity , to regulation of cellular growth.Their potential involvement in tumor promotion and progression has
been of concern for several decades. Purpose of review discuss the association between recent studies of human cancer by excess treated with growth hormon .
Pre-clinical studies and epidemiological observations in patients with an excess of hormone production or in patients chronically treated with GH does result in a small increase in cancer risk compared with untreated patients with GH deficiency although this is a distinction that is important mechanistically but not clinical .
Epidemiological studies of patients with acromegaly indicate an increased risk of colorectal cancer, although risk of other cancers is unproven, and a long-term follow up study of children deficient in GH treated with pituitary-derived GH has indicated an increased risk of colorectal cancer.
Finally, even if GH/IGF-1 therapy does result in a small increase in cancer risk compared to untreated patients with GH deficiency, it is likely that the eventual risk will be the same as the general population.
However, important questions remain unresolved concerns about the potential cancer-enhancing properties of GH.

Keywords:
growth hormone , insulin_ like growth factor , growth hormone deficiency

P186

The emergence of micro-isolator devices for high throughput exosome analysis: A technological leap towards personalized cancer treatment

Shabnam Shahrivari

Shabnam Shahrivari[1], Neda Saraygord Afshari[2*], Zeinab Bagheri[3]

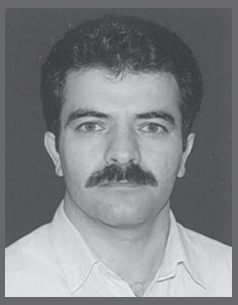
1) MSc. student of medical biotechnology; Student Research Committee, Iran University of Medical Sciences, Tehran, Iran
2*) Assistant professor; Department of Medical Biotechnology, Faculty of Allied Medical Sciences, Iran University of Medical Sciences, Tehran, Iran (neda.s.afshari@gmail.com)
3) Assistant professor; Protein research center, Shahid Beheshti University, Tehran, Iran Tehran, Iran

Abstract:
Exosomes, as the noteworthy extracellular compartments of liquid-biopsies, are vehicles aid the displacement of biomolecules (lipids, proteins and/or nucleic acids). Hence, they can play pivotal roles in cancer pathogenesis. The diversity of the exosomes' contents which dynamically reflects bio-situations, has made them a valuable biomarker for theranostic applications which fits the personalized medical attitudes. The role is more outstanding in the case of cancer as a complex disease. In these situations, using exosomes as personalized theranostic biomarkers demands the rise of rapid, precise and affordable technology. This has been recently achieved by the emergence of microfluidic technology which facilities exosome isolation and analysis.
Both physical and biological characteristics of exosomes have been used to design Lab-On-Chip micro-isolators. In bio-based isolators, exosome specific antibodies are immobilized on solid surfaces, specifically capture the vehicles. While, physical separators can either make use of particles' physical properties and/or physical forces (size-based separations on nonporous membranes and on-chip acoustic nano-filtration, respectively). Development of on-chip nanowires for trapping exosome-like vesicles and deterministic lateral displacement micro-sorter (based on the different displacement patterns of the large and small particles) are the other examples of micro-fabrications for exosome analysis.
Micro-isolators have proved that microfluidic technology has dramatically increased the efficiency of exosome-based analysis. Although at their infancy, micro-platforms have provided more accessible, affordable and convenient devices than today's conventional instruments (ultracentrifugation and size-exclusion-chromatography). They also provide more accurate and reproducible results but to fit the newly emerging personalized medicine in future they tend to be accompanied by downstream bio-analysis.

Keywords:
Exosomes; Microfluidic; Personalized medicine; Micro-isolator; Cancer diagnosis

P187

Metabolomics and Personalized Medicine: Benefits and Challenges in Undeveloped Countries



Abbas Ahmadi

Abbas Ahmadi[1*], Mehdi Zandi[2], Ali Salehi[2], Ali Tahmasebi[2]

1*) PhD of Molecular Medicine, Cellular and Molecular Research Center, Kurdistan University of Medical Sciences, Sanandaj, Iran
2) B.Sc. of Medical Laboratory Technology, Student Research Committee, Kurdistan University of Medical Sciences, Sanandaj, Iran.
*Corresponding author - abbasahmady1@gmail.com

Abstract:
Small molecules (metabolites) play key roles in all biological systems. Their comprehensive study provides the potential to understand physiology and pathobiology of human diseases. Metabolomics permits total, concurrent, and complete study of metabolites in a cell, tissue, organ or biological being. Due to complex genetic diversity, the results may vary among affected persons, from person to person, and also population to population.
Different analytical approaches and tools can be used in this field. After an extensive search in the Google Scholar and PubMed, related articles were chosen and summarized. Here we discuss the challenges for the use of metabolomics as a powerful disease biomarker. We will also address its uses for the finding of diseases biomarkers and treatment in the precision medicine.
In conclusion, metabolomics, is reforming our concept regarding the pathobiology, diagnosis, prognosis, and treatments in the current medicine era. However, as it is based on the individual and population diversities, the main challenges and obstacles for its uses in undeveloped countries are the lack of comprehensive population based studies. So, establishing powerful research and working groups for collecting bio-fluids and founding a reliable and robust bio-banking system is recommended.

Keywords:
metabolomics, challenges, precision medicine, bio-bank.

P189

The interaction between Berberine chloride with complex Histone (H1)-DNA by multi spectroscopic and molecular modeling

Louisa Rudini

Louisa Rudini, JamshidKhan Chamani

1Department of biology/Faculty of science, Mashhad branch, Islamic Azad University, Mashhad, Iran
2Department of biology/Faculty of science, Mashhad branch, Islamic Azad University, Mashhad, Iran
Rudini.louisa@gmail.com

Abstract:

DNA is the primary target of many anticancer drugs .Based on the former studies any changes in DNA structure has an important impact on the interaction of DNA-histone H1 complex and consequently on intercellular processes especially transcriptional regulation, since histone H1 is known as the inhibitor of gene expression. Some small molecules bind to histone-DNA complex and impair the important processes such as cell division, growth,and thus they lead to apoptosis in cancer cells.

Therefore the study of drug-histone (H1) DNA interaction is important for a better understanding of the mechanism of action and to design newer and more effective drugs.

In this study, the interaction of histone-DNA complex and Berberine chloride was investigated in Tris buffer (pH 6.8) using fluorescence spectroscopy, resonans light scattering, transition temperature, viscometry, circular dichroism, UV-visible and molecular docking and MTT assay techniques.

In fluorescence spectroscopy method emission reduction indicates quenching and complex formation that in a 351 excitation wavelength Berberine caused flourscence quenching of DNA, Histone H1 and DNA-Histone H1.

In competitive emission espectrum interacation between ethidium bromide and acridine orange as intercalator probs with Berberine was studied and it was showed that the addition of the Berberine to DNA-Ethidium bromide and DNA-Acridine orange complexes ,causes change in emission spectra of the complexes which indicates competition but in presence of Histone this competition between the ligand and probes was not observed.

So the competition between Berberine and intercalator probes represents that Berberine binds between DNA base pairs.

In resonans light scattering by adding ligand to macromolecules the number of particles were increased so the spectra was increased.

According to temperture transition studies adding Berberine to DNA increased DNA melting point and stability ,although melting point did not change in presence of Histone H1.

In viscometry method, the viscosity of DNA was increased by adding compound to DNA solution which was due to intercalating interaction but in the presence of the histone H1, viscosity decreased.

Also, due to intercalating compounds such as potassium iodide and sodium chloride ions, which compete with berberine chloride over binding sites in the absence of histone, it can be predicted that the Berberine binds between DNA base pairs.

In circular dichroism by additing ligands separately to DNA two peaks in positive and negative areas were observed, but for DNA-H1 complex just one peak in negative area was observed which was falling to a more negative point.

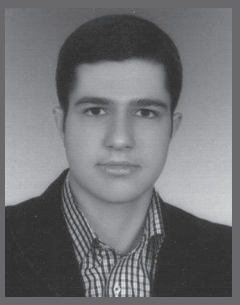
The results of the experiments showed that the type of Berberine interaction with DNA in absence of histone H1 is intercalation and in the presence of the histone Berberin binds to DNA grooves. Molecular docking also confirmed the above results.

Keywords:

ct-DNA , DNA-Histone, Berberine, Spectroscopy, Molecular Docking

P190

Expression of micro RNAs implicated in left ventricular hypertrophy; a systematic review



Hamed Motevalli

Aida Iranpour, MD[1], Reza Nekouian[2], Shokoufeh Hajsadeghi,MD[1], Reza Razzaghi[3], Fatemeh Mollaei[3], Hamed Motevalli[3*]

1) Research center for prevention of cardiovascular disease, Institute of Endocrinology & Metabolism, Iran University of medical sciences, Tehran, Iran
2) Pediatric growth and development research center , Institute of Endocrinology and metabolism Iran university of medical science, Tehran, Iran
3) Iran University of medical sciences, Tehran, Iran
*Corresponding author

Abstract:
Cardiovascular disease is one of the leading causes of human mortality and morbidity. Left ventricular hypertrophy (LVH) is a common finding and implicated as an important risk factor for sudden cardiac death. Recent efforts have been focused in determining novel molecular targets such as miRNAs with the goal of developing diagnostic or therapeutic tools especially in preclinical stage. Here we performed a systematically review of the literature to find correlations between miRNAs and LVH.
We reviewed three databases including Pubmed, Embase and Cochrane from 2012 to 2017 using left ventricular hypertrophy and micro RNA as keywords. It resulted in identification of 91 articles. Based on exclusion criteria, 13 articles were remained to study.
We observed higher expression levels of (miR-1, miR-2, miR-21, miR-22, miR-23a, miR-26b, miR-27a, miR29a, miR-29b, miR-29c, miR-133a, miR-155, miR-199a-5p, miR208, miR-208b,miR-499) and decreased levels of (miR-1, miR-9, miR-98, miR-132, miR-133, miR212, miR378) is associated with higher prevalence of LVH.
The finding of this systematic review shows that different types of miRNAs play significant roles in left ventricular hypertrophy and variable expression levels of them have been seen. Our data also indicates that they are dividing in two groups including stimulatory and inhibitory miRNAs. One of the most significant findings of our study is that some of the micro RNAs including miR-1 and miR-133 are in both groups. Thus, further investigation in order to determine the exact type of miRNAs is mandatory before considering them as diagnostic tools.

Keywords:
Left Ventricular Hypertrophy, Hypertrophy,left ventricular, MicroRNA, miRNA, Primary miRNA

P194

Spectroscopic and molecular modeling studies of interaction between ct-DNA and daunorubicin as a anticancer drug in absence and presence of histone H1

Samaneh Salehian

Samaneh Salehian[1], Jamshidkhan Chamani[2]

1) Department of biology , Faculty of science , Mashhad Branch, Islamic Azad University , Mashhad , Iran
2) Department of biology , Faculty of science , Mashhad Branch, Islamic Azad University , Mashhad , Iran
S8.salehian@yahoo.com

Abstract:
Many anticancer drugs like daunorubicin involved in transcriptional regulation that DNA is these drugs target . Histon H1 known as inhibitor of gene expression that can play a pharmacogenetic agent influence in interaction of small molecule with DNA during growth , cell division , inhibition and apoptosis in canser cells. In this research the interaction of DNA with daunorubicin ,that can kill MCF-7 in cell culture tecnique that used in this work, in absence and presence of histon H1 by using fluorescence spectroscopy , resonance light scattering , transition tempeture ,viscometry ,circular dichroism , UV_visible spectr.oscopy and molecular dockind techniques.
In transition tempture ,daunorobicin caused stability of DNA structure and DNA_Ligand complex ,with increasing melting point. In viscometry method by adding ligand to DNA and DNA_H1 complex ,viscometry of both solution. In circular Dichroism in DNA_Daunorubicin chart two peak in negative and positive area were created, but there is just one peak in negative area in Daunorubicin-DNA-H1 chart .Quenching in fluorescence spectroscopy, show the compete DNA with intercalators compound which located between DNA base pairs. In UV_visible decreasing of absorbtion and chang in poind diagram show intercalation future of Daunorubicin with DNA in absence and presence of H1. In resonance light scattering with adding ligand ,the intensity enhance that shows chang structure.
Results of molecular doching show groove binding that is diffrrnt with emperocal method ,although other results indicate intercalation mode.

Keywords:
DNA _Histon H1 complex , spectroscopy , intercalation ,daunorubicin

P196

A comprehensive model for cancer prevention and early detection

Mehrdad Zeinalian

Nafiseh Heidarzadeh Isfahani[1], Zahra Sadri[1], Mohammad Sajjad Zare'[1], Mahdi Hadian[1], Homayoun Naji[1], Mohammad Reza SharbafchiZadeh[1], Mehrdad Zeinalian[1,2*]

1) Ala Cancer Prevention and Control Center, Isfahan, Iran
2) Department of Genetics and Molecular biology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
*Corresponding author - zeinalianmehrdad@gmail.com

Abstract:
Some cancers develop as a result of genetic factors that occur in families. These cancers are linked to the heritable genetic pathogenic variants. About 5-10% of all cancers are related to hereditary syndromes in which the carriers have a higher chance to develop certain types of cancer. A charity-based institute in Central Iran, Ala cancer prevention and control center, has a department for genetic counseling of at-risk families for cancer. It provides some services such as the comprehensive genetic counseling sessions and education for risk reduction in the families registered in an established electronic database in center. The promotion of at-risk family members' awareness toward cancer risk factors (environmental and genetic factors) is considered in the educational preventive services including risk reduction advices and cancer early detection methods. Some of the health principles in Iranian traditional medicine are recommended to the audience as a complete package of health-related preventive rules.

At-risk families are invited for genetic counseling according to some criteria such as a positive familial history and early onset cancer. A risk assessment would be done by pedigree analysis, medical records and personal health history. In familial cases at-risk for hereditary syndromes genetic testing would be likely helpful. A second genetic counseling session should be arranged for interpreting the test results and explain the choices for medical prevention and early diagnosis. Some of these steps are done in partnership with psycho-oncology department to manage psychological outcomes. Follow-up services include annual phone and presence follow up for at-risk families to remind and emphasize the importance of early screening tests. Since 2014, 2224 families have been got genetic counseling and prevention services in this center. This is done for the first time in Iran and due to the growth of cancer rate, it should be provided at every cancer prevention center.

Keywords:
comprehensive model, cancer, prevention, early detection

P197

Personalized micro-RNA profiling and their individualized theranostic applications in cancer treatment

Shadi Abkhiz

Shadi Abkhiz[1], Neda Saraygord-Afshari[2*], Arshad Hosseini[2]
1) student research committee / Iran University of Medical Sciences, Tehran, Iran
2) Faculty of Allied Medical Sciences / Iran University of Medical Sciences, Tehran, Iran
*Corresponding author - afshari.edu@gmail.com

Abstract:
Micro-RNAs (miRNAs) are studied as class of theranostic markers suitable for personalized medicine; since they have some ideal characteristics such as specificity, stability and classification power for rapid and strong analysis, all of which need in theranostic application.

Considering the presence of microRNAs in all the cellular pathways, they possess undeniable roles in malignancies. For example, tumor suppressors and onco-miRs can cause proliferation, migration, epithelial mesenchymal transition and invasion. miRNA expression level can also indicate cancer initiation, progression, and metastasis, useful earlier detection of cancer. microRNAs can affect tumor environment and influence the pharmacokinetics and pharmacodynamics of patient-specific cancer drugs. Exact expression pattern of microRNAs not only indicates the origin of the tumor but also shows the degree of differentiation and classification of non-recognizable tumor tissues. The most important factor of microRNAs study is how to profiling microRNA expression which can be achieved by three major methods: amplification-based (real-time quantitative PCR, qRT-PCR), hybridization-based (microarrays), and sequencing-based (next-generation sequencing (NGS)) technologies. In addition, microRNAs can be detected in human tissue specimens, fresh or formalin-fixed paraffin embedded (FFPE).

However, each miRNA can affect large number of gene targets and each gene can be controlled with more than one miRNA complicated targeted detection, compare to other biomarkers, their important regulatory role in various biological processes, utilization as non-invasive diagnostic tests which are indigenous, safe and sensitive in pathology follow-up as well as convenient detection cause to achieve personalized hope for cancer diagnosis biomarker and computational/experimental biology with medical practices.

Keywords:
miRNA, cancer, personalized medicine.

P198

Personal tumor neoantigens and cancer immunotherapy

Neda Mohammadi

Neda Mohammadi[1], Neda Saraygord Afshari[2*]

1) Department of Medical Biotechnology; Student Research Committee, Iran University of Medical Sciences, Tehran, Iran
2*) Department of Medical Biotechnology, Faculty of Allied Medical Sciences, Iran University of Medical Sciences, Tehran, Iran
afshari.edu@gmail.com

Abstract:
Recently, immunotherapy and developing of cancer-specific vaccines have opened-up new windows for cancer treatment and helped to overcome tumor-induced immunosuppressions. But science the molecular profile of cancerous tissues has been proven to be varied from one individual to the other, demands for personalized immunotherapy of cancer has been risen; although this encounter fundamental challenges which have been lead to clinical failures in many. Personalized cancer vaccines based on individualized neoantigens (which are mutated proteins, specifically produced in tumor cells) are hoped to highly stimulate the specific anti-tumor responses. Fortunately, nowadays with the advent of high-throughput technologies, such as next-generation sequencing, array-based techniques and …, identification of mutated genes and subsequent synthesizing of neoantigens are made feasible. The events which facilitate the design and implementation of individualized neoantigens-based cancer vaccines.
Methodological overview of this procedure can be as follows: DNA and/or RNA of both tumor and normal tissues are extracted, mutated genes are identified and their specific mutated peptides are synthesized. Finally, neoantigens with powerful complementary immunoadjuvant (like checkpoint-blockade inhibitors) are administered to the patients for boosting the potency of their immune system especially their T cells. Hence, immune system can identify mutated antigens, and destroy tumor cells.
In spite of the encouraging results of new trials, like any other newly emerging technologies, personalized cancer vaccines has a lot of challenges ahead. Many efforts must be made to reduce the time for developing an individualized formulation of neoantigens-based cancer vaccines and to find a way for obtaining conclusive results.

Keywords:
Cancer; Personalized medicine; Vaccine; Neoantigens

P199

Producing Taxol from Iranian Yew

Sonia Daraei

Sonia Daraei[1], Shamsozoha Abolmaali[2*], Nafise Taromi[3]

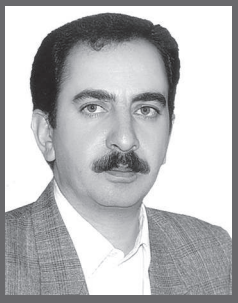
1) Campus Science and Technology, University of Semnan, Semnan, Iran
2*) Campus Science and Technology, University of Semnan, Semnan, Iran,
3) Personalized Medicine Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran
s_abolmaali@semnan.ac.ir

Abstract:
Frontotemporal dementia (FTD) is a progressive neurodegenerative disorder; with a gradual onset and progression of changes in behavior or language deficits. It is denoted to somewhat different clinical pictures including behavioral and personality changes, language difficulties and combination od theses symptoms with other neurological problems. In general FTD is now classified into several types including behavioral variant of FTD (bvFTD), semantic variant primary progressive aphasia (PPA), nonfluent agrammatic variant PPA, and FTD associated with motor neuron disease (FTD-MND).
The clinical varieties across the diagnosis of FTD are attributed to differences in the brain regions affected by FTD pathology which can cause degeneration of frontal and/or temporal lobes. Involvement of frontal lobe may develops symptoms such as behavioral Disinhibition, apathy or inertia, stereotyped or compulsive behaviors and executive deficits. Degeneration o temporal lobes lead to difficulty with language and hyperorality or dietary change.
Approximately 40 percent of FTD have a genetic based with autosomal dominant pattern of inheritance. Besides the major differences mentioned above, some types of gene mutations leading to FTD cause atrophy in especial regions of cerebral cortex. For instance, C9ORF72 expanded repeats lead to predominantly atrophy in the frontal lobes and some atrophy in the anterior temporal lobes, parietal lobes, occipital lobes, and cerebellum and thalamus. The atrophy in MAPT mutations predominantly involves the anteromedial temporal lobes and mutation in GRN gene which alters the progranulin protein lead to temporal, insular, and parietal lobe atrophy.
New progresses in genetic studies of FTD variants may enhance our knowlelge about diseases with frontotemporal degeneration and in the future, clinicians will need to know the genetic mutations occurred in every patient for proper treatment.

Keywords:
Personalized Medicine, Frontotemporal Dementia, Behavioral variant of FTD, Primary Progressive Aphasia, Gene Mutation

P201

Epigenetic alterations in hematologic malignancies



Ali Maleki

Ali Maleki
Allied Medical Sciences, Kermanshah University of Medical Sciences, Sanjabi street, Kermanshah, Iran
* Corresponding author - Maleki.hem@gmail.com

Abstract:
Background: Cancer development is not restricted to the genetic changes, but also to epigenetic changes. Epigenetic processes are very important in the development of hematological malignancies. The main epigenetic alterations are aberrations in DNA methylation, post-translational modifications of histones, chromatin remodeling and microRNAs patterns, and these are associated with tumor genesis. All the various cellular pathways contributing to the neoplastic phenotype are affected by epigenetic genes in cancer. These pathways can be explored as biomarkers in clinical use for early detection of disease, malignancy classification and response to treatment with classical chemotherapy agents and epigenetic drugs.
Materials and Method: A literature review was performed using PUBMED from 1985 to 2017. Cross referencing of discovered articles was also reviewed.
Results: In chronic lymphocytic leukemia, regional hypermethylation of gene promoters leads to gene silencing. Many of these genes have tumor suppressor phenotypes. In myelodysplastic syndrome (MDS), CDKN2B (alias, P15), a cyclin-dependent kinase inhibitor that negatively regulates the cell cycle, has been shown to be hypermethylated in marrow stem (CD34+) cells in patients with MDS. At present both Vidaza and Decitabine (DNA methyltransferase inhibitors) are approved for the treatment of MDS.
Conclusion: Unlike mutations or deletions, DNA hypermethylation and histone deacetylation are potentially reversible by pharmacological inhibition, therefore those epigenetic changes have been recognized as promising novel therapeutic targets in hematopoietic malignances. In this review, we discussed molecular mechanisms of epigenetics, epigenetic changes in hematological malignancies and epigenetic based treatments.

Keywords:
Epigenetic, hematological neoplasms, methylation, histone

P203

Effect of mutation in exon.4 of the LDL Receptor gene (LDLR) in familial hypercholesterolemia

Shima Parviz

Shima Parviz[1],Arghavan Hosseinpouri[1], Seyed Javad Hosseini[1,2], Ali movahed[3]

1) Department of cellular and molecular sciences, the Persian Gulf University, Bushehr, Iran
2) Assistant Professor ,Department of Biotechnology, the Persian Gulf Research and Studies Center, the Persian Gulf University, Bushehr, Iran
3) Assistant Professor, Department of Biochemistry, Faculty of Medicine,Bushehr University of Medical Sciences, Bushehr, Iran

Abstract:

Family Hypercholesterolemia (FH) is a common autosomal dominant genetic disorder that results from high levels of low-density lipoprotein cholesterol (LDL) and increases the risk of early-onset cardiovascular disease in men and women.As cardiovascular disease appears in heterozygous patients under the age of 20 years and in heterozygous patients under age 50.The incidence of this disease is 1 in 200 to 500 people in the world. It is not a rare disease, but it is fortunate to be diagnosed, and its treatment is possible. Early diagnosis and treatment can decrease the risk of atherosclerotic cardiovascular disease caused by the FH.Diagnosis can be done based on clinical criteria (including LDL, cholesterol and family history) or DNA testing. Over the past decades, cascade screening program has been conducted in many countries and regions that have led to the identification of a large number of these patients.

Most of the single-gene causes of FH-induced mutations in one of the three LDLR, APOB, and PSCK9 genes, of which about 90% occur in the LDLR gene and more than 1200 different mutations are detected. So far, all of the exons of the LDL receptor gene have been found to have various types of mutations associated with the disease, but because of the high percentage of mutations in exon 4 in the studies performed so far in the world, this study examines the mutations observed in this exon in patients with familial hypercholesterolemia.

P204

The therapeutic application of lipase, as an effective drug in the prevention, treatment and improvement of cancer progress

Asma Charkhabi

Asma Charkhabi[1*], Kamran Ghaedi[2], Bagher Yakhchali[3], Marzieh Alamatsaz[4]

1) MSc of Microbiology Biology, Noor Danesh Institute, Meymeh, Esfahan, Iran
2) PhD, Department of Biology, Faculty of Sciences, University of Isfahan, Iran
3) PhD, National Institute of Genetic Engineering and Biotechnology (NIGEB), Tehran, Iran
4) MSc of Cellular and Molecular Biology, Noor Danesh Institute, Meymeh, Isfahan, Iran
Asma.Charkhabi@gmail.com

Abstract:
Nowadays a variety of medicines are used to diagnose, treat, improve or prevent cancers. Cancers are a group of illnesses that are originated from uncontrolled proliferation of cells which lead to a tumor. For this reason, Food and Drug Administration (FDA) has focused a special attention on therapeutic enzymes to treat cancer because enzymes are specifically act, and they are highly capable to be used for treatments. Among the enzymes, lipase (triacylglycerol EC 3.1.1.3) is ranked as the third most widely used enzyme. Furthermore, due to its high stability in particular situations, is an appropriate molecule in the pharmaceutical industry for cancer treatment. According to the studies and reviews that were published by a number of researchers from 2006 to 2016: lipase, amylase, protease which easily digest fats, proteins and starch in the digestive tract are very effective in treating of gastrointestinal cancer. Nowadays, in USA and Sweden, using genetic engineering, recombinant enzyme is produced for treatment of skin, breast and lung cancers. Taken together, the high use and low cost of lipase made it an ideal approach for cancer therapy. In the present report we intend to review the literatures based on application of lipase as a therapeutic approach against cancer progress.

Keywords:
Therapeutic enzyme, Lipase, Cancer

P205

The cytotoxicity effect of Nigella Sativa extract and Thymoquinone on SW480 human colon cancer cell line

Saeede Mokhtari

Saeede Mokhtari, Forough Sanjarian, Hamidreza Soleimanpour Lichaei
National Institute of Genetic Engineering and Biotechnology(NIGEB), Tehran, Iran

Abstract:
Background: Thymoquinone (TQ), a compound isolated from black seed oil (Nigella sativa), has been shown to exert biological activity on various types of human cancers The goal of this study was investigation of the toxicity effects of the whole N. sativa's extract and pure TQ on SW480 human colon cancer cell line.
Methods: TQ content of extract was determined by HPLC technique. MTT assay was performed to examine the toxic effects of whole extract and pure TQ.
Results: We demonstrated that sub-cytotoxic doses of TQ (100µM) in 24 hours and 80µM in 48 hours and 40µM in 72 hours decreased SW480 cell viability by 50%. Nigella sativa extract inhibited cell proliferation with an IC50 of 2.5µl in 24 hours and 1.5µl in 48 hours and 1µl in 72 hours. The exact amount of Thymoquinine of Nigella sativa extract was 132.48 ppm) Part Per Million(
Conclusion: In the present study, we found that TQ and Nigella sativa's extract significantly reduced the viability of human colon cancer SW480 cells in a concentration- and time-dependent manner.

Keywords:
Thymoquinone , Nigella Sativa , Extract , SW480 cells

P206

Molecular Genetic of Familial Hypercholesterolemia and Personalized Medicine

Shima Parviz

Shima Parviz*[1], Seyed Javad Hosseini[1,2], Ali movahed[3]

1) Department of cellular and molecular sciences, the Persian Gulf University, Bushehr, Iran
2) Assistant Professor ,Department of Biotechnology, the Persian Gulf Research and Studies Center, the Persian Gulf University, Bushehr, Iran
3) Assistant Professor, Department of Biochemistry, Faculty of Medicine,Bushehr University of Medical Sciences, Bushehr, iran
*Sh.parviz@mehr.pgu.ac.ir

Abstract:
Cardiovascular disease(CVD) is one of the leading causes of death worldwide. Risk factors for CVD can be environmental and genetic. Family Hypercholesterolemia(FH) is a genetic factor with a dominant autosomal inheritance pattern resulting from high levels of low-density lipoprotein cholesterol (LDL) and increases the risk of premature cardiovascular disease. The disease, which is the most common genetic disease in the world, is due to a deficiency in the cholesterol recovery cycle using the conventional mechanisms of LDLR. FH can be monogenic or polygenic. Most FH-induced single-gene causes are mutations in one of the three LDLR, APOB, and PSCK9 genes, of which about 90% are generated in the LDLR gene. In more than 80% of cases, the FH clinical diagnosis without mutations in these genes is polygenic.DNA testing confirms FH diagnosis and helps identify at-risk relatives at an early age. But a negative genetic test does not deny FH diagnosis, especially when there is strong clinical phenotypic evidence. Despite genetic mutations known as a subset of this disorder and the availability of the commercial gene panel, the genetic testing for high costs is not normally performed in clinical care, FH is a complete example of personal medicine.If it is diagnosed at appropriate times, Largely prevented from the harmful consequences of the disease. On the other hand, the vital role of FH patients in the discovery of PCSK9 as a factor in the development of this disease, and as a result of the development of PCSK9 inhibitors, can be mentioned.Therefore, the participation of individuals is essential for development the drug.

P207

Effect of Fucoidan Extracted from Algae on Colon Cancer

Arghavan Hosseinpouri

Arghavan Hosseinpouri[1*], Shima Parviz[1], Mahdi Mohammadi[2], Narges obeidi[3]

1) Department of Cellular and Molecular Sciences,Faculty of Siences,Khalij fars University,Bushehr.
2) Departmet of Biotechnology,Persian Gulf Studies and Research Center, Khalij fars University,Bushehr.
3) Department of Hematology, Faculty of paramedicine, Bushehr University of Medical Sciences.
*A.hosseinpouri@gmail.com

Abstract:

Colorectal cancer is the third most common cancer in the world, with around 1.4 million new cases in 2012. Recently, the use of natural ingredients, such as fucoidan in seaweed, due to its non-toxic and marine natural product, Many have been caught up in controlling many diseases, such as invasive cancers. The first anticancer effects of this substance were reported in 1980, and so far 142 articles have been published. Most of these papers, Laboratory studies such as adding fucoidan to the cell-line growth culture of different cancers, such as stomach adenocarcinoma, blood, melanoma, Liver, bladder, prostate, breast, colon and lung.

Positive effects of fucoidan on HCT-15, HCT-29, HCT-116, colon cancer, respectively, as morphology and cytoplasmic disturbance, inhibition of proliferation Cell proliferation and increase of signaling pathways of apoptosis, interaction with activation of Caspase 3 and 7, increased deaths and cytotoxic effects.In spite of the wide resemblance of different species of fucoidans, it is sometimes seen that the effect is different. for example, Cladosiphon okamuranus, did not have an effect on breast cancer treatment, while in the colon cancer, it weakened tumor growth and increased survival. Another use of Fucoidan in cancer use has been associated with the reduction of side effects of chemotherapy such as gastrointestinal mucositis and tolerance of further chemotherapy.Also, the effect of fucoidan on reducing inflammation and maintaining the epithelial integrity to treat inflammatory bowel conditions is very promising due to the strengthening of tight joints.

P208

Gene Expression Profiles in Radiation Workers Occupationally Exposed to Low Levels of Ionizing Radiation in Al-Tuwaitha Site in Baghdad

Zainab A. Ouda

Zainab A. Ouda[1], Abulsahib K, Ali[2], Abd AL-Ameer, N. AL Rekaby[1]
1) Al- Mustansiriyah University, Science College , Biology Dep.
2) Ministry of Science and Technology, Central Laboratories Directorate
wow.2000@ymail.com

Abstract:
Ionizing radiation (IR) imposes risks to human health and the environment. IR at low doses and low dose rates has the potency to initiate carcinogenesis. Genotoxic environmental agents such as IR trigger a cascade of signal transduction pathways for cellular protection. Physical dosimeter records indicated that the total accu¬mulated radiation doses in these individuals varied from 0.696 to 39.088 mSv. In this study, using cDNA Real time polymerase chain reaction (RT-PCR) technique, we monitored the gene expression profiles in lymphocytes derived from 20 male radiation workers occupationally exposed to low ionizing radiation as well as 10 male blood samples as control. Total RNA was isolated using Trizol method from blood for the study groups mentioned. The RNA concentration was determined spectrophotometrically by measuring their absorbance using Nano- drop spectrophotometer that dependent on the ratio A260/A280 of the wavelength which lead to the determination of RNA purity, it ranged from 1.79-2.1 in all groups. RNA integrity and quality were confirmed by agarose gel electrophoresis. Three bands such as 28s, 18s and 5s appeared in a visible manner. This study involved the reverse transcription (RT) of the RNA for the manufacture of complementary DNA (cDNA) using the polymerase chain reaction (PCR) for investigation on above –mentioned groups of study.
Complementary DNA was used in amplification of genes used in the present study, three types of specialized primer genes were selected for the genes such as RHOA, CDKN1A and GADD45A, which have a relation with ionizing radiation in addition to the primers for internal control (β-actin) gene. All of these genes play an important role in the organization of the Cell cycle/proliferation and DNA repair. Therefore, the study was contributed to the possibility of using it as a biological evidence for the detection of radiation exposure or contamination and thus may contribute to understand some of unknown mechanisms that may occur during the process of cancer formation perhaps caused by radiation.
The optimal conditions for PCR were determined using a dye (SYBR® Green 1).This should be done before using the device quantitative real time-PCR (QRT-PCR) in experiments. The products of replicated specialized primers for the genes concerned and the cDNA for the studied samples were electrophoretically separated in agarose gels .The banding profiles were visualized by ethidium bromide staining, as the molecular weight were 135 bp , 165 bp and 185 , bp, (nitrogen-base pair) for RHOA ,CDKN1A, GADD45A genes , respectively.Gene expression analysis revealed statistically significant transcriptional changes in a 3 genes (RHOA, GADD45A up-regulated and CDKN1A down-regulated) . Some of the genes that showed altered expression profiles in this study can be used as biomarkers for monitoring the chronic low level exposure in humans. Additionally, alterations in gene expression patterns observed in chronically exposed radiation workers reinforces the need for defining the effective radiation dose that causes immediate genetic damage as well as the long-term effects on genomic instability, including cancer.

Keywords:
Ionizing radiation / Radiation workers / Occupational exposure / Gene expression profiles.

The International Personalized Medicine Congress of Iran

Personalized Medicine Painting Festival (<13 age)

نیکی مینایی ۸ ساله از کرج

لاوین حسن زاده اسکویی ۱۲ ساله از اهواز

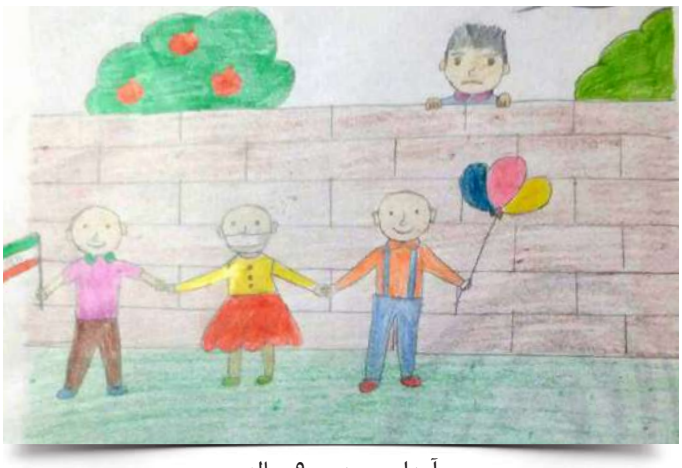
مهسا ایمانی ۱۱ ساله از پل دختر

سامان دادبخش ۱۱ ساله از شیراز

عرشیا تلخ آبی ۶ ساله از تهران

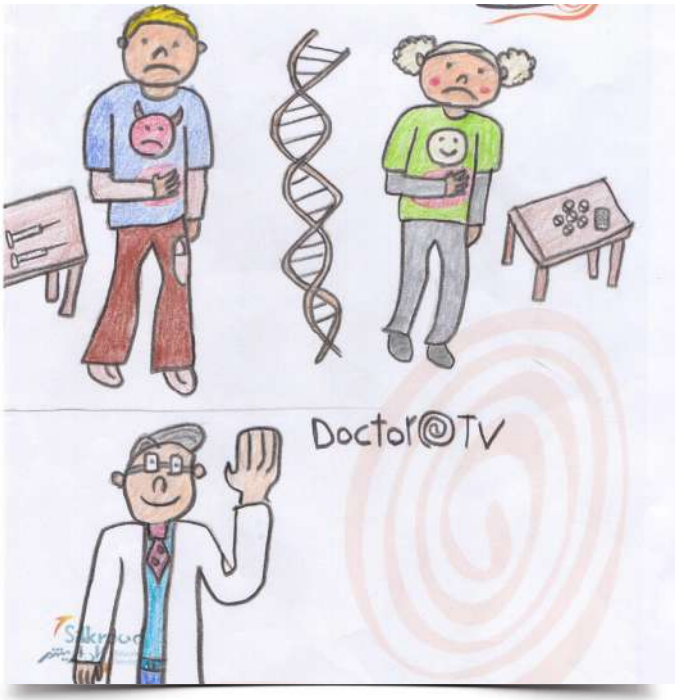
آریو حبیبی ۵ ساله از تهران

زهرا معصومی ۱۰ ساله از شیراز



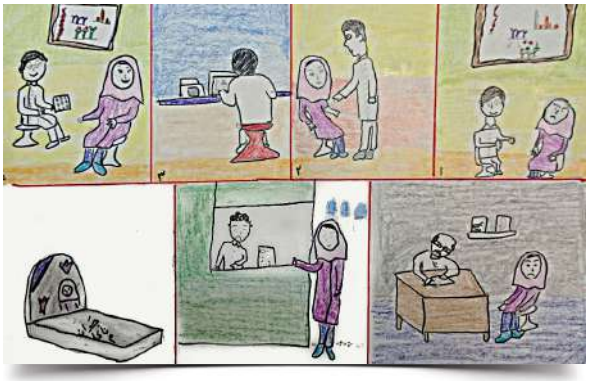
آیدا محمدی ۹ ساله

ارنیکا گلشنی ۱۰ ساله از شیراز



ارسطو عالمشاهی ۱۲ ساله از شیراز

ملیکا منتظمی ۱۱ ساله از شیراز



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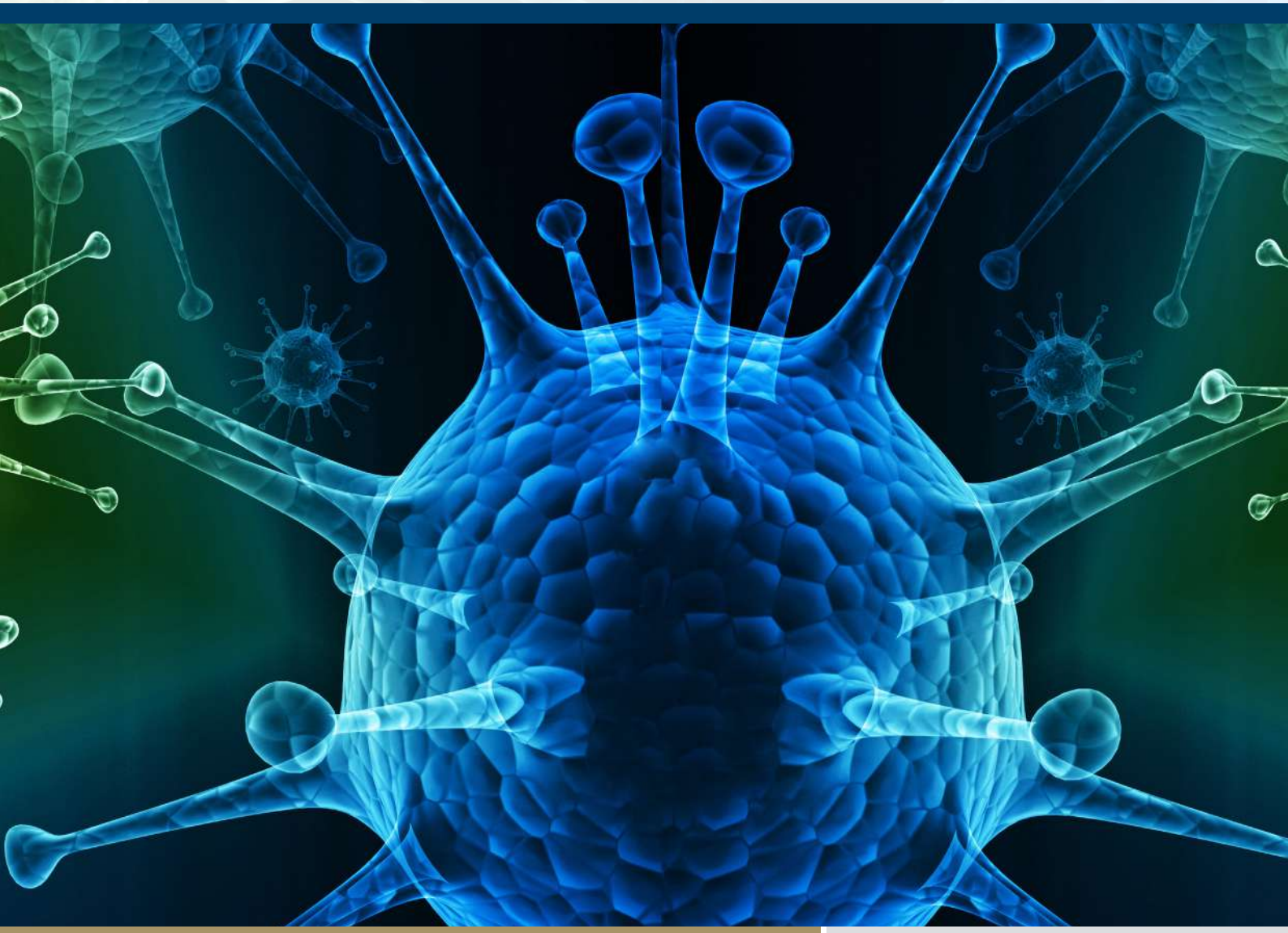
AusDiagnostics

Multiplexed Diagnostics | Affordable Healthcare

کمپانی AusDiagnostics از کشور استرالیا با ارائه ی روش مولکولی Multiplex PCR برای شناسایی پاتوژن ها به ویژه برای پاتوژن هایی که بسیار آهسته و یا سخت در محیط کشت رشد می کنند ، به دلیل حساسیت زیاد و سریع و آسان بودن به عنوان یک استاندارد طلائی معرفی شده است.
یکی دیگر از فوائد روش سیستمیک پی سی آر چندگانه، توانایی تشخیص چندین عامل از جمله عوامل ویروسی، باکتریایی، پروتوزئا، مخمر و قارچ ها در یک دوره آزمایش می باشد و نتایج بسیار کاربردی را برای تشخیص های مختلف به همراه دارد.

Molecular methods are becoming the gold standard for the detection of pathogens because of their superior sensitivity, rapid turnaround time, simplicity and ability to identify pathogens that are slow growing or difficult to culture.
Another advantage of Multiplex PCR is their capability to detect viruses, bacteria, protozoa and yeasts in one go, bringing great benefits for differential diagnostics.



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درمانگاه تخصصی ژنتیک دکتر فقیهی

مرجع تخصصی نسل جدید توالی یابی ژنتیکی (NGS) در ایران

دارای تاییدیه وزارت بهداشت درمان و آموزش پزشکی به عنوان
آزمایشگاه مرجع سلامت در کشور

خدمات تخصصی ژنتیک بالینی

- پانل ناقلین برای تشخیص بیماری های نهان در خانواده های دارای ازدواج فامیلی .
- تشخیص اختلالات ژنتیکی ناشنوایی نابینایی ، قلبی- عروقی ، کلیوی ، مغزی ، . . .
- تشخیص بیماری های متابولیک و تک ژنی (PKU, Albinism, G6PDD, . . .)
- تشخیص بیماری های تکرار نوکلیوتیدی (Fragile X, ALS, . . .)
- تشخیص بیماری های تحلیل برنده عضلانی (SMA, DMD) با روش MLPA
- تشخیص سرطان ها شامل پستان ، تخمدان ، ریه و کولون و سایر (BRCA1, BRCA2, . . .)
- تعیین دقیق مولکولی HLA با استفاده از نسل جدید توالی یابی ژنتیکی NGS

خدمات ژنتیکی پیش از تولد

- تشخیص پیش از تولد بیماری های ژنتیکی PND (Prenatal Diagnosis)
- تشخیص ژنتیکی پیش از لانه گزینی جنین PGD و PGS
- تست غیر تهاجمی تعدادی کرومزوم های جنین (NIPT) یا (Cell Free-fetal DNA) و با دقت ۹۹.۹%
- آمینوسنتز و نمونه برداری از پرزهای جنین CVS
- بررسی تعدادی کرومزوم های جنین (QF-PCR)
- کاریوتایپ با رزولوشن بالا Karyotype
- سونوگرافی غربالگری سلامت جنین سه ماه اول و سه ماه دوم بارداری
- سونوگرافی قلب جنین

مشاوره ژنتیک

- مشاوره ژنتیک قبل از ازدواج
- مشاوره ژنتیک پیش از بارداری
- مشاوره ژنتیک حین بارداری
- مشاوره ژنتیک ناباروری زنان و مردان
- مشاوره ژنتیک علل سقط مکرر

خدمات تخصصی توالی یابی ژنتیکی (NGS) در ایران

- تعیین توالی تمام ژنوم Whole Genome Sequencing
- تعیین توالی تمام اگزون های کد کننده پروتئین Whole Exome Sequencing
- تعیین توالی گروهی از بیماری های خاص Targeted_Sequencing

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این یک حقیقت تلخ است، اما سال‌هاست با مشارکت شما حمایت از همه کودکان مبتلا به سرطان ایران با امید رسیدن به شیرینی سلامتی محقق شده است.

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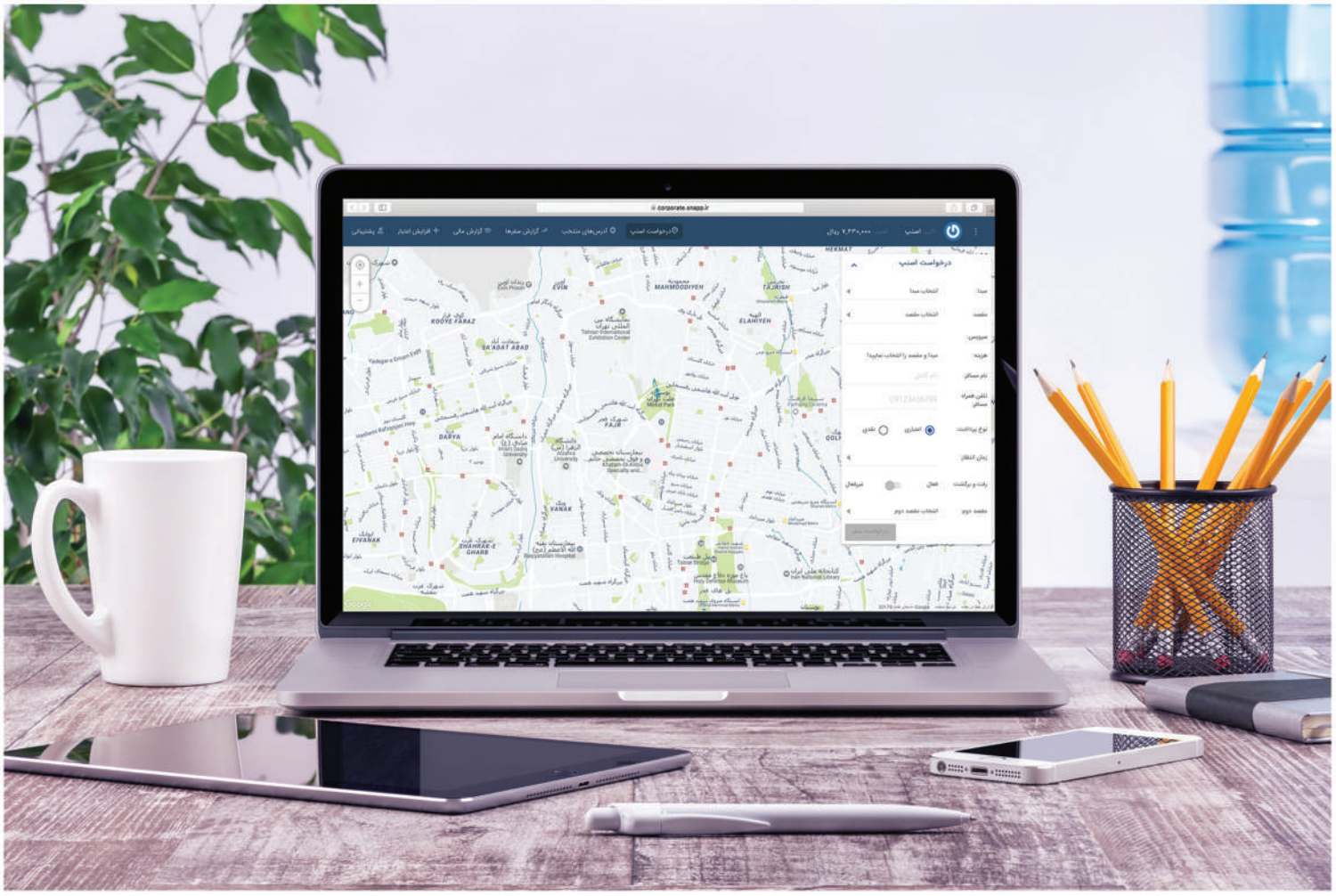
از اینکه به پیام ما توجه می کنید، سپاسگزاریم.

فرصت درج این آگهی به صورت رایگان در اختیار محک قرار گرفته است.



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