Personalized Medicine
JOURNAL

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The First International Congress of Iranian Personalized Medicine

Congress Personalized Medicine
The First International Iranian

Congress highlights:

- Genomics & Personalized Medicine
- Advances in Molecular Diagnostics
- Personalized Drug Therapy
- Clinical Case Reports
- Lifestyle Medicine
- Paths of Biomarkers
- Perventive Medicine
- Bioinformatics
- Pharmacogenomics
- P4 Medicine (Perdictive, Preventive, Personalized & Participatory)
- Ethics in Personalized Medicine
- Future of Personalized Medicine
- (Neuroscience,Nanomedicin,Cardiovascular Diseases, Cancer and Metabolic Syndrom)

Feb. 2017, Tehran, Iran
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The Future of Medicine is Personalized

Congress
Medicine
Personalized
The First International Iranian

Personalized Medicine Journal

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Designer: Shahab Razagh

Cover Designer: Shahab Razagh

Technical Supervisor Printing: Yousef Golmohammadi

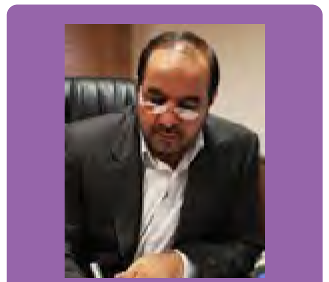
Lithography, Printing, Binding: Parvin Publisher - No. 1115, St. Damavand, Tehran, Iran

Telephone: +98(21)88985293

Email: info@PersonalizedMedicineJournal.com

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

Message of Congress Chairmans



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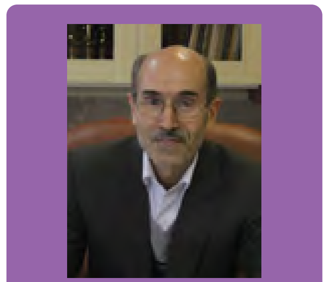

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IRAN UNIVERSITY OF MEDICAL SCIENCE

NIGEB

Greetings and respect to scientists, professors and all audiences who are active in the field of medicine. We are proud to announce that with the grate grace of God Almighty and the best efforts of scientists and scholars the first International personalized medicine of Iran will be held in February 2017 in Tehran, Iran.

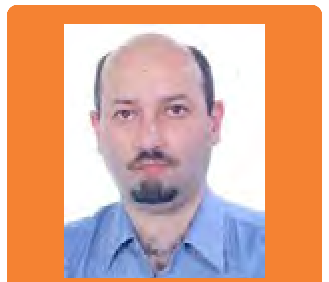
As the whole medicine society believe Personalized Medicine is the future of medicine and various fields and the human beings will benefit from its advantages in near future.

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 who helped us to make this event more effective and even possible.

Dr.Alireza Jalali **Dr.J.Miresmaeil** **Dr.M.Zamani**

Message of Congress Scientific Secretaries



Dr. Massoud Houshmand
Scientific Secretary
National Institute of Genetic Engineering and Biotechnology

Dr. Reza Nekouian
Scientific Secretary
Iran University of Medical Sciences

Dear Colleagues,

We would like to kindly welcome each of you to the First Iran International Personalized Medicine Congress. It`s an exciting time for Iran`s medical advances as we continue to grow and adapt, remaining always adaptable, motivated and responsive for prediction, prevention, better diagnosis and higher quality of health care system. Baqiatallah University of Medical Science (BUMS) along with Iran University of Medical Science (IUMS) and National Institute of Genetic Engineering and Biotechnology (NIGEB) are confronting a time of many changes and we are meeting these changes during a time of larger nation-wide and global. The world of personalized medicine is an exciting area in which to research and work, and we will continue to meet and bring inspired people together in forums like this, to ensure our prospective remains at the cutting edge.

We would like to give you an idea of what you can expect and what we hope to achieve during our congress. The congress will be held in February 2017 from 25th to 29th. Different scientific panels are designed together to meet variety of aspects of personalized medicine and their correlation with each other, which hopefully frames a network that might lead to a change in our health care system.

We are transforming the way we operate to continuously improve our ability to predict and prevent human diseases, and personalized our medical protocols and of course induce the soul of participation between patients and their health providers. Our health care decision makers and partners in the field of medicine have continued to meet the challenges of our field and to excel despite setbacks. We should all be very proud of where we are today and excited about where we are headed.

Before we close, we would like to thank each of you for attending our conference and bringing your expertise to our gathering. You, as organization leaders, have the vision, the knowledge, and the experience to help us pave our way into the future. You are truly our greatest asset today and tomorrow, and we could not accomplish what we do without your support and leadership. Throughout this conference, we ask you to stay engaged, keep us proactive and help us shape the future of Personalized Medicine. Our personal respect and thanks goes out to all of you.

Dr. Massoud Houshmand **Dr. Reza Nekouian**

Message of Personalized Medicine Journal Board

Dr.Mohammad Ali Saremi
Chairman of AmitisGen
Med TECH Group

Nayyere Moslehi
Editor In Chief
Personalized Medicine
Journal

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Personalized Medicine JOURNAL

By the special grace of God Almighty and the greatest efforts of our country’s professors, the first Personalized Medicine congress will be held from February 2017.

While Personalized Medicine has a thousand years of antiquity in recent years individualistic approach has gradually expanded in all branches of medicine.This field of science is being used more and more in the daily medicine and it seems that in near future it will be one of the main areas of medicine.

We are sure that the future of medicine is personalized, and the Personalized Medicine Journal is a pioneered one which is taking the duty of this field notification. We hope that with special grace of God Almighty and the greatest efforts of our country’s professors, in a not far future we reach to our goal of right treatment to the right patient at the right time.

Dr.Mohammad Ali Saremi **Nayyere Moslehi**

Congress Main Topics

Personalized Medicine in Frontotemporal Dementia and its variants..8

Role of personalized medicine to customized risk evaluation ,treatment and surveillance in gastric cancer......................9

Personalized Medicine for Radiation Therapy...10

Personalized treatments in lung cancer...11

Modulation of neutrophil extracellular trap formation in health and disease...12

Stem Cell Technology and Personalised Medicine...13

Hematopoietic Stem Cell Transplantation :A curative treatment for potentially fatal disorders...14

New perspective therapy of breast cancer based on pharmacogenomics study of dopamine receptor DRD2....................15

Personalized Medicine in Pulmonary Infection...16

Asthma and Personalized Medicine Care..17

New perspective therapy of breast cancer based on pharmacogenomics study of dopamine receptor DRD2..................18

P4 Medicine – A Predictive, Preventive, Personalized and Participatory Approach in modern Health Care 19

Advances in personalized medicine in the ALS research..20

The First international Congress of Iranian Personalized Medicine- Tehran, February 25-27, 2017 Toward a World Alliance of Health and Wellness based on Systems P4 Medicine and Citizen Science 21

Ethical Issues of Personalized Medicine and Genetic Information Banks...22

Paving the Way for Personalized Medicine in Cancer: Experience in Iran...23

Genome wide association study in Tehran cardio-metabolic genetic study could promotes precision medicine in Iran.......24

The challenges in development of Pharmacogenetics and Preventive genetic testing...25

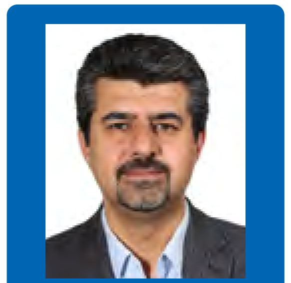
Personalized treatment in colon cancer...26

Coordinators of Congress Main Topics (In Alphabetic Order)

Dr.M.Asadi
Personalized Medicine in Cancer

Dr.S.Ghafari
Personalized Medicine in Drug Treatment

Dr.M.Haghjoo
Personalized Medicine in Cardiovascular Disease

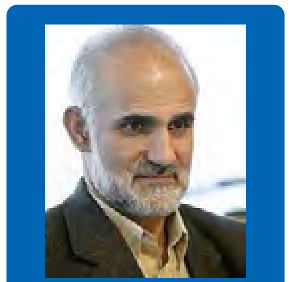


Dr.A.Hamidiye
Personalized Medicine in Cell Therapy

Dr.M.T. Joghataei
Personalized Medicine in Neuroscience

Dr.S.Kooranifar
Personalized Medicine in Pulmonary Diseases

Dr.E.Nabipur
Personalized Medicine in Metabolic Syndrome



Dr.M.Moeen
Personalized Medicine in Asthma and Allergies & Medical Ethics

Key Speakers
(In Alphabetic Order)

Dr.K.Afshar
Swiss Society of Medical Genetics (SSMG),The Genetics Society of America,The American Society of Cell Biologists

Dr.G.Ahangari
Department of Medical Genetics, National Institute of Genetic Engineering and Biotechnology, Iran

Dr.M.Almasi-Dooghaee
Neurology Department, Iran University of Medical Sciences, Iran

Dr.M. Assadi
Alborz University of Medical Science, Iran

Dr.C. Auffray
European Institute for Systems Biology & Medicine (EISBM)- Lyon - France CNRS-ENS-UCBL-INSERM - Campus Charles Mérieux – Université de Lyon

Dr.F.Azizi
Research Institute for endocrine sciences Shahid Beheshti University of Medical Sciences, Iran

Dr.M. Daneshpour
Cellular and molecular endocrine research center, Research Institute for endocrine sciences Shahid Beheshti University of Medical Sciences, Iran

Dr.M.Fakhr Taha
Department of Stem Cell and Regenerative Medicine, Institute for Medical Biotechnology, National Institute of Genetic Engineering and Biotechnology (NIGEB), Iran

DR.K.Guity
Research Institute for endocrine sciences Shahid Beheshti University of Medical Sciences, Iran

Dr.A. Hosseinzadeh
Division of Immunology, Department of Clinical Microbiology, Umeå University, Sweden

Dr.E. Karbasi
Radiation Oncologist, Azad University of Medical Sciences, Iran

Dr.A. Kazemi
Biotechnology Research Center, Tabriz University of Medical Sciences, Iran

Dr.F.Mahjoubi
Clinical Genetic Department, NIGEB, Iran

Dr.R.Malayeri
Firoozgar Hospital, Iran

Dr.M.Mehdizadeh
Shahid Beheshti university of Medical Sciences, Iran

Dr.V.Moradians
Iran University of Medical Sciences, Iran

Dr.R.Naghshin
Iran University of Medical Sciences, Iran

Dr.L.Sadeghi
Assisstant Professor of Shahid Beheshti University of Medical School, Iran

Dr.M. Sagner
Principal Investigator. University of Lausanne, Faculty of Medicine and Biology

Dr.B.Sedaghatikhayat
Research Institute for Endocrine Sciences Shahid Beheshti University of Medical Sciences, Iran

Dr.R.Rofougaran
Förste forskningsassistent, Department of Phamacology and Clinical Neuroscience, Umeå University, Sweden

Dr.C.Urban
Division of Immunology, Department of Clinical Microbiology, Umeå University, Sweden

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KO1077

Personalized Medicine in Frontotemporal Dementia and its Variants

Mostafa Almasi-Dooghaee
Neurology Department, Iran University of Medical Sciences : a_mostafa108@yahoo.com

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

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KO1117

Role of Personalized Medicine to Customized Risk Evaluation ,Treatment and Surveillance in Gastric Cancer

Mojan Assadi
Alborz University of Medical Science : mojanassadi@yahoo.com

Abstract:
Role of personalized medicine to customized risk evaluation ,treatment and surveillance in gastric cancer Personalized medicine is used to learn about a person’s genetic makeup and how their tumor grows.Using this data,physicians hope to find prevention,screening and treatment strategies that may be more effective.By performing genetic tests on the cancer cells and on normal cells ,doctors can customized treatment to each patient with fewer side effects. Gastric cancer is the most common cancer in male population in Iran with high mortality rate.Criteria for risk evaluation of gastric cancer is based on personal and family history of gastric and breast cancer.Most gastric cancers are sporadic ,but 5-10% have a familial component and 3-5%are associated with an inherited cancer predisposition such as hereditary diffuse gastric cancer,lynch syndrome,juvenile polyposis syndrome,peutz-jeghers syndrome and familial adenomatosis polyposis. Treatment protocols is variable according to stage,performance status, comorbidities and genetic profiles.surveillance recommendations based on genetic factors such as CDH1 mutation carriers,Lynch syndrome and… . In all aspects it seams that personalized medicine play an important role with more effective outcomes

Keywords:
gastric cancer treatment

KO1167

Personalized Medicine for Radiation Therapy

Ehsan Karbasi
Radiation Oncologist, Azad University of Medical Sciences : ehsonkarbasi@gmail.com

Abstract:
Radiation therapy (RT) plays an essential role in treatment of most cancers. For example, examination of Surveillance, Epidemiology and End Results data revealed an estimated 29% of patients with cancer received RT during their initial treatment course. However, it can have significant side effects both during and after treatment and also newer techniques such as IMRT, could be so expensive. Thus, there is a significant need for tools to predict the utility of RT in individual patients and personalized medicine for RT could be a potential effective way to predict what patients would receive the best gain and less toxicity from radiation therapy.

Gene expression and cellular radiosensitivity in a database of 48 human cancer cell lines representing a wide array of primary sites, including breast, colon, leukemia, melanoma, non-small-cell lung, ovarian, renal and prostate cancer to identify 500 genes associated with radiosensitivity, have been investigated. From these 500 genes, a ten-gene network were proposed to play a central role in determining radiophenotype. A modele of cellular radiosensitivity as a linear function of gene expression for the ten genes have been studied. The Radiosensitivity index (RSI) is modeled on the cellular survival after RT in the cell lines, therefore a low RSI indicates a higher response to RT (i.e., radiosensitive).

The radiosensitivity index, or any other assay that can predict response to radiotherapy, will have a transformative impact on the practice of radiation oncology and can predict radiation sensitivity which is associated with improved outcomes for patients treated with radiotherapy. This is seen for a number of different end points (response rate, locoregional control, distant metastasis-free survival and relapse-free survival) and different tumor types.

As a matter of fact, RSI may impact clinical decisions in radiation oncology in multiple ways – for example, in patients who are in the low RSI spectrum (radiosensitive) RT is predicted to be effective. Depending on the disease site it may be reasonable for these patients to undergo radiotherapy rather than surgery. In contrast, patients in the high end of the RSI spectrum (radioresistant) may be better off treated without radiotherapy. A clinical example would be in rectal or esophageal cancer where radioresistant patients may proceed directly to surgery without preoperative RT.

Finally, there might be patients that will fall in the intermediate range for RSI and these are the patients where RT dose modifications or concurrent chemotherapy might significantly impact their clinical outcome. Future clinical trials may seek to modulate the dose of radiotherapy based on radiosensitivity; a lower dose of radiotherapy should result in less risk of short- and long-term side effects.

Keywords:
Personalized medicine, radiation therapy

KO1174

Personalized Treatments in lung cancer

Reza Malayeri
Firoozgar Hospital, Tehran, Iran : r.malayeri@gmail.com

Abstract:
The past decade has seen an enormous advancement in the therapy for non-small cell lung cancer, predominantly seen in adenocarcinoma.The first achievement was the knowledge that certain histologies respond better to certain drugs. This was the introduction of histology-based drugs. Then came the discovery of targetable mutations. We have many mutations in this disease, mostly still untargettable. These events have led to a personalized therapeutic approach with the delivery of drugs that target specific oncogenic pathways active in a given tumor with the intent of acquiring the best response rate. Patients benefitting here were mostly non- or never smokers. The discovery of sensitizing mutation in the epidermal growth factor receptor gene as the basis for clinical response to tyrosine kinase inhibitors led to a systematic search for other molecular targets in lung cancer. Currently, there are several molecular alterations that can be targeted by experimental drugs, such as ALK and ROS. These new discoveries would not be possible without a parallel technological evolution in diagnostic molecular pathology. Next-generation sequencing (NGS) is a technology that allows for the evaluation of multiple molecular alterations in the same sample using a small amount of tissue. Selective evaluation of targeted cancer genes, instead of whole-genome evaluation, is the approach that is best suited to enter clinical practice. In the era of immunotherapy, another lesson was learnt and that was showing a benefit in patients who did not show any of the mutations mentioned above, thus a treatment was mainly for squamous cell lung cancer and smokers.

Keywords:
EGFR, ALK, Adenocarcinoma, mutations

KO1177

Modulation of neutrophil extracellular trap formation in health and disease

Ava Hosseinzadeh[1] ، Constantin Urban[2]

1) Division of Immunology, Department of Clinical Microbiology, Umeå University, Sweden : ava.hosseinzadeh@gmail.com
2) Division of Immunology, Department of Clinical Microbiology, Umeå University, Sweden

Abstract:
The critical prompt innate immune response is highly built upon the influx of neutrophils from the blood stream to the site of infection. In the battlefield, neutrophils sense pathogen-associated molecular patterns (PAMPs) through their pattern-recognition receptors (PRRs) to launch a number of responses with the goal to defeat the invading pathogen. Neutrophils` wide spectrum of responses ranges from reactive oxygen species production (ROS), phagocytosis, cytokine secretion, and neutrophil extracellular trap (NET) formation. The NET scaffold is composed of nuclear chromatin which is armed with antimicrobial proteins. DNA traps are able to ensnare and kill microbes. NETs impose deleterious effects on the host itself in addition to their antimicrobial activity. These hazardous effects mainly stem from pro-inflammatory and tissue-destructive activity of NETs. Therefore, it seems rational that NET formation is tightly regulated and not happening spontaneously. Positive and negative regulators of NET formation were investigated in a mechanistic fashion.

As unbalanced inflammation is harmful to the host, we aimed to find molecules, which are able to inhibit NET formation. Thus, we introduced the non-toxic agent tempol that efficiently blocked NET induction. We therefore proposed tempol as a potential treatment during inflammatory disorders where NET formation is out of balance. In quest for positive regulators of NET formation we found the major addictive component of tobacco and electronic cigarettes, nicotine, as compelling direct inducer of NET release. Interestingly, nicotine is associated with exacerbated inflammatory diseases exerting its pro-inflammatory activity via acetylcholine receptor by targeting protein kinase B activation with no effect on NADPH oxidase complex in a ROS independent fashion. In consideration of neutrophils role in smoking-related diseases we propose targeting Akt could lower the undesirable effect of NET.

In conclusion, we identified new modulators of NET formation which might have implications in forthcoming therapies.

Keywords:
neutrophil extracellular trap (NET), Candida albicans, Tempol, Nicotine

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KO1178

Stem Cell Technology and Personalised Medicine

Masoumeh Fakhr taha

Department of Stem Cell and Regenerative Medicine, Institute for Medical Biotechnology, National Institute of Genetic Engineering and Biotechnology (NIGEB), Tehran, Iran. : mftaha@nigeb.ac.ir

Abstract:
Stem cells are a rapidly evolving field of biological research with great importance in the study and treatment of many diseases. Patient's stem cells can be used to either determine the molecular mechanisms underlying disorders or study drug responses of the diseased cells. It may also be used to test safety and effectiveness of different therapies. Moreover, mesenchymal stem cells and induced pluripotent stem cells represent two promising sources of stem cells with great potential in cell transplantations and regenerative medicine. Based on current evidence, stem cell technology has a significant prospect in personalised medicine.

Keywords:
Stem cells; Drug responses; Cell transplantations; Regenerative medicine.

KO1182

Hematopoietic Stem Cell Transplantation: A curative treatment for potentially fatal disorders

Mahshid Mehdizadeh
Shahid Beheshti university of medical sciences : mahshid_mehdizadeh@yahoo.com

Abstract:
A variety of hematological disorders of the bone marrow, such as acute leukemia, chronicmyelocytic leukemia and severe aplastic anemia, were invariably known as fatal disorders. In the past two decades, physicians have been able to change this reality into a more hopeful outcome byreplacing the diseased bone marrow with stem cells from either a family or an unrelated donor with identical human leukocyte antigens (HLA).Based on the rapid progression in the field of stem cell transplantation donor banks now are considered a necessity. Considering stem cell transplantation we can treat some malignant disorders with Intending to cure.Timing of hematopoietic stem cell transplantation is the most important point to achieve cure in malignant disorders. Distinct indications are shown for HSCT in Acute myeloblastic and lymphoblastic leukemia, aplastic anemia, multiple myeloma and relapsed Hodgkin and non Hodgkin lymphomas which benefit the most. Preparing the patients for on time HSCT is key point of success. Achievement of complete remission before HSCT and finding the best donor in family members or unrelated ones are corner stones of transplantation .There are someethical concerns for donors and families, concerns that need to be discussed and understood by patients, donors and health care professionals.

Keywords:
stem cell,hematopoietic,transplantation,malignancy

KO1183

New perspective therapy of breast cancer based on pharmacogenomics study of dopamine receptor DRD2

Ghasem Ahangari
Department of Medical Genetics, National Institute of Genetic Engineering and Biotechnology, Tehran : ghah@nigeb.ac.ir

Abstract:
Breast cancer is the most common cancer among females worldwide and a most prevalent malignancy in Iranian women. Chronic stress may make an important contribution to cancer, especially in the breast. Numerous studies showed roles of neurotransmitters in the occurrence and progression of cancers which are mediated by their various types of receptors. This study was conducted to evaluate alterations in the expression profile of dopamine receptor genes in peripheral blood mononuclear cells (PBMC) as stress factors in breast cancer patients and the human breast cancer cell line (MCF-7). Peripheral blood samples were obtained from 30 patients and 30 healthy individuals. Total mRNA was extracted from PBMC and MCF-7 cells and RT-PCR was performed to confirm the presence of five dopamine receptors (DRD1-DRD5). Expression changes of dopamine receptor genes were evaluated by real time. We observed that DRD2 in PBMCs of breast cancer patients were increased compared to healthy individuals. Furthermore, study was to determine the pattern of dopamine receptors gene expression on MCF-7 cells and to evaluate the selective dopamine receptors agonist and antagonist effects on them. In addition, some other discoveries which are patented for the treatment of breast cancer are reviewed in this article. To determine the pattern of dopamine receptors gene expression in human breast cancer cells (MCF-7), RT-PCR was performed. Then, MCF-7 cells were treated by different doses of bromocriptine and remoxipride for 48 hours. Cell viability was evaluated by MTT assay. Thus, nuclear morphology of cells was analyzed by mixed dye florescent staining. Real time PCR technique was performed to determine the decreasing rate of proliferating cell nuclear antigen (PCNA) gene expression in treated MCF-7 cells. Finally, quantification of apoptosis and its difference with necrosis at the single cell level were assessed by Flowcytometery technique. This study revealed that, unlike remoxipride, bromocriptine suppressed proliferation of the MCF-7 cells (54.3% at 12.5µM bromocriptine concentration), but remoxipride could suppress the effect of bromocriptine. Bromocriptine has inhibitory effects on MCF- 7 cells by induction of apoptosis via D2-like receptors. Therefore, in future studies, bromocriptine can be used as a new choice for the treatment of tumoral breast cancer cells.

Keywords:
breast cancer

KO1184

Personalized Medicine in Pulmonary Infection

Vahan Moradians
IUMS : moradians.v@iums.ac.ir

Abstract:
After sequencing the human genome, it became possible to find minor differences between individuals which without affecting the phenotype, could have important consequences in certain conditions. These are called Single Nucleotide Polymorphism (SNP). SNPs are the cornerstone for the concept of Personalized Medicine which is now gradually replacing the old Programmatic Medicine (a fixed recipe for every patient). The simplest example is the slow and fast acetylators and hepatotoxicity of anti-tuberculosis drugs.

Pulmonary infections are one of oldest diseases in medical literature and the chronic lung infections are one of the most challenging areas in medicine for prevention, diagnosis and treatment.

Finding new bio markers for example can help us to predict which patient with latent tuberculous infection will progress to active disease and should receive prophylactic therapy.

I will try to discuss the latest research and biomarkers especially in chronic pulmonary infections.

Keywords:
Biomarkers, Personalized Medicine, Chronic, Pulmonary Infection, Tuberculosis, Aspergillosis

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KO1185

Asthma and Personalized Medicine Care

Roozbeh Naghshin
IUMS : rnaghshin@yahoo.com

Abstract:
After decades of improvement in diagnosis techniques and new treatment modalities, asthma outcomes have stalled. Mortality has decreased in developed countries, but despite effective therapies, hospitalizations, exacerbations and symptom control remain sub-optimal.

The disease burden remains huge and in Iran 8 to 9 percent of population suffer from asthma. In controlled trials, most patients gain high levels of control, but in ‘real-life’ routine clinical practice most patients do not. Avoidable factors are found in most asthma deaths and hospital admissions.

Audits of prescribing patterns in primary care clinicians often show prescribing not in accord with guideline recommendations, including overprescribing of Salbutamol (SABA), underuse of inhaled corticosteroids (ICS), use of long-acting β2-agonists (LABAs) as monotherapy and over-use of Injections of corticosteroids.

The most common reasons for poor control are that many patients either do not take treatment regularly or have poor inhaler technique. Unfortunately non-adherence is a common form of self-management in asthmatic patients. Many patients use their inhaler badly, most will make some errors and many make ‘critical errors’ that result in little or no medication delivery and it`s too important for physician to educate each individual patient “how to use inhalers and spacer”.

Psychological dysfunction is six times as common in people with asthma, and asthma-related quality of life correlates more closely with psychological and social status than lung function or treatment step.

It is unlikely in the foreseeable future that we can ‘cure’ asthma, but we should be able to characterize our patients individually, in particular those who, for one reason or another, are not doing well, and for most there will be effective strategies for improving outcomes. However, the most effective intervention(s) will vary greatly between patients, and a ‘one size fits all’ approach will no longer suffice. We now need to put our information together into coherent, patient-orientated personalized care.

Keywords:
Asthma, Patient Care, Personalized Medicine

KO1187

New perspective therapy of breast cancer based on pharmacogenomics study of dopamine receptor DRD2

Ghasem Ahangari
Department of Medical Genetics, National Institute of Genetic Engineering and Biotechnology, Tehran, : ghah@nigeb.ac.ir

Abstract:
Breast cancer is the most common cancer among females worldwide and a most prevalent malignancy in Iranian women. Chronic stress may make an important contribution to cancer, especially in the breast. Numerous studies showed roles of neurotransmitters in the occurrence and progression of cancers which are mediated by their various types of receptors. This study was conducted to evaluate alterations in the expression profile of dopamine receptor genes in peripheral blood mononuclear cells (PBMC) as stress factors in breast cancer patients and the human breast cancer cell line (MCF-7). Peripheral blood samples were obtained from 30 patients and 30 healthy individuals. Total mRNA was extracted from PBMC and MCF-7 cells and RT-PCR was performed to confirm the presence of five dopamine receptors (DRD1-DRD5). Expression changes of dopamine receptor genes were evaluated by real time. We observed that DRD2 in PBMCs of breast cancer patients were increased compared to healthy individuals. Furthermore, study was to determine the pattern of dopamine receptors gene expression on MCF-7 cells and to evaluate the selective dopamine receptors agonist and antagonist effects on them. In addition, some other discoveries which are patented for the treatment of breast cancer are reviewed in this article. To determine the pattern of dopamine receptors gene expression in human breast cancer cells (MCF-7), RT-PCR was performed. Then, MCF-7 cells were treated by different doses of bromocriptine and remoxipride for 48 hours. Cell viability was evaluated by MTT assay. Thus, nuclear morphology of cells was analyzed by mixed dye florescent staining. Real time PCR technique was performed to determine the decreasing rate of proliferating cell nuclear antigen (PCNA) gene expression in treated MCF-7 cells. Finally, quantification of apoptosis and its difference with necrosis at the single cell level were assessed by Flowcytometery technique. This study revealed that, unlike remoxipride, bromocriptine suppressed proliferation of the MCF-7 cells (54.3% at 12.5µM bromocriptine concentration), but remoxipride could suppress the effect of bromocriptine. Bromocriptine has inhibitory effects on MCF- 7 cells by induction of apoptosis via D2-like receptors. Therefore, in future studies, bromocriptine can be used as a new choice for the treatment of tumoral breast cancer cells.

Keywords:
breast cancer

KO1188

P4 Medicine – A Predictive, Preventive, Personalized and Participatory Approach in modern Health Care

Dr Micheal Sagner
Principal Investigator. University of Lausanne, Faculty of Medicine and Biology : sagner@esprevmed.org

Abstract:
Chronic diseases (i.e., noncommunicable diseases), mainly cardiovascular disease, cancer, respiratory diseases and type-2-diabetes, are now the leading cause of death, disability and diminished quality of life on the planet. Moreover, these diseases are also a major financial burden worldwide, significantly impacting the economy of many countries. Healthcare systems and medicine have progressively improved upon the ability to address infectious diseases and react to adverse health events through both surgical interventions and pharmacology; we have become efficient in delivering reactive care (i.e., initiating interventions once an individual is on the verge of or has actually suffered a negative health event). However, with slowly progressing and often `silent` chronic diseases now being the main cause of illness, healthcare and medicine must evolve into a proactive system, moving away from a merely reactive approach to care. Minimal interactions among the specialists and limited information to the general practitioner and to the individual receiving care lead to a fragmented health approach, non-concerted prescriptions, a scattered follow-up and a suboptimal cost-effectiveness ratio. A new approach in medicine that is predictive, preventive, personalized and participatory, which we label here as “P4” holds great promise to reduce the burden of chronic diseases by harnessing technology and an increasingly better understanding of environment-biology interactions, evidence-based interventions and the underlying mechanisms of chronic diseases. In this lecture, we present a ‘P4 Health Continuum’ model as a framework to promote and facilitate multi-stakeholder collaboration with an orchestrated common language and an integrated care model to increase the healthspan.

Keywords:
Preventive, Approach

KO1189

Advances in personalized medicine in the ALS research

Reza Rofougaran

Förste forskningsassistent, Dept. of Phamacology and Clinical Neuroscience, Umeå University, Sweden : rofougaranreza@yahoo.com

Abstract:

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disorder that eventually leads to the death of motor neurons and fatal paralysis. Numerous different gene mutations have been found in familial cases of ALS, such as mutations in superoxide dismutase 1 (SOD1), TAR DNA-binding protein 43 (TDP-43), fused in sarcoma (FUS), C9ORF72, ubiquilin-2 (UBQLN2), optineurin (OPTN) and others. Importantly, the genetic and phenotypic heterogeneity of ALS leads to a variety of responses to similar treatment regimens. The application of personalized medicine in ALS first requires genetic screening among ALS patients. As better drugs become available, it will be important to take into account the genetic profile status of the patient to determine if individuals with certain mutations would respond better to particular treatments. The genetic screening has other advantage in which it is possible to study the connections between gene modifiers with age of onset and disease progression in ALS populations. The recent study that conducted at Umeå university showed, depending on the mutation, the progression rates, distribution, end-stage SOD1 aggregate levels, and histopathology were differed in ALS mice model. These results will be discussed. Next generation sequencing (NGS) technologies have emerged as a powerful tool for the genetic screening of causative mutations and subgrouping of ALS patients. In this section, I will present some recent results. In the presentation, in the context of personalized medicine, I will also discuss more about patient-derived fibroblast lines expressing different mutant SOD1 as a tool to study the role of misfolding SOD1 in the ALS pathogenesis. I consider that gene therapy has great potential for personalized medicine approaches in ALS, either by antisense oligonucleotide, small interference RNA or any other method such as antibodies targeting pathological proteins. These techniques have already been tested and appear to be effective in SOD1, TDP-43, C9ORF72 and FUS animal models. I will review application of gene therapies relevant in personalized medicine approach in the ALS research.

Keywords:
personalized medicine

KO1191

The First international Congress of Iranian Personalized Medicine- Tehran, February 25-27, 2017 Toward a World Alliance of Health and Wellness based on Systems P4 Medicine and Citizen Science.

Charles Auffray

European Institute for Systems Biology & Medicine (EISBM)- Lyon - France CNRS-ENS-UCBL-INSERM - Campus Charles Mérieux – Université de Lyon : cauffray@eisbm.org

Abstract:

Systems biology approaches are combining high-dimensional functional genomics data with biological, clinical, environmental and lifestyle assessments through iterative statistical analyses, computational modelling and experimental validation. They are transforming biomedical research and clinical practice, triggering the transition from a reactive to a proactive practice of medicine (1-2). This is revolutionizing how medicine will be practiced in the 21st century (3-5). The effective development of participatory, personalized, predictive and preventive (P4) systems medicine requires harmonization of experimental and computational methods for data, information and knowledge collection, storage, analysis and sharing on a big data scale using high-performance cloud computing infrastructures ensuring data security and compliance with personal data and privacy protection regulations. In order to address the associated ethical, legal and social issues, the active participation of all stakeholders including researchers and clinicians in academy and industry, regulatory and funding bodies, individuals and patient organizations is thus essential.

Two examples of individuals who have managed to anticipate the occurrence of disease and take preventive measures through a regular assessment of their exposome monitored through connected mobile devices (environmental and occupational exposures, nutrition, sleep, exercise, stress), clinicome (biological and clinical features), and integrome (metabolomics, proteomic, transcriptomic, epigenomic, genomic and genetic features) provide the basis for effective implementation of systems P4 medicine (6-7). The Vistera Project initiated by EISBM in Lyon, Nantes and Paris in partnership with ISB have been designed to scale up the monitoring of wellness, health and disease through the collection of billions of data points for increasing numbers of individuals who are healthy, at risk of developing disease, or in the course of disease development, with the active participation of individuals through social networks (8). The EISBM-ISB pilot studies form the basis for the development of a worldwide network of systems medicine centres including prominent research and hospital centres such as the Luxembourg, New Delhi and Shanghai Centres of Systems Biomedicine. Through their commitment to implement the open standard protocol of the Vistera Project and enforce full compliance with personal data and privacy protection regulations under the umbrella of a World Alliance for Health and Wellness, this network will catalyse the transformation of healthcare delivery and the transition toward emphasis on management of wellness through citizen science.

By monitoring individuals over a long period of time, the Vistera Project will provide them with actionable recommendations to maintain their state of health and wellness, detect early events indicative of a risk or a transition to disease, enabling their management and reversal. The expectation is that expanding the monitoring from one to millions then billions of individuals over the next 25 years, the Vistera Project will trigger in one generation a reversal of the escalating costs of healthcare management, drug and diagnostic development, providing the basis for a more cost-efficient and sustainable integrated healthcare system.

Keywords:
Iranian Personalized

KO1192

Ethical Issues of Personalized Medicine and Genetic Information Banks

Abdolhassan Kazemi
Biotechnology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran : Kazemi1338@Gmail.com

Abstract:

Biobanks are an essential and important tool of new idea in health system such as Personalized Medicine, genetic epidemiology and screening. Biobanks could investigates the roles, effects and influences of genetic factors and their interaction with environmental factors such as nutrition, stress, etc (in a broad meaning) for the occurrence of behaviors, health conditions, diseases, and quality of life in human populations. Application of biobanks in Personalized Medicine are to understand the influence and impact of genetics parameters on the development of behaviors, health conditions, diseases, and quality of life, their course and the clinical implications, with the final goal to improve prevention, diagnostics and therapy. The unexpected progress of genetics fields in the last two decades - with respect to the understanding of the meaning of genes for human health, as well as the availability of cost-effective high throughput methods in the lab and techniques, has opened massive opportunities to study genetic factors and their influence in human life and health condition. In addition, for establishment of an effective biobank access to large cases and samples of patients or from the population is needed. This can be realized via collaboration of several biobanks. Large biobanks with 500,000 or more participants are being established or planned in the UK, Japan, Iceland, Taiwan, Canada, Australia, Italia, Sweden and the US. However, in Germany only two smaller activities are ongoing, KORA-gen in the south and POPGEN in the north. Possibilities to reach larger numbers for Germany, based on existing cohorts or disease networks, are discussed between scientist and government. For the implementation and use of biobanks, stringent ethical, social and legal boundary circumstances have to be taken into account. The opinion of the German National Ethics Council on Biobanks for Research as well as the new advices of the Telematic Platform (TMF), which has been developed in close collaboration with the Data Protection Officers, improve transparency and legal security.

Keywords:
Biobank, Personalized Medicine, Ethics issue, Privacy Policy, Genetic privacy

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KO1194

Paving the Way for Personalized Medicine in Cancer: Experience in Iran

Forouzandeh Mahjoubi
Clinical Genetic Dept. NIGEB : frouz@nigeb.ac.ir

Abstract:

The vision of matching the right patient to the right treatment at the right time has always been the main goal of cancer therapy particularly in cancer therapy. For instance, the drug Gleevec (imatinib)that can stop the effect of the new fusion products produced by Philadelphia translocation in patients with leukemia. Similarly, it turns out that Erbitux (cetuximab) improves the survival of people with colorectal cancer whose tumour cells carry a mutated EGFR gene but not a mutated KRAS gene. However, until recently, very few cancer patients enjoyed the benefits of truly (personalized) / precision therapy. With the exploding knowledge of tumor genotype, as well as increasingly available targeted treatment options, it seems that the era of precision cancer medicine is nigh. The story of cancer therapy in Iran is more or less similar to the rest of the world. Every day, thousands of people are taking medications that will not help them. The very expensive drug, Herceptin, that supposed to do target therapy in breast cancer woman with Her2 gene amplification, could only help the survival of about 50% of patients. In addition, the toxic side effects of anticancer drugs can be a major limitation to their effective use. Moreover, the effectiveness of chemotherapy is limited by drug resistance. This is a major obstacle in cancer chemotherapy in Iranian cancer patients. Knowing that genotypic differences, with consequent phenotypic expression could be one of the main resean of differences in response to therapy. Also, it is important to note that targeted therapies should ideally be accompanied by a diagnostic marker, we aimed to investigate possible genetic biomarkers which could lead to better diagnosis, prognosis and prediction to response to chemothepy in Iranian patients with colorectal cancer and breast cancer which in this talk I will present some of the data.

Keywords:
Personalized Medicine, Cancer

KO1197

Genome wide association study in Tehran cardio-metabolic genetic study could promotes precision medicine in Iran

Maryam Daneshpour[1] ، Bahareh Sedaghatikhayat[2] ، Kamran Guity[2] ، Fereidoun Azizi[2]

1) Cellular and molecular endocrine research center, Research Institute for endocrine sciences Shahid Beheshti University of Medical Sciences, Tehran, Iran
2) Research Institute for endocrine sciences Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract:
In recent decades trying to identify the role of genetic changes and their effect on the prevention and disease is one of the most fundamental goals of medicine. Since the physicians` instructions are based on the specification set is an average that cannot be completely effective for wide range of patient. Therefore, precision medicine or personal medicine have used of certain genetic characteristics, genomics and clinical information for each individual. By the end of the genome-wide project, planning for more recognition of genetic pattern was done. The original version of the genome as a book is not edited and non-readable and lots of researchers around the world had tried to extract and categorize information. Also, developing large scale of genomic data banks like HapMap and 1000 Genomes Project would help make more accurate readings do this great book. Genome-wide study on participant of Tehran Lipid and Glucose Study as the oldest and largest prospective study has been conducted to by Iranian researchers removed a small step toward understanding the genome of the Iranian population. The prospective of this lecture is reviewing the findings from genome-wide studies in precision medicine in whole of the word in recent years then introduce the genome-wide study on the Iranian population.

Keywords:
Genome wide association study, precision medicine, Tehran Lipid and Glucose Study

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KO1201

The challenges in development of Pharmacogenetics and Preventive genetic testing

Katayoun Afshar
Swiss Society of Medical Genetics (SSMG),The Genetics Society of America,The American Society of Cell Biologists
afshar.katayoun@gmail.com

Abstract:
Genetic research and the recent technological advances have contributed tremendously in increasing the number of the routine diagnostic test and has opened a venue for genomic and personalized medicine. Nevertheless, assessment of the variants and the determination of the combinatorial effects of several genetics and environmental factors remains the most challenging step for the interpretation of the results or evaluation of the risks of the disease development in the patients. Close collaboration between the health care providers, research and diagnostic laboratories as well as development of bioinformatics tools and algorithms have been proven to be neccessary for efficient utilisation and interpretation of the high throughput data in the diagnostics testing. Our laboratory has overcome some of these challenges and has developed many products for Pharmacogenetics, Predictive and Preventive medicine. In this presentation, I will describe examples of the development and utilisation of the genetic tests for evaluation of risks and side effects associated with consumption of specific or combined drugs. In particular, I will describe a product that provides evaluation of the risk of venous thromboembolism associated with taking oral contraceptives, taking into account genetic factors, age, environmental factors and the type of the contraceptive pills.

Keywords:
Pharmacogenetics

KO1202

Personalized treatment in colon cancer

Leila Sadeghi
Assisstant professor of shahid beheshti university of medical school : l_sadeghi4650@yahoo.com

Abstract:
Colorectal cancer is the 3rd leading cause of cancer mortality worldwide with an estimate 639000 deaths per year.the past 5 years have witnessed extraordinary advances in the field of DNA sequencing tecnology.NGS allowed researchers to sequence individual genomes and match combinations of mutations with specific diseases.As cancer is inherently a disease of the genome,it is not surprising to see NGS tecnology already being applied to cancer research with promises of greater underestanding of carcinogenesis.Now we are going to discuss recent advances in NGS and spiculate on future directions for the application of this tecnology to colorectal cancer diagnosis and treatment.

Keywords:
Personalized,treatment

O1014

Determination the level of PTEN and CDKN1C/ p57kip2 Tumor Suppressor Gene expression in tumor tissue of patients with gastric cancer compared with its peripheral healthy tissues

Sareh Sohrabi[1] ، Massoud Saidijam[2]
1) Department of Molecular Medicine and Genetics, Molecular Medicine Research Center,
2) Department of Molecular Medicine and Genetics, Molecular Medicine Research Center : sjam110@yahoo.com

Abstract:
Background: Gastric cancer is the third most common cause of cancer-related death in the world. In the Islamic Republic of Iran, stomach malignancy have the highest incidence and mortality rates of cancer. Unfortunately gastric cancer remains difficult to cure, because the most patients present with advanced disease so early diagnosis and treatment leads to improved survival. Genetic and epigenetic changes in tumor suppressor genes (TSGs) frequently occur in human cancers. Some studies indicated that loss of TSGs is a key event in gastric carcinoma. Many TSG candidates have been studied, but based on epigenetic alteration each population is valuable to evaluate. So this study investigated the expression rate of PTEN and CDKN1C in a small available population in Iran.
Methods: 64 gastric samples (32 tumoral gastric tissues and 32 healthy adjacent tissues) were collected from patients referred to Imam Khomeini Hospital Cancer Institute during 2008-2011. Total RNA was extracted, cDNA synthesized, then expression level of PTEN and CDKN1C was detected by Real time-PCR.
Results: Our results displayed PTEN and CDKN1C expression significantly decreased in cancerous tissues compared to healthy adjacent tissues (P
Conclusion: A significant expression decrease of both tumor suppressor genes (PTEN and CDKN1C) in tumoral tissues compared with healthy adjacent tissues suggest that these genes have important role in gastric cancer incidence and future researches may reveal their advantage in treatment and diagnosis.

Keywords:
Stomach Neoplasms, Gene Expression, PTEN, Cyclin-Dependent
Kinase Inhibitor p57, Real-time PCR

O1022

Association of Expression of Selenoprotein P in mRNA and Protein Levels with Metabolic Syndrome in Subjects with Cardiovascular Disease: Results of Selenegene Study

Mojgan Gharipour[1] ، Masoumeh Sadeghi[2] ، Mehrdad Behmanesh[3] ، Mansour Salehi[4] ، Elham Khosravi[5]
1) cardiovascular research institute : mojgangharipour@gmail.com
2) Cardiac Rehabilitation Research Center
3) Tarbiat Modaress
4) Isfahan University of Medical Sciences
5) Isfajan University of Medical Sciences

Abstract:
Background/Objectives: Selenoprotein P (SeP) is involved in transporting selenium from the liver to target tissues. As SeP confers protection against disease by reducing chronic oxidative stress, this study is aimed to assess the level of SeP in the serum of patients with metabolic syndrome (MetS) with a history of cardiovascular disease (CVD).
Subjects/Methods: A cross-sectional study was conducted on 63 and 71 subjects with and without MetS in presence of documented CVD hospitals (Isfahan, Iran) Participants were recruited from December 2015 until March 2016. All demographic, anthropometric and with cardiometabolic variables (lipids, blood glucose, blood pressure) were assessed. Lifestyle related factors and personal history and familial CVD risk factors were recorded. The expression of SELP in mRNA and protein levels in the serum were measured and MetS was determined using ATPIII criteria. The level of SeP was obtained by human ELISA kit and RNA isolated by research kits and measured by real-time PCR. Binary logistic regression analysis demonstrated MetS and SeP as dependent and independent variables, respectively.
Results: The prevalence of women was higher in the MetS group. There is no significant difference between mean age of subjects with MetS and without MetS. Mean of systolic and diastolic blood pressure, triglyceride, HDL-C, fasting blood sugar (FBS), BMI, and waist circumference were higher among subjects with MetS ($P=0.05$). Mean of SeP was lower among subjects with MetS ($P< 0.04$). Furthermore, the association between MetS and SeP levels remained marginally significant even after adjusting for potential confounders such as age, gender, family history, smoking status, and nutrition. SeP and WC has a significant relationship (OR, 0.995; 95% CI, 0.990 to 1.00), $P<0.033$). There is no significant relationship between SeP and the other components of MetS such as FBS, HDL-C, and blood pressure after controlling for
confounders.
Conclusions: In conclusion, we demonstrated a significant decrease in circulating SeP levels according to MetS status in patients with documented cardiovascular disease.

Keywords:
Gene Expression, Selenoprotein P, mRNA, Protein, Metabolic Cardiovascular Disease

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O1163

Toll-like receptors 4 cell membrane level in T lymphocytes of patients undergoing percutaneous coronary intervention (PCI)

Samaneh sadat Enayati[1] ، Seyed Kianoosh Hosseini[2] ، Majid Yakhkeshi[2] ، Sepideh Borhan[3]
1) Metabolic Disorders Research Center, Endocrinology andMetabolismMolecular-Cellular Sciences Institute, Tehran Universityof Medical Sciences, Tehran, Iran.
2) Department of Cardiovascular Disorders, Division of Interventional Cardiology,Tehran Universityof Medical Sciences, Tehran, Iran.
3) Metabolic Disorders Research Center, Endocrinology andMetabolismMolecular-Cellular Sciences Institute, Tehran Universityof Medical Sciences, Tehran, Iran.

Abstract:
Introduction: Atherosclerosis, the leading cause of cardiovascular disease (CVD), is driven by inflammation. Increasing evidence suggests that toll-like receptors (TLR) are key orchestrators of the atherosclerotic disease process. Toll-like receptor 4 is expressed by different cell types in the atherosclerotic vessel wall. Activation of TLR4 in atherosclerotic lesions stimulates mononuclear phagocytes to secrete chemokines which are recognized for their involvement in the recruitment of monocytes and T- lymphocytes in the arterial wall. Few studies have been done on TLR4 and its roles in T- lymphocytes recruitment and subsequent inflammatory response and hence, atherogenesis. Hence in this study the expression level of TLR4 in CD3+ T-lymphocytes was evaluated in Coronary artery disease (CAD).
Material and methods: 45-65 years old patients that participated in this case-control study, were referred to shariati hospital for diagnostic angiography coronary for 13 months. Patients were derived into two categories, normal corner (n=38) and 3VD (n=38). Clinical information was recorded and angiography was performed, then patients CD were read by the intervention cardiologist. SYNTAX score for each patient was calculated. Cell surface markers, TLR4 were investigated by the flowcytometry in CD3+ T-lymphocytes.
Results: T-test analysis showed that the means of the cell surface markers TLR4 ($P=0.027$) were enhanced in patients with coronary artery disease compared to the control group in coronary artery disease patients. Pearson test of synthax score and TLR4 level in CD3+ T-lymphocytes show significant ($P= 0.04$) positive correlation (0.224).
Conclusion: Our findings illustrate that TLR4 is a risk marker against coronary artery disease. Synthax score, which grades the complexity of coronary artery disease, have positive correlation with TLR4 level. This result demonstrates TLR4 level augmentation on CD3+ T-lymphocytes is a marker of CAD severity.

Keywords:
Coronary artery disease (CAD), Toll Like Receptor4 (TLR4), SYNTAX score

O1025

Assessing the dietary patterns and rs1333048 polymorphism interaction on cardiovascular disease risk factors in healthy Tehrani people

Mehdi Mollahosseini[1] ، Mohammad Hossein Rahimi[2] ، Mir Saeed Yekaninejad[3] ، Zhila Maghbooli[4] ، khadijeh Mirzaei[2]

1) Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences (TUMS), Tehran, Iran. 2 Osteoporosis Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences , Tehran , Iran. :
2) Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences (TUMS), Tehran, Iran : mirzaei_kh@tums.ac.ir
3) Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
4) Osteoporosis Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences , Tehran , Iran

Abstract:
Introduction: Genome Wide Association Studies (GWAS) showed that risk alleles of chromosome 9P21 region are related to increasing hazard of cardiovascular diseases without any association with their risk factors such as lipid profile and inflammation markers. No study have been performed to evaluate the interaction between these single nucleotide polymorphisms (SNP) and dietary patterns (DP) on cardiovascular disease risk factors.
Materials and methods: This cross-sectional study conducted on 265 Tehrani healthy adults (age range: 18-55 years). DPs were extracted by a 147-items semi-quantitative food frequency questionnaire (FFQ) and factor analyzing method. Bioelectrical impedance analysis (BIA) method was used for body analysis. Weight, height, waist circumference, waist to height ratio (WHtR), body mass index (BMI), lipid profile, fasting blood glucose and high sensitivity C-reactive protein (hs_Crp) were measured. Blood sampling was done after 10-12 hours fasting. rs1333048 were genotyped by restriction fragment length polymorphism (PCR-RFLP) method.
Results: Prevalence of C allele was 52.85% and A allele was 47.15%. AA genotype compared to CC had greater odds for general obesity (OR=3.11; 95% CI =1.008-9.60, P=0.048) and central obesity (OR=2.63; 95% CI =1.12-6.17, P=0.026). Significant Interactions were observed between legumes based DP and rs1333048 SNP on waist circumference (P-interaction= 0.047), body fat percent (P-interaction = 0.048), hs-Crp (P-interaction =0.042), BMI (P-interaction =0.073), WHtR (P-interaction =0.063) and odds for general obesity (P-interaction =0.051) in this way that last tertile of this DP compared to first tertile, reduced all mentioned items for individuals with CC genotype whereas increased them for who with CA and AA genotypes.

Conclusion:
Results of this study indicates significant associations between A allele of rs1333048 SNP and general and central obesity and significant interactions between this SNP

O1027

Linkage between bioethics ans steam cell

Ghazaleh Arabzadeh
nourdanesh : ghazaleharabzadeh11@gmail.com

Abstract:
AIM & INTRODUCTION:
Bioethics is a new science and interdisciplinary in applied ethics field which is to analyze the challenges and problems of moral, philosophical, religious and legal concerns associated with the emergence and spread of new biological technologies.
Effects of certain or probable risk arising from the application of technology such as cloning, genetic manipulation, biomedical experiments on human subjects has caused international institutions at various levels in the formulation and adoption of the Declaration while explaining the general principles and guidelines for countries and ask them to adjust domestic legislation and regulations and its efforts to adopt comprehensive legislation.
Research using stem cells derived from human embryonic or adult cell, great promise to reduce the suffering of patients and difficulties to treat diseases but it also has its own ethical considerations and concerns. These concerns cover the whole important subjects such as safety and respect for the human embryo.No doubt, enjoy the benefit of such studies depends on proper and consistent compliance with ethical requirements and special considerations. Here, the most important considerations are reviewed.
MATERIAL & METHOD:
review of 50 researches which published since 2011 till 2016 from

Keywords:
Bioethics , steam cell , genetic manipulation

O1042

Quantification and clinical value of cell-free circulating DNA in colorectal cancer

Abolfazl Akbari[1] ، Shahram Agah[2]
1) Colorectal Research Center, Iran University of Medical Sciences, Tehran, Iran : akbariia2006@gmail.com
2) Colorectal Research Center, Iran University of Medical Sciences, Tehran, Iran

Abstract:
Background and objectives: Development of a non-invasive sensitive and specific biomarker is the upmost importance in early detection of cancers. Colorectal cancer (CRC) as the second leading cause of cancer worldwide is not excluded from this fact. Circulating nucleic acids including cell-free circulating DNA (cfcDNA) in patients with cancers have been recognized as promising biomarkers for diagnosis, prognosis and treatment. This study aimed to quantify cfcDNA in CRC to evaluate its potential value as a non-invasive blood-based source for investigating biomarker candidates.
Methods: Total DNAs were extracted from plasma samples of 62 patients with stages II, III and IV CRC and 24 healthy controls. The quality and quantity of DNA were studied by spectrophotometry. Quantification of baseline cfcDNA was determined as the amount of free GAPDH in plasma, by using real-time quantitative polymerase chain reaction (RT-qPCR).
Results: RT-qPCR data revealed that the concentration of cfcDNA in CRC patients was significantly different from healthy controls ($P<0.05$). Further analysis showed that the concentrations of cfcDNA were correlated with the degree of differentiation ($r=0.87$, $P<0.05$) and tumor size ($r=0.72$, $P<0.05$) but not with other clinicopathological factors.
Conclusion: The significantly elevated plasma DNA level in CRC was shown to be correlated with clinicoplathological features. In conclusion, cfcDNA could be served as a suitable source of molecular biomarkers which can benefit to clinical settings of CRC. Hence, gene analysis of cfcDNA might be at the forefront of advance in personalized medicine, particularly for cancer early detection and management.

Keywords:
Biomarker, cell-free circulating DNA, Colorectal cancer,

O1045

Evalition of mir-10a in CLL Patients and Healthy People using RT-qPCR

Monir Sayahian[1] ، Mansoor Salehi[2] ، Parisa Mohammadinejad[3]
1) Department of basic science, Islamic Azad University, Shahrekord Branch, Shahrekord, Iran
2) Department of Genetics and Molecular Biology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran u8002010@hotmail.com
3) Biology Dept., Shahr e Kord Branch, Islamic Azad University, Shahr e Kord, of Iran

Abstract:
Background: Chronic Lymphocytic Leukemia (CLL) is the most common human leukemia occurring as indolent or aggressive form. MicroRNAs are small non-coding RNAs involved in several cellular processes and expressed in a tissue-specific manner. In CLL, microRNAs can function as oncogenes or tumor suppressors. The aim of the present study was to compare the expression level of mir-10a in normal and neoplastic samples from CLL patients by RT-qPCR.
Methods: The number of 15 blood samples from patients with CLL and 15 blood samples from healthy group under the direct supervision of a pathologist specialist due to clinical presentation and laboratory findings were collected. After extracting RNA from normal and tumor blood samples, cDNA synthesis method according to the protocol and RT-qPCR was performed. mir-10a expression level was calculated using Livak method. All data were analyzed using SPSS software.
Results: The results of RT-qPCR indicated that miR-10a down-regulation was significantly correlated with CLL cancer clinic pathological features. Expression level of mir-10a was 7.43% in CLL patients and 92.57% in healthy group (p value=0.001).
Conclusion: Due to the previous reports, mir-10a act as tumor suppressor in CLL, which could be used as biomarker for CLL diagnosis. In this study we propose that miR-10a is a potential diagnostic marker and therapeutic target of CLL.

Keywords:
Chronic lymphocytic leukemia, microRN

O1049

Cancer Detection as a First Step of Personalized Medicine Using Circulating microRNAs in Peripheral Blood

Hanieh Sadeghi[1] ، Ali Sharifi Zarchi[2] ، Aryan Kamal[3] ، Bahareh Shayesteh Pour[1] ، Hamid Gourabi[4] ، Andreas Keller[5] ، Mehdi Totonchi[6]

1) Department of Genetics, 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 Biology and Technology, ACECR, Tehran, Iran
3) Department of Mathematical Sciences, Sharif University of Technology, Tehran, Iran
4) Department of Genetics, Reproductive Biomedicine Research Center, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran
5) Department of Clinical Bioinformatics, Saarland University, Saarbr¨ ucken, Germany
6) 2. Department of Genetics, Reproductive Biomedicine Research Center, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran

Abstract:
The use of personalized medicine to advance both the prevention and cure of disease is potentially possible. The main step to success in this filed depends on having proper diagnostic tests that identify patients who can benefit from targeted therapies. microRNAs (miRNAs) are a class of non-coding RNAs that regulate many cellular processes including tumorigenesis. Circulating miRNAs are known as less invasive markers in many malignancies such as cancer. Recent studies have shown that some specific miRNAs are deregulated in blood of early stage cancer patients compared to healthy controls. In this study, we aim to design subsets of circulating miRNAs can detect each type of cancer from unaffected controls and other types of cancers with high accuracy. We used miRNA expression profiles from the cancer genome atlas (TCGA) and analyzed 6104 next-generation sequencing (NGS) data related to 14 different types of cancer tissues encompassing 5493 cancer samples and 611 healthy controls. We were using feature selection algorithm and support vector machine with 10 fold cross validation as machine learning method for improving detection accuracy. By focusing on five miRNAs, we could separate all cancer samples from all normal samples with 97% accuracy. We obtained subsets with maximum 5 members and also acceptable accuracy for each cancer type. The highest accuracy received for thyroid carcinoma (98%) and kidney renal clear cell carcinoma (97%) with subset of three and two miRNAs, respectively. We also could classify samples in 3 classes (breast invasive carcinoma, normal breast tissue and all other normal and cancer tissues) just with 3 miRNAs. Using these bioinformatics approach we identified various subsets of miRNAs that could distinguish every type of cancer from unaffected controls. These subsets have potential to be evaluated in blood samples of each cancer type.

Keywords:
Personalized medicine, Early detection, Circulating microRNA, Biomarker, Bioinformatics

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O1055

Investigation of the CYLD promoter methylation pattern in gastric cancer

Elham Ghadami[2] ، Novin Nikbakhsh[2] ، Mohadese Kosari[1] ، Maryam Pilehchian[1] ، Sadegh Fattahi[3] ، Haleh Akhavan- Niaki[1]

1) Department of Genetics, Faculty of Medicine, Babol University of Medical Sciences, Babol, Iran : halehakhavan@yahoo.com
2) Department of Surgery, Rouhani Hospital, Babol University of Medical Sciences, Babol, Iran
3) Cellular and Molecular Biology Research Center, Babol University of Medical Sciences, Babol, Iran

Abstract:
Intoduction: Gastric cancer is one of the most common malignancies and cause of cancer death in the world. DNA methylation plays an important role in development and prognosis of gastric cancer. Hypermethylation of tumor suppressor genes is involved in initiation and progression of many types of cancer. Tumor suppressor gene CYLD negatively regulates various signaling pathways including Wnt, Shh, and Notch. In this study we evaluated promoter methylation pattern of CYLD gene in gastric cancer patients.
Materials and methods: Tumoral tissues of thirty gastric cancer patients and their adjacent non-tumoral counterparts were studied. DNA extraction and bisulfite treatment followed by sequencing of PCR products were performed.
Results: Promoter hypermethylation of the CYLD gene was found in 14(46%) of the 30 tumoral tissues. Also, 6(20%) hemi-methylated tumor margin tissues were observed.
Discussion: CYLD promoter hypermethylation can be associated with gastric cancer risk. Because of DNA methylation is a reversible process, it may be a new target to prevent progression of gastric cancer.

Keywords:
Gastric cancer, CYLD, Promoter methylation

O1060

Association between polymorphisms of TOX3 gene and breast cancer risk in Persian women

Hamidreza Agha heydarali naghash[1] ، Ali Salehzadeh[2] ، Ashkan Alborzi[3] ، Shima Forouzan[3] ، Ali Hajizadeh[3] somayeh Saeidi[3] ، Bahareh Abbasi[4] ، Nafiseh Ansarinejad[5] ، Massoud Houshmand[4]

1) Karaj Branch, Islamic Azad University,Karaj,Iran
2) Department of Biology, Rasht Branch, Islamic Azad University, Rasht, Iran
3) Islamshahr Branch, Islamic Azad University, Islamshahr, Iran
4) National Institute of Genetic Engineering and Biotechnology (NIGEB),Tehran,Iran : massoudh@nigeb.ac.ir
5) Iran University of Medical Sciences, Tehran,Iran

Abstract:

Several epidemiological studies have evaluated the association between TNRC9 (also known as TOX3) polymorphisms and breast cancer risk, but the results remain inconclusive according to different ethnic groups (Zheng et al., 2009; Li et al., 2009; Ruiz-Narváez et al., 2010).

TOX3 the locus on 16q includes a gene TNRC9 and a hypothetical gene LOC643714. TOX3 is a gene of uncertain function containing a trinucleotide repeat motif and encoding a member of the high-mobility group family of non-histone chromatin proteins. The presence of a putative high-mobility group box motif suggests that it might function as a transcription factor (Easton et al., 2007). Several studies have shown that susceptibility loci at TOX3 predispose to sporadic breast cancer.

The TOX3/LOC643714 locus on chromosome 16q12.1 was one of the first breast cancer regions identified through genome-wide association study (GWAS) in populations of European and East Asian Origin.

5 SNPs including rs3803662, rs12443621, rs8051542, rs3104746 and rs4784227 inTOX3 and the hypothetical gene LOC643714 identified novel risk loci for breast cancer in populations of European and East Asian origin. In this study, we will evaluate the association between TOX3 polymorphisms (rs3803662 , rs12443621, rs8051542, rs3104746 and rs4784227) and breast cancer risk in Persian women.

Keywords:
TOX3,breast cancer , SNP,association, polymorphism

O1081

Omics-based sample collection and biobanking for development of personalized medicine

Dr Mohammad Javad Hajipour1 ، Zohreh Mahmoudi2 ، Negar Mahmoudi3 ، Shirin Djalalinia4 ، Arezoo Dilmaghani5 ، Kamyar Rezaee5 ، Nazanin Keyvan5 ، Shilan Foroomand5 ، Bahman Damerchilo5 ، Nazila Rezaei5 ، Farshad Farzadfar2

1) The Persian Gulf Marine Biotechnology Research Center, The Persian Gulf Biomedical Sciences Research Institute, Bushehr University of Medical Sciences, Bushehr, Iran
2)Non-Communicable Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran farzadfar3@yahoo.com
3) Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran
4) Deputy of Research and Technology, Ministry of Health and Medical Education, Tehran, Iran,
5) Non-Communicable Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

Abstract:

Omics-based studies provide valuable information on personal and public health status. These analytical approaches provide unique opportunities to discover biomarkers that specifically feature different disease stages and determine the emerging risk factors involved in disease prevalence/progress. Access to high-quality biological samples is required to make omics-based analysis unbiased and fit for purpose. We collected the biological samples (e. g. blood, plasma, buffy coat and urine) from 21000 participants randomly selected from the urban and rural area of 31 provinces of Iran, as a sub-component of STEPs survey (Large-Scale Cross-Sectional Studies of Surveillance of Risk Factors of Non-Communicable Diseases) 2016 in Iran. These samples were collected, processed, transferred and stored based on the standard protocols that ensure the quality and fitness of biological samples for all fields of omics analyses. The quality assured and validated protocols were developed for long-time storage of biological samples in the biobank. All variable parameters (i. e. contamination, maintenance, temperature, time, the number of freeze-thaw cycle and storage condition) that affect the quality of biological samples and Omic outcomes were considered in protocol development. The laboratory information management software was also developed to improve data recording/storage and biobank management. We develop consensus SOPs that are generalizable and feasible for every research group in every laboratory. Besides biological samples, Valuable information on demography, socioeconomic status, diet, physical activity, smoking, lifestyle, diabetes, hypertension, urine sodium and creatinine and hyperlipidaemia treatment of all participants was also collected. The crosstalk among these factors and genome/proteome/metabolome/epigenome determines the individual resistance and susceptibility to different diseases/risk factors. Various “omics” approaches investigate the influence of these factors on a molecular level, with the intention of developing personalized approaches to disease diagnosis and treatment.

O1091

in-silico analysis of potential role of miR137 in patients with Schizophrenia

seyedeh azdeh Abtahi[1] ، Naghmeh Gholipour[2] ، nourodin moradi[3]
1) sana institute of higher education, Sari, Mazandaran, Iran
2) national institute of genetic engineering and biotechnology (nigeb), tehran, iran
3) Tehran university, Tehran, Iran

Abstract:
Background: Schizophrenia is a complex genetic disease and characterized by affective, cognitive, neuromorphological, and molecular abnormalities that may have a neurodevelopmental origin. MicroRNAs (miRNAs) are critical to neurodevelopment and adult neuronal processes by modulating the activity of multiple genes within biological networks. Noncoding variants in the human MIR137 gene locus increase schizophrenia risk with genome-wide significance.MiR137 as a brain-enriched microRNA, plays important roles in regulating embryonic neural stem cells (NSCs) fate determination, neuronal proliferation and differentiation, and synaptic maturation.
Methods: To determine the gene targets of the differentially expressed miRNAs, we used three of the leading miRNA target prediction algorithms: mirwalk2, PicTar, and TargetScan. Mirwalk2 found the miRNA-target genes in the Carcinogenesis pathway and verified by KEGG pathways. KEGG pathway is derived from Kanehisa Lab, Kyoto University, Japan. This analysis is used to determine the position and role of this MIR137 in controling carcinogenesis pathway. The position and function of genes in a pathway are crucial for recognizing the mechanism of intervention or regulation of MIR137 in carcinogenesis.

Results: Among the 638 predicted targets of mir137 with 7, 8 and 9 score. Our data manifested KEGG signaling pathways “pathway in cancer and Schizophrenia” as the most statistical relevant pathways with mir137 targetome. Several genes were identified that probably indicate a role for sustained Schizophrenia is a complex genetic disease. This is predicted that critical mRNAs in cholinergic synapse pathway.
Conclusions: Our data suggests that miR137 acts as a regulator molecule by targeting some important mRNAs which are necessary in cholinergic synapse pathway, so it could be used as a prognostic biomarker in Schizophrenia.

Keywords:
Schizophrenia, miR137, biomarker

O1099

Regulation of Stemness, Metastasis and Drug Resistance By MicroRNAs in Gastric cancer

Mahnaz Azimi[1] ، Marzieh Ebrahimi[2] ، Mehdi Tootoonchi[3] ، Parisa Sahranavard[3] ، Jazad Firoozi[3]
1) Department of Genetics, University of Science and Culture, ACECR, Tehran, Iran.
2) Department of Stem Cells and Developmental Biology at Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran : mebrahimi@royaninstitute.org
3) Department of Genetics, Reproductive Biomedical Research Center, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran.

Abstract:
Objective or background: Cancer stem cells (CSCs) have a significant role in spread out and cancer metastasis as well as resistance to conventional therapy. MiRNA is one of the regulatory elements which can regulate metastasis, stemness and drug-resistance properties simultaneously. Therefore, in this study, by using literature learning and data mining, 30 miRNAs obtained that are able to regulate any third of these properties in gastric cancer.
Materials & methods: published articles from PubMed online database were obtained using search strategy: ((stem cell OR sphere OR side population) AND (miRNA OR microRNA) AND (profiling)).
138 studies were collected from mentioned search strategy and after removing duplicates, non-full-text and non-related topics and abstracts, 21 studies were selected (figure 1).

Figure 1. Flowchart of study selection.
A total of 200 miRNAs which regulate stemness, were observed in 21 studies.
For extracting miRNAs that regulate metastasis, we used the miRCancer database. Then we observed 76 miRNAs are common between metastasis and stemness.
And for the drug resistance feature, we used the PUBMED database and analyzed 30 common miRNAs in these three properties. (figure 2).
2. Venn diagram shows the Number of common miRNAs.
RESULTS: Based on different sets of data, 30 miRNAs including: hsa-miR-197, hsa-let-7f, hsa-miR-34a, hsa-miR-21 , hsa-miR-7g , hsa-miR-107, hsa- miR-7d , hsa-miR-149 , hsa-miR-375 , hsa-miR-30a , hsa-miR-103a , hsa-miR-224 , hsa-miR-129-1, hsa-miR-197, hsa-miR-125b, hsa-miR-24, hsa-miR-20a, hsa-miR-223, hsa-miR-129-2, hsa-miR-149, hsa-miR-23b, hsa-miR-27a, hsa-miR-338, hsa-miR-181b, hsa-miR-27b, hsa-miR-140, hsa- miR-19b, hsa-miR-92, hsa-miR-524 and hsa-miR-106b play a role in resistance to conventional therapy, stemness, metastasis in gastric cancer.

O1103

Personalized Breast Cancer Screening Using Circulating MicroRNAs as Potential Biomarker in Whole Blood

Bahareh Shayestehpour[1] ، Aryan Kamal[2] ، Ali Sharifi zarchi[3]، Hanieh Sadeghi[1] ، Hamid Gourabi[4] ، Andreas Keller[5] ، Mehdi Totonchi[4]

1) Department of Genetics, Faculty of Basic Sciences and Advanced Technologies in biology, University of Science and Culture, ACECR, Tehran, Iran
2) Department of Mathematical Sciences, Sharif University of Technology, Tehran, Iran
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 Genetics at Reproductive Biomedicine Research Center, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran : m.totonchi@royaninstitute.org
5) Chair for Clinical Bioinformatics, Saarland University, Saarbrucken, Germany

Abstract:
Personalized medicine is defined as studying a person’s genes, proteins and environment to increase the efficiency of diagnosis and treatment. The first step in personalized medicine is diagnostic testing to separate patients into different groups. MicroRNAs are a new class of small non-coding RNAs that have a regulatory role at the post-transcriptional level of gene expression. Aberrant expression of miRNAs is related to many diseases such as cancer so it can be used as a biomarker for diagnosis and prognosis. Circulating microRNAs are stable in body fluids such as blood, serum, plasma etc. We investigated to find the best group of candidate microRNAs and design a panel for early detection of breast cancer.

We analyzed miRNome data from the cancer genome atlas (TCGA) with a computational approach. In the first step, we analyzed 6104 samples from 14 different types of cancers and normal tissues, and then Differential Expression between 778 Breast cancer samples, 87 control samples and all other cancer and normal samples were done. We also performed Differential Expression between candidate list with 105 circulating miRNA microarray data sets from invasive ductal carcinoma samples to validate the candidates.

We found that miRNAs can distinguish normal samples from tumors so they can be regarded as good biomarkers. The candidate list with a threshold of adjusted P values less than 0.001 and absolute log fold changes more than one were selected. A list of 54 differentially expressed miRNAs can separate Breast Cancer from all normal tissues with a good P value. As 16 of the 54 candidates are significantly deregulated in all cancers, we focused on the other 38 by considering their different features and then compared this list with circulating miRNA data sets to achieve the final candidate list comprising 17 miRNAs for the early detection of breast cancer.

Although miRNA profiling using whole blood is a potential biomarker for early detection of breast cancer, clinical validation of these new candidate biomarkers in the wet lab is necessary.

Keywords:
Personalized medicine, Circulating MicroRNA, Biomarker, Breast cancer, Early detection, Bioinformatics

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O1111

Expression level study of EGR family genes in schizophrenic patients

Mozhdeh Amini faskhodi[1] ، Reza Mahdian[2] ، Arvin Haghighatfard[3] ، Mehrdad Hashemi[4]
1) Department of biology, Tehran medical branch, Islamic azadi university, Tehran, Iran
2) Department of medical biotechnology,Pasture Institute,Tehran, Iran
3) Department of biology, Tehran North Branch, Islamic Azad University, Tehran , Iran
4) Department of biology, Tehran medical branch, Islamic Azad University, Tehran, Iran mozhdeh.amini@yahoo.com

Abstract:
Schizophrenia (SCZ) is a major psychiatric disorder with 1 percent prevalence and unknown etiology with acute and chronic positive, negative and cognitive symptoms. Early growth response (EGR) family genes including EGR1 to EGR4 are transcription factors that are essential for development and function of central and peripheral nervous system. Previous studies were reported involvement of EGR1 and EGR3 with etiology of schizophrenia and addiction.

mRNA level of EGR1, EGR2, EGR3 and EGR4 were studied in blood samples of 150 Iranian schizophrenic patients and 50 non-psychiatric subjects using quantitative Real time PCR. Also positive and negative symptom scale (PANSS) from patients and Wechsler Adult Intelligence Scale (WAISE) from all subjects were obtained.

Significant down regulation of EGR1, EGR2 and EGR3 were detected in SCZ vs. non-psychiatrics. No significant expression alteration was revealed in EGR4 between SCZ vs. non-psychiatrics. Correlations were found between EGR1 and EGR2 down expression and higher scores of negative symptoms in PANSS and memory deficit in Digit span memory subscale of WAISE.

Results were suggested EGR family role in etiology of schizophrenia. In addition findings indicate down regulation of transcription factors may lead to negative symptoms and memory deficiency. EGR family genes may present as biomarker for schizophrenia.

Keywords:
EGR family - schizophrenia - gene expression

O1113

Several novel biomarkers in bioenergetic pathways have detected in schizophrenia and paranoid personality disorder

Arvin Haghighatfard[1] ، Amir Hossein Ghaderi[2] ، Soha Sadeghi[3]
1) Department of Biology ,Tehran North Branch,Islamic Azad university,Tehran,Iran : arvinland@yahoo.com
2) Cognitive Neuroscience Lab, Department of Psychology, University of Tabriz, Tabriz, Iran
3) Laboratory of Medical Genetics, National Institute of Genetic Engineering and Biotechnology (NIGEB), Tehran, Iran

Abstract:

Schizophrenia (SCZ) is a chronic neuropsychiatric disorder with 1 % prevalence worldwide and no certain known etiology. Paranoid personality disorder (PPD) is one of the type A personality disorders which characterized by paranoia and a pervasive, long-standing suspiciousness and generalized mistrust of others with 0.5%–2.5% occurrence in general population and no clear etiology .Present study aimed to assess the role of mitochondrial complex I and cell bioenergetic pathways in etiology and characteristics of SCZ and PPD.

mRNA level of all genomic and mitochondrial genes which encoding mitochondrial complex I subunits(44 genes) assessed in blood with quantitative Real time PCR, associated by comprehensive psychiatric and psychological assessments, electroencephalography and biochemical evaluations in 634 SCZ , 340 PPD patients and 528 non psychiatric subjects.

Significant expression changes of 18 genes in SCZ patients and 11 genes in PPD patients detected in mitochondrial complex I. Most of these genes were novel candidate biomarkers for SCZ and PPD. Significant over expression of NDUFS1 was found in paranoid schizophrenic patients and PPD patients in compare with other subtypes of schizophrenia. There was a direct correlation between antipsychotic resistance in patients and over expression of NDUFS1 and NDUFV1 and down expression of NDUFB11 and NDUFA1.Several correlations between mRNA levels and severity of symptoms, drug response, and deficits in attention, working memory, executive functions and brain regions activities were found.

Findings suggest that deregulations of both core and supernumerary subunits of complex I are involved in etiology of SCZ and PPD. These deregulations have effects on brain activity as well as disorders characteristics. NDUFS1as largest subunit of complex I presented as a special biomarker for paranoid behaviors along with antipsychotic resistance and prefrontal cortex dysfunctions in psychotic patients. Also all of the 11 candidate genes found in PPD were among the 18 differentially expressed genes found in schizophrenia and their change direction were the same in both disorders which refer to important and upper hand effects of cell bioenergetic pathways in behavior and psychosis.

Keywords:
Schizophrenia, Paranoid personality disorder, mitochondrial complex I, gene expression, NDUFS1

O1116

Genetic risk factors for tendency to suicide detected in a GWAS study

Arvin Haghighatfard[1]، Atieh Alizadenik[2] ، Elham Rastegari Moghaddam[3] ، Noshin Nejati[2]
1) Department of biology ,Tehran North Branch,Islamic Azad university,Tehran,Iran : arvinland@yahoo.com
2) Department of biology, Damghan branch, Islamic Azad University, Damghan, Iran
3) Department of microbiology, Damghan branch, Islamic Azad University, Damghan, Iran

Abstract:

Suicide is a major public health problem, which kills almost one million individuals each year in world population. Psychological risk factors for suicidal behaviors are including, psychiatric and medical illness, impulsivity, aggression, alcohol and drug abuse specially stimulants, and low stress resilience. Genetic risk factors of suicide are not completely clarified. Present study aimed to detect genetic risk factors that increasing the vulnerability to committing suicide. DNA was extracted from blood samples of 100 saved suicide victims with at least one attempt to suicide in last 12 months and 150 healthy subjects. Genotyping for the subjects was performed using the Affymetrix Genome-Wide Human SNP Array 6.0 (Affymetrix, Santa Clara, CA) according to the manufacturer’s protocol. Several SNPs were detected with genome-wide significance. The significant association found in 77 SNPs involved in dopaminergic pathway and neurodevelopment of CNS. 56 of significantly related SNPs were found as risk factors of psychiatric disorders specially schizophrenia and obsessive compulsive disorder; other 21 SNPs were related to the mitochondrial complexes, transcription factors and growth factor genes. The study was showed genetic bases of suicidal thoughts and could be used for providing genetic prognostic markers for prediction of suicide risk especially in subjects with psychosis. Also importance of mitochondrial complexes and growth factors in neuorobilogical functions and decision making processes in brain has been showed.

Keywords:
Suicide tendency, SNP array, mitochondrial complexes, growth factors

O1121

BsmI (rs1544410) polymorphism of vitamin D receptor gene influences improvement of vitamin D status in overweight women with hypovitaminosis D

Samira Ebrahimof[1] ، Sakineh Shab_bidar[2] ، Pooneh Angoorani[3] ، Somayeh Abedini[3] ، Mehdi Hedayati[4]

1) National Nutrition and Food Technology Research Institute, Faculty of Nutrition and Food Technology, Shahid Beheshti University of Medical Sciences, Tehran, Iran : s.ebrahimof@sbmu.ac.ir
2) Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences
3) National Nutrition and Food Technology Research Institute, Faculty of Nutrition and Food Technology, Shahid Beheshti University of Medical Sciences
4) Cellular and Molecular Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences

Abstract:
The aim of the present study was to evaluate the possible influence of BsmI (rs1544410) polymorphism of vitamin D receptor (VDR) gene on response to vitamin D supplementation in women with hypovitaminosis D. Seventy-five apparently healthy overweight women aged 20-40 years with hypovitaminosis D were assessed. Hypovitaminosis D was described as plasma 25(OH)D3 level less than 30ng/mL. BsmI polymorphism of VDR were detected using PCR-sequencing. Subjects were given 50000 IU/w vitamin D3 for 12 weeks. Demographic data as well as dietary and physical activity habits were obtained by interview. Fasting blood samples were obtained from each subject at the beginning and after 12 weeks to evaluate the efficacy of vitamin D3 supplementation. Distribution of the genotypes of the BsmI polymorphism was as follows: GG (41 %), GA (45 %) and AA (14 %). Supplementation resulted in significant increase in 25(OH)D3 level in the studied subjects. The most increase in the 25(OH)D3 level was in the GG genotype of the BsmI variant. In the GG genotype group 51.5±22.1 ng/mL increase in the 25(OH)D3 level was observed. The increase in the 25(OH) D3 level in the GA genotype and AA genotype groups was 43.7±14.6 and 38.0±6.6 ng/mL, respectively. In conclusion, subjects carrying GG genotype of BsmI polymorphism of the VDR gene may response better to vitamin D supplementation compared to other genotypes of this VDR polymorphism.

Keywords:
Vitamin D, vitamin D receptor gene polymorphism, BsmI, supplementation

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O1123

Analysis of VEGF Gene Methylation Pattern and Metabolic Syndrome

Eng nahid talebzadeh[1] ، Saeid Ghorbian[1]

Department of Molecular Biology, Ahar Branch, Islamic Azad University, Ahar, Iran. ghorbian20@yahoo.com

Abstract:
Introduction: Metabolic syndrome (MS) involved multiple disorders such as diabetes, hypertension and obesity, which were associated considerably with changes in gene expression that are originated through genetic, epigenetic and environmental factors. DNA methylation is a most common epigenetic variation that regulates gene expression in physiologic and pathologic conditions. We aim to assess methylation patterns of promoter regions of vascular endothelial growth factor gene (VEGF), which may be acts a critical role in the pathogenesis of MS.
Materials and Methods: In this case-control investigation, we were assessed a total of 100 subjects, which were included 50 of cases diagnosed as MS and 50 in healthy individuals as a control group. Methyl specific polymerase chain reaction (MS –PCR) method was performed to analysis of VEGF gene promoter methylatin patterns.
Results: The frequencies of VEGF gene promoter methylation observed in 32% (16/50) and 20% (10/50) of case and control individuals, respectively. Our findings revealed that the frequencies of the gene methylated was not statistically significant difference between two groups (p-value >0.05).
Conclusions: Due to the small sample size suggested that more evidence will be needed to approve the present results, which was not considered the VEGF gene methylation as a predisposed factors in feature of MS.

Keywords:
VEGF, Metabolic syndrome, Methylation, Promoter

O1125

Pharmacogenetics in management of Epilepsy

Massoud Houshmand
NIGEB, Department of Human Genetics

Abstract:
There are large variation between the cases in efficacy, adverse reactions and optimal dose of anti-epileptic medications. The genetic variations are seen in the genes that are responsible in pharmacokinetics and pharmacodynamics of Anti-Epileptic drugs (AED). The best defined indication for testing relates to HLA-B*15:02 genotyping to identify those individuals of Iranian cases who are at high risk for developing serious adverse cutaneous reactions to carbamazepine. . The use of genetic testing to guide epilepsy treatment is likely to increase in the future, as better understanding of the function of epilepsy genes will permit the application of precision medicine targeting the biological mechanisms responsible for epilepsy in the specific individual. Here we review the current state of epilepsy pharmacogenetics focusing on phenotyping questions and discuss what characteristics we need to study to get answers and we discuss on rate and prevalence of HLA-B*15:02 variation in our cases.

Keywords:
Pharmacogenetic, Epilepsy, Carbamazepine

O1127

Adherence to a healthy dietary pattern is associated with reduced risk of endometrial cancer: evidence from a meta-analysis with 2617 cases and 78082 participants/controls

Shahab Alizadeh
Department of Cellular and Molecular Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences (TUMS), Tehran, Iran : alizadeh.mnutr@gmail.com

Abstract:
Background: Compared with investigating single food or nutrient effects, an assessment of whole diet using dietary patterns might be a more appropriate method to explore the combinatorial effects of dietary factors on health outcomes. Studying the association between dietary patterns and risk of endometrial cancer (EC) is an emerging literature; however, the results from published studies are not entirely conclusive. The current meta-analysis was conducted to comprehensively elucidate these associations. Methods: Pertinent studies published prior to September 2016 were systematically searched and retrieved through PubMed and Scopus databases. The most common dietary patterns with high loadings of foods or nutrients were selected and the most adjusted risk estimates were derived by comparing the highest with the lowest categories of dietary pattern scores. Data were pooled using random-effects model when heterogeneity was significant; otherwise, the fixed-effects model was applied. Statistical analysis was performed by STATA (version 14). Results: A total of 5 studies, including 2617 cases and 78082 participants/controls were included in this meta-analysis. Adherence to a healthy dietary pattern, featured by a higher intake of all types of fresh fruits and vegetables, legumes, fiber, fish, poultry, whole grains, and low-fat dairy products, was found to be significantly associated with decreased risk of EC (OR=0. 80, 95%CI: 0.61–0.98, random effects), whereas no significant association with Western/unhealthy dietary pattern was observed (OR=1. 14, 95%CI: 0.95-1.34, fixed effects). Conclusion: This meta-analysis proposes that adherence to a healthy dietary pattern is related to a lower risk of endometrial cancer.

Keywords:
Dietary patterns, endometrial cancer, meta-analysis

O1128

Combined effects of obesity and metabolic status on the risk of incident chronic kidney disease events: pooled analysis of longitudinal studies

shahab alizadeh
Department of Cellular and Molecular Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences (TUMS), Tehran, Iran. alizadeh.mnutr@gmail.com

Abstract:
Background: Emerging evidence has shown that obesity has different phenotypes and a subset of obese individuals, known as metabolically healthy obese (MHO) subjects, might be at lower risk for developing obesity-derived complications than their metabolically unhealthy obese (MUHO) peers. Although most previous studies have linked obesity to chronic kidney disease (CKD), reports regarding the association between MHO phenotype and risk of CKD are inconsistent. This meta-analysis was conducted to comprehensively analyze the risk of CKD in different phenotypes of body size. Methods: The EMBASE, MEDLINE, and Web of Science databases were systematically searched until May 2016 to identify all prospective cohort studies exploring CKD risk associated with metabolic phenotypes of body size. Body size phenotypes were defined based on the combination of the presence/absence metabolic syndrome and categories of body mass index. The estimated risks and 95% confidence intervals (CIs) were extracted and pooled using a random-effects model. Results: A total of 7 studies, with 3596 cases and 142824 participants were included in the meta-analysis. The analysis revealed that individuals with metabolically healthy obesity were at increased risk for CKD compared with healthy normal-weight participants (OR =1.45; CI =1.26-1.64, fixed effects), but had lower risks than metabolically unhealthy obese (OR =2.04, 95%CI =1.40–2.68, random effects) individuals. In addition, normal-weight individuals with metabolically unhealthy status had almost similar risk for CKD as those with metabolically healthy obesity phenotype (OR =1.44, 95%CI =1.16–1.72, fixed effects). Conclusion: These findings suggest that persons with metabolic aberrations, however at normal-weight, have an increased risk for incident CKD. Healthy obese subjects had higher risk; refuting the notion that metabolically healthy obesity is a benign condition.

Keywords:
Obesity, chronic kidney disease, meta-analysis

O1133

personalized medicine in obstetric

Maryam Rahimi
Maryam Rahimi assistant professor : me616us@yahoo.com

Abstract:
Personalized medicine seeks to identify the right dose of the right drug for the right patient at the right time. Typically, individualization of therapy is based on the pharmacogenomic make-up of the individual and environmental factors that alter drug disposition and response. In addition to these factors, during pregnancy a woman's body undergoes many changes that can impact the therapeutic efficacy of medications. Yet, there is minimal research regarding personalized medicine in obstetrics. Adoption of pharmacogenetic testing into the obstetrical care is dependent on evidence of analytical validity, clinical validity, and clinical utility
. Here, briefly present information regarding the potential utility of personalized medicine for treating the obstetric patient for pain with narcotics, hypertension, and preterm labor and discuss the impediments of bringing personalized medicine to the obstetrical clinic.
Obstetrics is a discipline focused on the care of women during pregnancy, an inherently normal phase of life. Unlike other medical specialties, obstetric care providers oversee a natural process which has been successfully navigated by women for thousands of years, even before modern medicine. Over time, care for the patient with abnormal pregnancy or medical complications of pregnancy has been added to the spectrum of care provided by obstetricians. These conditions are often corrected through procedural interventions on the mother or fetus, or through medical management.
Beyond medications used for obstetric indications, pregnant women are also exposed to treatments for medical co-morbidities complicating pregnancy. The selection of a medication to treat a given pathology) rests on evidence of efficacy in the non-pregnant population, balanced against teratogenicity or correlation with poor obstetric outcomes. Historically, the FDA has maintained a pregnancy drug rating system to summarize the known information on risk of drug usage in pregnancy. This A-B-C-D-X letter rating has been misinterpreted by many clinicians and has led to the withholding of therapy due to the perceived risk of medications within specific classes3. As early as 1997, the FDA recommended changes in drug labeling to move towards a descriptive rating system to encourage clinicians to more carefully consider the evidence supporting the use of a drug in pregnancy4
Peripartum pain is commonly treated by narcotic pain relievers, such as codeine and hydrocodone. These prodrugs require biotransformation through CYP2D6 metabolism to their active moieties, morphine and hydromorphone, respectively. CYP2D6 activity is induced during pregnancy
In addition, more than 80 pharmacogenomic variants have been reported for CYP2D6 (many of which alter the activity of the enzyme (Approximately 7% of Caucasians have a variant that leads to a CYP2D6 poor metabolizer (PM) phenotype, which results in reduced enzyme activity. For instance, these individuals have reduced capacity to convert codeine to morphine and do not obtain adequate pain relief from codeine. Conversely, about 2–3% of Caucasians possess multiple copies of active CYP2D6 alleles, leading to an ultrarapid metabolism (UM) phenotype. In these individuals, codeine is rapidly converted to morphine, potentially leading to toxicity. While rare, cases of death in UM individuals treated with clinical doses of codeine have been reported. In some of these individuals, the presence of a variant that reduces the activity of UDP-Glucuronosyltransferase-2B7 (UGT2B7), the enzyme responsible for inactivation of morphine, may have also contributed to the toxic concentrations of morphine. After the report of an infant death associated with the CYP2D6 UM genotype of a breastfeeding mother taking codeine for post-Cesarean pain relief21, the U.S. FDA issued a Public Health Advisory cautioning women on the use of narcotic analgesics during breastfeeding22. Additionally, the Clinical Pharmacogenomics Implementation Consortium (CPIC) has issued guidelines on the use of codeine with respect to CYP2D6 genotype
. While hydrocodone and oxycodone undergo similar metabolic activation via CYP2D6, there are not adequate data regarding the consequences of PM or UM phenotype for use of these agents.

Keywords:
personalized medicine ,pharmacogenetic,narcotic,CYP2D6

O1136

The role of Twin Hearts Meditation Practice on fatigue in breast cancer patients

Pouran Varvani farahani[1] ، Samira Azghandi[2] ، Amir Hossein Khonsari[3]
1) School of Nursing and Midwifery, Arak University of Medical Science Sciences
2) Cancer Research Center, Shahid Beheshti University of Medical Science : s.azghandi@yahoo.com
3) Jalal All Ahmad, Tehran, IR. Iran.

Abstract:
Introduction: Due to the prevalence of fatigue in women with breast cancer during chemotherapy and its impact on the psychological state of patients and also the prevalence of depression, they encounter a reduction in life expectancy. Therefore, this study was aim to determine the effect of twin hearts meditation on fatigue in breast cancer patients undergoing chemotherapy.

Method: The current study was a clinical trial. All the women with breast cancer who referred to chemotherapy clinics of Shohadaye Tajrish hospital were recruited in this study using purposive sampling method and allocated into two groups randomly. Research Tools: demographic questionnaire and fatigue severity questionnaire were completed by patients before the intervention. Throughout the intervention, twin heart meditation was taught to the patients in the experimental group by the experimental fellow and they were asked to perform it at least 3 times a week for two weeks. After two weeks of intervention data was analyzed using SPSS version 20 and α=0.05 was considered.

Results: The two groups of experimental and control were similar in demographic data (P>0.05) and no significant difference was seen in the fatigue severity mean score.

However, there was a significant in the mean score of the two groups after the intervention (P<0.001). Fatigue severities mean score in the control group changed from (47.3) to (54.4). No significant difference was seen in the mean score before and after the intervention.

Conclusion: The twin hearts meditation exercise reduces the fatigue of breast cancer patients undergoing chemotherapy. Therefore, meditation is recommended as a complementary therapy beside medication in these patients.

Keywords:
Twin Hearts Meditation, Breast Cancer, Fatigue, Chemotherapy

O1137

The factor analysis of health related quality of life among women with polycystic ovary syndrome (PCOSQ-50)

Fatemeh Nasiri amiri[1] ، Fahimeh Ramezani Tehrani[2]
1) BABOL MEDICAL SCIENCES UNIVERSITY
2) Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences : ramezani@endocrine.ac.ir

Abstract:
Background: More studies indicate diminished health related quality of life (HRQoL) among women with polycystic ovary syndrome (PCOS) due to emotional, psycho-social, infertility, marital and hirsutism problems. The purpose of this study was to Exploratory and Confirmatory factor structure of HRQoL in women with PCOS (PCOSQ-50). In addition, internal consistency and test–retest analyses were used to assess the reliability of the instrument.

Patients and Methods: A cross-sectional study was conducted to assess the construct validity of the PCOSQ-50. First, the development of HRQoL in women with PCOS was designed based on qualitative research. The details of this phase have been previously published. After that by convenience sampling method 350 women with PCOS attending three clinics (gynecologic, endocrinology, and dermatology) at two teaching hospitals, affiliated to the Babol University of Medical Sciences, were selected. After explaining the objectives of the study, written informed consent was obtained from each participant and they were requested to complete the questionnaires. The Kaiser-Meyer Olkin test was used to assess the sampling adequacy, a cutoff point of 0.40 was considered as the minimum load factor required in maintaining each item of the factor being extracted. The Exploratory and Confirmatory Factor Analysis was done by SPSS software version 18 and LISLER software version 8.8 respectively.

Results: The principal component analysis indicated a six -factor structure for the questionnaire (psychosocial and emotional, self-body image, fertility, sexual function, obesity and menstrual disorder and hirsutism) that jointly accounted for 50.83 % of variances observed. Reliability of questionnaire with Cronbach's alpha coefficient for six factor showed that the range between 0.87 -0.95 and for whole questionnaire 0.92. The 43-item model was supported by the confirmatory factory analysis. Compared to the 50-item model, the 43-item model showed a marked improvement on several incremental fit indices and achieved a more parsimonious model fit. The fit indexes were as follows: RMSEA = 0.09, NFI = 0.90, CFI = 0.91, IFI = 0.91, GFI = 0.60 and SRMR = 0.09.

Conclusion: The 43-item PCOSQ is psychometrically superior to the original. However, its predictive efficacy needs to be examined in longitudinal studies.

Keywords:
Polycystic ovary syndrome; Quality of life; Factor analysis; Reliability

O1139

Genotype-phenotype correlation and risk assessment in patients with diagnosis Brugada Syndrome

Siamak Saber[1] ، Amir-farjam Fazelifar[2] ، Majid Haghjoo[2] ، Abolfath Alizadeh[2] ، Zahra Emkanjoo[2] ،
Seyed Mohammad Dalili[2] ، Mahmoud Eftekharzadeh[3] ، Alireza Heidari Bakavoli[4] ،
Seyed Massoud Houshmand[5] ، Elena V Zaklyazminskaya[6]

1) Research center of Electrophysiology & pacemaker, Rajaie Cardiovascular Medical Hospital
2) Cardiac Electrophysiology Research Center, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran.
3) Tehran Arrhythmia Clinic, Tehran, Iran.
4) Cardiovascular Research Center, Ghaem Hospital Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
5) National institute of genetic Engineering and Biotechnology
6) Head of Genetic Lab,6. Petrovsky Russian Research Center of Surgery, RAMS, Moscow, Russia zhelene@mail.ru

Abstract:

Introduction:

Brugada syndrome (BrS) is an autosomal dominant inherited channelopathies characterized by ST-segment elevation in V1-V2 leads followed by negative T-wave on standard ECG, and high risk of sudden cardiac death (SCD). The disease was considered of the high frequency in Southeast Asia, but current estimation of BrS is at least 1:10000 in all ethnic groups. Approximately 15-30% of individuals with BrS cases are affected by loss of function mutations in SCN5A gene (more than 370 mutations).

In this study, we study genotype-phenotype correlation and risk stratification in our group of patients.

Materials and methods:

The present study was performed in accordance with the Helsinki Declaration and local ethics committee. Written informed consent for clinical and genetic evaluation was obtained from each member.

The clinical follow-up included a review of personal and familial history, complete physical examination, 12-lead ECG, 24-hour Holter ECG monitoring, echocardiography, and sodium channel blocker challenge test. Genetic analyzing of SCN5A gene was performed.

Results:

Age of first detection of Brugada syndrome is 37±13 years old, male/female ratio is 8:1.

In our group, the most common symptoms have been a history of SCD cases in the family (56%), syncope (51%). Brugada Pattern type 1 detected in 44% of our group, in superficial 12-leads ECG. Ventricular tachycardia was detected in 32% of patients.

We had found 17 mutations in SCN5A gene in 17 unrelated probands (21%). 11 of 17 mutations (65%) are reported as first time. Functional study was performed for all new mutations by In-Silico and cellular electrophysiological study was done for one of them.

All mutations were found in Male gender. Regards to our SCN5A gene analysis, around 50% of mutations are missense and in half of them had recorded not any history of life-treating symptoms.

Conclusion:

Correlation between Syncope and positive familial history of SCD under 45 years old in BrS patients and SCN5A mutations were found ($P<0.01$).

ECG study in our group was shown strongly correlation between SCN5A gene mutations and prolonged PR interval (PR>200msec). Regards to at least 3 years follow up, Prognosis in BrS patients who carrier of haploinsufficiency mutations in SCN5A gene are poor compare with missense mutations ($p<0.05$). ICD implantation is recommended in patient with mutation in SCN5A gene.

It seems, our data on the role of SCN5A gene study help us not only to BrS diagnostics but also in prognosis for patients

Keywords:
SCN5A gene ,Brugada syndrome, Sudden Cardiac Death

O1147

Messenger RNA expression analysis panel in urinary sediment cells in diabetic patients in order to predict the individualized risk of diabetic nephropathy in each patient

Mahdieh Salimi

Department of Medical Genetics, Institute of Medical Biotechnology, National Institute of Genetic Engineering and Biotechnology (NIGEB) : shaghayeghit@yahoo.com

Abstract:

BACKGROUND: The initiation and progression of diabetic nephropathy (DN) is complex. Quantification of mRNA expression in urinary sediment has emerged as a novel strategy for studying renal diseases. Considering the numerous molecules involved in DN development, the mRNA expression of a panel comprised of 7 genes (MCP-1, KIM1, MDM2, MST1, BMP7, SWV and IRS2) were analysed in urinary sediment cells of diabetic, diabetic nephropathy patients in early stage of the disease and normal control groups using Real- Time RT PCR. Methods: To quantify the mRNA expression of 7 genes panel in 150 individual comprised of diabetic, diabetic nephropathy patients in early stage of the disease and normal control groups, the Urinary cell pellet was collected from each study participant and after RNA extraction and cDNA synthesis the Real-Time RT-PCR was used. Results: Our data showed that the expression of MCP-1 , KIM1, SWV and IRS2 genes were significantly increased in diabetic nephropathy patients even at very early stages of the disease ($p \leq 0.001$). The expression of MDM2 and BMP7 were decreased in urinary sediment cells of DN compared with diabetes and control groups ($p \leq 0.001$) where as the expression of MST1 gene expression showed no significant difference in DN patients compared other groups ($p< 0.05$). Conclusion: In patients with diabetic nephropathy, urinary mRNA expression of MCP-1, KIM1, SWV and IRS2 genes correlated with baseline renal function. Our result suggests that serial measurement of urinary expression of these genes may have a value for the predict the personalized diabetic nephropathy risk or very early detection of renal injury in diabetic patients.

Keywords:
diabetic nephropathy, biomarker, early detection, risk assessment, urinary sediment cell

O1156

Cut-off Point Selection for Biomarkers from a Personalized Medicine Perspective: A Practical Approach

Farideh Bagherzadeh-khiabani[1] ، Davood Khalili[2]

1) Prevention of Metabolic Disorders Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2) Department of Biostatistics and Epidemiology, Research Institute for Endocrine Science, Shahid Beheshti University of Medical Sciences, Tehran, Iran : dkhalili@endocrine.ac.ir

Abstract:

Objectives: Despite its drawbacks, converting continuous biomarkers into either “positive” or “negative” is common in medicine; the reason is that a physician usually needs to choose between two options i.e. to classify someone as healthy or unhealthy. According to personalized medicine, to allow for incorporating preferences into decision-making, cut-points should be selected based on individualized costs and benefits of treatment/decision i.e. based on a cost jointly agreed upon by physician and/or patient. Traditional measures such as Youden`s Index fail to do dichotomization at the patient level and modern ones such as net-benefit-fraction are not comprehensible to physicians. We went deep into these measures to help select individualized cut-points.
Study Design and Setting: Dichotomization methods were outlined focusing on cost-sensitive measures including Misclassification-cost-term (MCT), generalized-Youden (GY), and net-benefit-fraction (NBF) and their consistency in selecting the optimal cut-off point was proved mathematically. Convertible terms representing preferences such as cost, harm-to-benefit ratio and threshold probability for treatment were clarified. In an experiment, sex-specific cut-points were identified to dichotomize fasting blood sugar (FBS) for pre-diabetes definition in a cohort of 1212 men and 1758 women, aged 20-60 years with 12-year follow-up.
Results: The area under the curve (AUC) as a measure to show the discrimination power of FBS for incidence of Type-2 diabetes was 0.77 (95% CI: 0.73-0.81) and 0.79 (95% CI: 0.76-0.82) for males and females, respectively. The Youden`s index resulted in the cut-off points of 94 for males and 95 for females. As a practice, the two threshold probabilities of %10 and %20 for developing diabetes resulted in FBS cutoffs of 89 and 95 respectively in females. For males, cutoff selection resulted in 94 at both probabilities. These cut-offs could be helpful to decide for prevention strategies regarding physician/patient`s preferences.
Conclusion: The probability threshold for treatment is suggested as a tangible cost index for patients/physicians and Net Benefit Fraction as an understandable and practical tool for cut-off selection. The probability threshold for treatment is an understandable index which is defined as the specific probability of disease at which the clinician prefers to make intervention (i.e. treatment or diagnostic test) for each individual patient. It could easily be specified by formal methods (such as clinical trials, clinical decision analysis) or subjective estimate (the domain expert and/or the patient opt for). The NBF is an understandable unitless measure which is defined as the fraction of the incidence rate that could be predicted and prevented appropriately regarding harm-to-benefit of treatment.

Keywords:
Marker; Dichotomization; Cut-off; Harm; Benefit; Decision Making

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P1024

Assosiation between VKORC1 Gene Polymorphisms and patient characteristics with Warfarin Dose Requirement in Kerman City, South East of Iran.

Naghmeh Satarzadeh[1] ، Mohammad Javad Soltani Banavandi[2]

1) Dep of Microbiology, Kerman Branch, islamic Azad University, Kerman, Iran. : naghmeh.satarzadeh@gmail.com
2) Dep of Microbiology, Kerman Branch, islamic Azad University, Kerman, Iran.

Abstract:

Background:Warfarin is commonly used as an oral therapeutic anticoagulant in patients either with atrial fibrillation, heart valves implants or a confirmed episode of thrombosis or thromboembolism .Variation in dose requirements is different for everyone, and genetic factors are effect on Dose variation.polymorphism of VKORC1 gene is identified as the maingenetic factors involved in warfarin dosage requirement variations.

Objectives: this study aims to determine the frequency of vkorc1 polymorphism in patients using warfarin from kerman city and investigated assosiation between vkorc1 gene polymorphism with Warfarin Dose Requirement.

Materials and methods: A total of 112 patients taking warfarin with stable dose requirements enrolled in the study. DNA samples from these patients were genotyped for VKORC1 Gene Polymorphism by using the polymerase chain reaction restriction fragment length polymorphism method (PCR-RFLP) and Examined associations between demographic characteristics(e.g. sex ,age , smoking,…) , maintenance dose of warfarin and genetic factors.

Results: the most common genotype was VKORC1GA (48.2%). genotype frequency subjects carried VKORC1 AA and GG were 12.5% and 39.3% respectively. In addition, a significant relationship was found between VKORC1(–1639G>A) and Daily dose of warfarin.

Conclusion:The frequencies of the VKORC1 –1639 A alleles were significantly lower than VKORC1 –1639 G alleles and required fewer warfarin dose. Age have found a significant effect on warfarin dosing.

Keywords:
warfarin, VKORC1, polymorphism

P1005

Designing and Developing Avicennapp Mobile Health Application: A Stride toward Prevention and Management of Diabetes and Cardiovascular Diseases in Iran

Ali Amidi[1] ، mahin nomali[2] ، mohammadreza hemmati[3]
1) CEO of Avicennapp company : ali@avicennapp.com
2) University of tehran
3) CTO of Avicennapp company

Abstract:

Introduction: Cardiovascular diseases (CVDs) and diabetes with increasing prevalence and high mortality rate imply high economic burden on health care systems and patients. According to the importance of prevention, early detection and management of these disease, availability of a mobile phone for majority of population and tendency to self-monitoring of health status by mobile health applications, the aim was to design and develop of Avicennapp mobile health application.
Materials and Methods: The engineering team from Tehran University (TU) designed the research and development session of this application. The medical content prepared and approved by medical team from Tehran University of Medical Sciences (TUMS) and converted to codes to be entered in the application.
Results: This application consists of different sections. They include guidance for using the application and its measurement devices for blood pressure, blood glucose and cholesterol, personal profile, CVDs and diabetes risk calculators and providing smart recommendations based on the level of risk, smart reminders, the self- care status determinant and providing recommendations based on the self- care scores, calling emergency medical services and health care team in emergency situation.
Conclusions: Designing and developing the mobile health application in prevention and management of CVDs and diabetes in Iran by multidisciplinary team can be a stride toward health care improvement in our country.

Keywords:
Mobile application, Prevention, Disease management, Diabetes, Cardiovascular disease.

P1006

Nanotechnology Applications in Personalized Medicine

Alina Abdolahi[1] ، Shima Rahmati[2]
1) Student Research Committee, Kurdistan University of Medical Sciences, Sanandaj, Iran. : alina.abdolahi@yahoo.com
2) Student Research Committee, Kurdistan University of Medical Sciences, Sanandaj, Iran

Abstract:

Introduction and Objectives: Due to the limitations of standard diagnostic and therapeutic strategies, the disease treatment is moving towards tailored treatment for individual patients, considering the inter-individual variability in therapeutic response. Personalized medicine, medical treatments are tailored to the specific characteristics of individual patients because No single therapeutic agent is recognized to produce the same effect in different patients with a single type of disease. Nanotechnology-based tools and techniques are rapidly emerging in the fields of medical imaging and targeted drug delivery. Employing constructs such as dendrimers,
liposomes, nanoshells, nanotubes, emulsions and quantum dots, these advances lead toward the concept of personalized medicine and the potential for very early, even presymptomatic, diagnoses coupled with highly-effective targeted therapy.
Materials and Methods: The retrieved studies were searched through the PubMed (MEDLINE), Google Scholar, Scopus, databases. Different studies have been demonstrated that Some applications of nanotechnology in medicine including: Nanodiagnostics (Molecular diagnostics Imaging with nanoparticle contrast materials), Nanobiosensors, Nanopharmaceuticals (Nanotechnology-based drugs, Targeted drug delivery to site of action, Drug delivery from implanted nanopumps and nanocoated stents), Reconstructive surgery (Tissue engineering with nanobiotechnology scaffolds, Implantation of rejection-resistant artificial tissues and organs), Nanorobotics (Vascular surgery by nanorobots introduced into the vascular System, Remote controlled nanorobots for detection and destruction of cancer, Nanosurgery (Nanosensors implanted in catheters to provide real-time data during surgery, Nanolaser surgery.
Results and Conclusions: Applications of nanobiotechnology are beginning to show an impact on the practice of conventional medicine. Nanotechnology will enable design and delivery of more effective drugs with targeted delivery increasing efficacy and reducing toxicity.

Keywords:
Nanotechnology, Personalized medicine, Nanodiagnostics, Nanobiosensors

P1007

Personalized medicine in cancer targeted therapy

Shima Rahmati[1] ، Alina abdolahi[2]
1) Student Research Committee, Kurdistan University of Medical Sciences, Sanandaj, Iran. : rahmati_may66@yahoo.com
2) . Student Research Committee, Kurdistan University of Medical Sciences, Sanandaj, Iran

Abstract:

Introduction and Objective: 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. Molecular characterization of tumour cells enables refinement of classifications for many cancers and can sometimes guide treatment.
Materials and Methods: The retrieved studies were searched through the PubMed (MEDLINE), Google Scholar, Scopus, databases. Different studies have been demonstrated that the application of novel compounds in clinical trials has revealed promising results. Furthermore expanded knowledge of the molecular basis of cancer has shown that significant differences in gene sequence and expression patterns can guide therapy for a variety of solid tumors such as breast cancer (HER2 overexpression test, approved drug is Herceptin), colorectal cancer (KRAS and BRAF testing, Panitumumab; Cetuximab), lung cancer (EGFR amplification testing, Gefitinib, Erlotinib) and CML- chronic myeloid leukaemia (BCR-ABL Mutation Analysis Test, Imatinib).
Result and Conclusion: Profiling and identifying the complete landscape of genomic changes in individual cancers would be invaluable not only for understanding the basic mechanisms of cancer development and progression, but also in developing personalized cancer treatments. Therapies over the past decade, use of more-specific therapies that are targeted to each tumour

Keywords:
personalized medicine, cancer, Targeted therapy

P1008

association of single nucleotide polymorphism rs76121131[C>t] in CD44 related with hsa-miR-3929and Gastric cancer

Samaneh Samani1 ، Mansoureh Azadeh[2] ، Pardis Saadatmand[3] ، Kamran Ghaedi[4] ، Mohammad Hosein Sanati[5]
1) Division of cellular and Molecular biology,Department of biology, Nour danesh institute of higher education ,Meymeh,Iran
2) Department of Biochemistry, Faculty of Basic Science, Najafabad Branch, Islamic Azad University, Najafabad, Isfahan, Iran
3) Zist fanavary Novin, Biotechnology Institute, Isfahan, Iran
4) Division of Cellular and Molecular Biology, Department of Biology, Faculty of Sciences, University of Isfahan, Isfahan, Iran kamranghaedi@yahoo.com
5) National Institute of Genetic Engineering and Biotechnology, Tehran, Iran

Abstract:

Nowadays, treatment can be done with genetic variation. SNPs are the most important biomarkers for personalized medicine.MicroRNAs (miRNAs) participate in diverse biological pathways and may act as oncomir or tumor suppressors, so they could be used as a prognostic biomarker. The aim of our study is to expand current knowledge about molecular function of hsa-miR-3929 and its relatede SNP in gastric cancer cells by using bioinformatics tools.Validated and predicted targets of hsa-miR-3929 were obtained from miRbase and miRwalk databases respectively. miRBase and DAVID databases were used for further analysis. miRNASNP database predicts single nucleotide polymorphism in 3’UTR of a gene (CD44) related to hsa- miR-3929.It is predicted that hsa-miR-3929acts as a critical tumor suppressor micro RNA by inhibiting some important genes in sustained angiogenesis pathway.
Our data manifested KEGG signaling pathways “pathway in cancer” as the most statistical relevant pathways with hsa-miR3929 targetome.According to our data, hsa- miR-3929 and its related SNP may be involved in gastriccancer prognosis by altering regulation of angiogenesis and some vital signaling pathways mRNAs.
To sum up, C allele in this location can have prognostic value for angiogenesis and metastasis phenotypes in patients with gastric carcinoma.

Keywords:
gastric cancer, hsa-miR-3929, SNP,KEGG

P1009

A bioinformatic method for sorting variants in the region of genome

Vahid Akbari[1] ، Mohammad Taghi Akbari[2] ، Marziyeh Kallhor[3]
1) student
2) Associate Professor mtakbari@Modares.ac.ir
3) MSc student

Abstract:
Next-generation sequencing technologies made a revolution in genome sequencing and our understanding about genome architecture. Comprehensive survey of genetic variants and their relationship with disease could be possible by these technologies. Deciphering of genome sequences is essential for the mapping of genetic diseases and risk evaluation. Numerous computational algorithms for identifying and characterizing variants have been developed, but most of them are neither integrated nor interoperable and considering of research purposes we have to use different methods and algorithms. In the past for few years human genome structural variation discoveries has enjoyed increased attention from the genomics research community.
One of the things that significant for determination of relevance between variants and disease is to find and sort variants in a particular region of the genome. Numerous algorithm and software developed for this purpose, but working with these tools requires high skill or proficiency in programming, such as R program. In this paper we want to introduce an easy way without need in programming for this purpose. In this way we use GALAXY a web-based program for sorting variants, we import our target sequences into GALAXY from UCSC or other similar databases.

Keywords:
Next-generation sequencing, Variant, Algorithm, Galaxy

P1012

Personalized medicine in cancer targeted therapy based on Gold Nanoparticles

Hanife Shariatifar
Kurdistan University of Medical Sciences : hanife1365@yahoo.com

Abstract:
Cancer is a major health problem worldwide as the second leading cause of death. Each year, over 10 million new cases and over 5 million deaths from the disease are reported, so it is essential to develop new technologies for accurate early detection and treatment of cancer. Site-specific drug delivery is an important area of research that is anticipated to increase the efficacy of the drug and reduce potential side effects. This manuscript focuses on the work done in the last several years developing gold nanoparticles as cancer therapeutics and diagnostic agents.

Keywords:
Personalized Medicine, Cancer therapy, Gold Nanoparticle, Drug delivery

P1011

From whole exome sequencing to functional study: A bioinformatic framework

Vahid Akbari[1] ، Marziyeh Kallhor[2] ، Mohammad Taghi Akbari[3]
1) student
2) MSc student
3) Associate Professor mtakbari@Modares.ac.ir

Abstract:
Genome-wide association (GWA) studies suggest that common genetic variants explain only a modest fraction of heritable risk for common diseases, raising the question of whether rare variants account for a significant fraction of unexplained heritability. Although the proportion of structural variants and small insertions and deletions (indels;
When we perform WES for specific disease such as breast cancer it is possible that we found numerous variants in various genes, but if we want to figure out which of these variants actually associated with our interest disease, requires intricate bioinformatic works. First of all you have to filter your variants ,Respectively, based upon these items: allele frequencies, data mining, various software that predict effect of variant on protein (e.g. Polyphen, SIFT), Prioritize genes using bioinformatics tools (e.g. ToppGene, GPSy) , also by using bioinformatics tools such as i-tasser we can anticipate structure of protein product of interest gene and compare it with normal protein; when you filter your data and find those variants and genes which more likely associated with disease then you should perform functional study to proof this association. In this paper we want to introduce best practical software and databases for this framework and show you how to choose best case between founded variants and genes for functional study; we also illustrate how to choose The most appropriate vector and cell line for functional analysis moreover best software for in-silico cloning before any in-vivo analysis.

Keywords:
WES, variants, disease, bioinformatic, functional analysis

P1013

Study of association between hsa-miR-940 targetom signaling pathways it is related SNP(rs3859431)functionally with the incident of LHON

Samaneh Samani[1] ، Pardis Saadatmand[2] ، Negin Hoghoughi[2] ، Mansoureh Azadeh[3]

1) Division of cellular and Molecular biology,Department of biology, Nour danesh institute of higher education ,Meymeh,Iran s_samani43@yahoo.com
2) Zist fanavary Novin, Biotechnology Institute, Isfahan, Iran
3) Department of Biochemistry, Faculty of Basic Science, Najafabad Branch, Islamic Azad University, Najafabad, Isfahan, Iran

Abstract:
LHON is one of the usual disorder, optic neuropathy that makes a loss of central vision and always is associated with mitochondrial point mutation. the first cells lost are Retinal ganglion and they are so sensitive to incomplete ATP and oxidation. the genetic of LHON is connected to Mt genetic.Genetic in this case is one of the important reasons, more than the environment. In LHON often lost vision is part of clinical appearance and the patients suffer from Neurological disorder. the Men are more exposed. Abnormal function of Mt is dependent on Energetic disorder, that it can spoil nerves pathway and Retinal cells.Nowadays, treatment can be done with genetic variation. SNPs are the most important biomarkers for personalized medicine.MicroRNAs (miRNAs) participate in diverse biological pathways and may act as oncomir or tumor suppressors,and Operating regulation so they could be used as a prognostic biomarker. The aim of our study is to expand current knowledge about molecular function of hsa-miR-940and its relatede SNP in LHON by using bioinformatics tools.Validated and predicted targets of hsa-miR-940were obtained from miRbase and miRwalk databases respectively. miRBase and DAVID databases were used for further analysis. miRNASNP database predicts single nucleotide polymorphism in 3UTR of a gene (CRX) related to hsa- miR-940. Our data manifested KEGG and DAVID signaling pathways Acxon Guideance Pathway1 2and Prion Diseaseas , Glioma3 4the most statistical relevant pathways with hsa-miR940 targetome. To sum up, the genotyping of the C allele in this location(23808) in the CRX gene can have prognostic of LHON.

Keywords:
LHON, hsa-miR-940,KEGG,DAVID,miRbase,miRNASNP

P1015

Identification of B and T cell epitope based peptide vaccine from IGF-1 receptor in breast cancer

Manijeh Mahdavi[1] ، Majid Kheirollahi[2] ، Violaine Moreau[3] ، Mehrnaz Keyhanfar[4] ، Roya Kelishadi[5]

1) Applied Physiology Research Center, Cardiovascular research institute, Isfahan University of Medical Sciences, Isfahan, Iran gmahdavi2002@yahoo.com
2) Department of Genetics and Molecular Biology, School of Medicine, Pediatric Inherited Diseases Research Center, Research Institute for Primordial Prevention of Non-communicable disease, Isfahan University of Medical Sciences, Isfahan, Iran.
3) CNRS UMR5048– UM- INSERM U1054, Centre de Biochimie Structurale, 29, rue de Navacelles, 34090 Montpellier Cedex, France.
4) Isfahan university. Biotechnology department. Isfahan. Iran
5) Department of pediatrics, child growth and development research center, Research Institute for Primordial Prevention of Non-communicable Disease, Isfahan University of Medical Sciences, Isfahan, Iran.

Abstract:
The insulin-like growth factor-1 receptor (IGF-1R) plays a key role in proliferation, growth, differentiation, and development of several human malignancies including breast and pancreatic adenocarcinoma. IGF-1R targeted immunotherapeutic approaches are particularly attractive, as they may potentially elicit even stronger antitumor responses than traditional targeted approaches. Cancer peptide vaccines can produce immunologic responses against cancer cells by triggering helper T cell (Th) or cytotoxic T cells (CTL) in association with Major Histocompatibility Complex (MHC) class I or II molecules on the cell surface of antigen presenting cells. In our previous study, we set a technique based on molecular docking in order to find the best MHC class I and II binder peptides using GOLD. In the present work, molecular docking analysis on a library consisting of 30 discontinuous peptides from IGF-1R identified peptides 249 and 86, as the best MHC binder peptides to both MHC class I and II molecules used in the study. The most often targeted receptors for the peptide 249 were HLA-DR4, HLA-DR3 and HLA-DR2 and also for peptide 86, were HLA-DR4, HLA-DP2 and HLA-DR3. These findings, based on bioinformatics analyses, can be conducted in further experimental analyses in cancer therapy and vaccine design.

Keywords:
Docking, MHC, Bioinformatics, Peptide vaccine, IGF-1 receptor

P1016

Analysis of the CYP3A4 gene variant (rs2740574) in an Iranian Population: Pilot base study

Arezu Karimpur zahmatkesh[1] ، Abolfazl Movafagh[2]
1) 1Shahid Dr Beheshti Medical Sciences University, Faculty of medicine, Medical Genetics Department : a.karimpur.z@gmail.com
2) Shahid Dr Beheshti Medical Sciences University, Faculty of medicine, Medical Genetics Department

Abstract:
Various studies revealed that, CYP3A4*1B, as a variant allele of CYP3A4 gene, has variations in populations with different ethnic background. In this pilot research work, we studied 183 healthy non consanguinity men of an Iranian origin for this genetic variation. We applied RFLP-PCR technique for this research study. In contrast with other researches, in Asian country (such as China and Japan with 0% allele frequency) our study showed that frequency of this allele in Iranian men among an Asian continent is 3%. This finding is an important attempt in pharmacogenetics research endeavor.

Keywords:
CYP450, CYP3A4, CYP3A4*1B, genetic variant /

P1079

applications of nanotechnology to solve challenges of cardiac tissue engineering

Narges Esmaeilzadeh[1] ، Ehteram Hosseinzadeh[1]
1) Department of Medical Nanotechnology, Faculty of Advanced Technologies in Medicine, Iran University of Medical Sciences, Tehran, Iran : n.esmailzadeh90@yahoo.com

Abstract:
Cardiovascular diseases are the highest cause of mortality in the world. Cardiomyocytes (cardiac muscle cells) have limited proliferation, therefore repair of the damaged tissue will not occurred and necrosis or fibrosis tissue will be replaced. Myocardial mass loss and lack of contractility are precursors to heart failure. Nowadays, medication, surgery and heart transplantation are methods that used for treatment of these diseases.

Tissue engineering is an interdisciplinary field that help to treat medical problems such as tissue loss or severe organ failure. Despite all the progress made in this field over the last few years, there is still some limitations such as delivering nutrients to cells, defects in cellular function and immune response to engineered scaffolds. These limitations are greatly affected by nanotechnology.

Nanotechnology is the development of new systems that mimic natural tissue complex structure and boost cellular signal, attachment, cell growth and differentiation. nanotechnology in cardiac tissue engineering help to precise control over the engineered constructions and enhance the mechanical and electrical properties of the cardiac patches. Scaffolds with Gold nanoparticles promote massive cardiac sarcomeric actinin expression, significantly higher contraction amplitudes and rates.

Keywords:
cardiac tissue engineering- nanotechnology- nano particle- cardiomyocyte

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P1088

Multiplex PCR optimization for coamplification of int-2 and y-IFN genes

Atefeh Arbabi barzoki[1] ، zohreh zahraie[2]
1) Cell and Molecular Biology Department, Faculty of Chemistry, University of Kashan, Kashan, IRAN : a.kashanuni94@gmail.com
2) Cell and Molecular Biology Department, Faculty of Chemistry, University of Kashan, Kashan, IRAN

Abstract:
Multiplex PCR optimization for coamplification of int-2 and -IFN genes Atefeh Arbabi, Zohreh Zahraei Cell and Molecular Biology Department, Faculty of Chemistry, University of Kashan, Kashan, IRAN Fibroblast growth factor 3 (FGF3), is encoded by the int-2 gene which is involved in cellular functions such as: proliferation, angiogenesis and metastasis. This gene is amplified in some cancer patients and may be associated with advanced tumor progression. In this study, for evaluation the amplification of int-2 gene in patient's blood samples, Multiplex PCR (Polymerase Chain Reaction) technique was used. After extracting genomic DNA from human blood by salting out procedure, amplification of int-2 gene was determined by optimizing coamplification of single-copy gene, -IFN and the target gene (int-2) in PCR reaction. The 25 µl reaction mixture contained 10mM Mgcl2, 0.2 mM dNTP, 0.7 µM of primer int-2, 0.5 µM of primer -IFN and 100 ng of genomic DNA in the presence of 2 U of Taq DNA polymerase. Further optimization of PCR conditions were achieved, when the melting point of the primers set the upper limit on annealing temperature (Touchdown PCR). For the first phase (5 cycles), the annealing temperature was reduced 10C per cycle, so that at the second phase (25 cycles) the annealing temperature was adjusted at 580C.

Keywords: Multiplex PCR, Optimization, int-2 gene

P1090

applications of nanotechnology to solve challenges of neural tissue engineering

Ehteram Hosseinzadeh[1] ، Narges Esmaeilzadeh[3]
1) Department of Medical Nanotechnology, Faculty of Advanced Technologies in Medicine, Iran University of Medical Sciences, Tehran, Iran : Ehteramhosseinzadeh92@gmail.com

Abstract:
According to the anatomical and physiological structure of the nervous system, regeneration and repair of the nervous system is complex. Extensive studies in this field such as stem cell therapies and tissue engineering, nerve regeneration has provided new methods. Recent advancements in nerve regeneration have involved the application of tissue engineering principles and this has evolved a new perspective to neural therapy. Tissue engineering involves seeding of cells on bio-mimicked scaffolds providing adhesive surfaces. However researchers though face a range of problems in generating tissue which can be circumvented by employing nanotechnology. Nanotechnology provides substrates for cell adhesion and proliferation and agents for cell growth and can be used to create nanostructures and nanoparticles to aid the engineering of different types of tissue. Gold NPs (AuNPs) are of particular interest due to their excellent stability and various biocompatibility properties, including nontoxicity, non-immunogenicity, and high tissue permeability without hampering cell functionality. (AuNPs) can be incorporated into macro porous scaffolds or other bioengineering materials to increase the conductivity and enhance the electrical signal transfer between neural cell.

Keywords: neural tissue engineering- nanotechnology- nano particle

P1017

Circulating Tumor Cells (CTCs) count and personalized management of breast cancer: A systematic review

Fatemeh Khatami[1] ، Ramin Heshmat[2] ، Hamid Reza Aghayan[2] ، Maryam Sanaei[2] ، Negar Sarhangi[3] ، Bagher Larijani[3] ، Seyed Mohammad Tavangar[4]

1) Chronic Disease Research Center, Endocrinology and Metabolism Population Science Institute, Tehran University of Medical Sciences, Tehran, IRAN : fatemehkhatami1978@gmail.com
2) Chronic Disease Research Center, Endocrinology and Metabolism Population Science Institute, Tehran University of Medical Sciences, Tehran, IRAN
3) Endocrinology & Metabolism Research Center, Tehran University of Medical Sciences , IRAN
4) Department of Pathology, Doctor Shariati Hospital, Tehran University of Medical Sciences, IRAN

Abstract:
Objectives:
Circulating tumor cells (CTCs) detection and characterization in the peripheral blood of breast cancer patients has proven practical and predictive value in different studies. However, the clinical significance of CTCs enumeration in personalization of breast cancer diagnosis and treatment remains under the debate.
Methods:
A literature search in PubMed, Web of Science and Scopus was performed from October 1990 to June 2016 for studies which evaluating CTCs and its association with clinical and pathological characteristics and medical outcome in the field of breast cancer personalization for both diagnosis and treatment categories. The treatment outcomes were progression-free survival (PFS) and overall survival (OS) or relapse in different patients.
Results:
Sixty nine studies met the inclusion criteria. The sample size varies from 1 to 2026. Median follow-up was 15 months (range 3-27). Different molecular techniques have been applied for research but theymostly are based on CTCs enrichment and then detection by using FDA-approved Cell SearchTM. By far the most studies define CTCs as cytokeratins (CK) positive and CD45 negative cells. Despite the differences in methodology, twenty eight studies for breast cancer diagnosis and prognosis were mainly focusedon CTCs isolation and enumeration.
Conclusions:
In the way of precision treatment, detection of CTCs before initiation of first-line therapy or during therapy in patients with breast cancer is highly valuable but in the way of precision medicine it should be supported with some molecular characteristics of CTCs like CTCs phenotypic changes, gene expression analysis of CTCs and molecular characteristics of CTCs
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Keywords:
Circulating Tumor Cells, CTCs, Breast Cancer, Personalized Medicine

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P1020

Effect of Hydroalcholic extract of saffron on cysts of Giardia lamblia in Invitro

Ali Pouryousef
MSc in Parasitology, Faculty Member at Torbat Heydariyeh University of Medical Sciences,Torbat Heydariyeh Iran apouryousef67@gmial.com

Abstract:
Aims: Giardia lamblia is one the most important of intestinal flagellate protozoan which in terms of medical parasitology and public health is important in our country and many countries. Considering the importance of Treatment of infection in patients, particularly with the use of medicinal plants and the presence of parasite resistance to chemical drugs, this study was performed to evaluate the effects of saffron extract on Giardia lamblia cyst in vitro.
Materials & methods: In this experimental study hydroalcholic extracts of saffron in 1, 10, 50 and 100 mg⁄ml concentrations and times 1,2,30,60,180 and 1440 minutes, and cysts of Giardia isolated from stools of patient by sucrose solution 0.85M. Then, hydroalcholic extract after diluting affected on Giardia cysts. Data were analyzed by SPSS version 20.
Findings: Results of this study indicated that concentration of 50 and 100 mg⁄ml of hydroalcholic extracted of saffron after 3 and 24 hours has the most killing and cytotoxicity activity on G. lamblia cysts in vitro.
Conclusion: According to our results, the concentration of 100mg⁄ml of saffron after 24 hour has the highest cytotoxicity effect relatively on G. lamblia cysts. Therefore, the in vivo study on saffron in animal models is recommended.
Keywords: Giardia lambelia, Crocus sativus, hydroalcholic extract, invitro

P1196

Investigation of the mitochondrial haplogroups in a selective population of Isfahan province

Dr Elham Iranpour [1] ، Massoud Houshmand[2]
1) mobarakeh :
2) Supervisor : housh62@yahoo.com

Abstract:
In order to investigate the mitochondrial haplogroups in a selective population of Isfahan province, 96 unrelated men in Isfahan province with at least two generations in this province were token blood. Then DNA was extracted and quality assessed. 25 coding SNPs defining the major haplogroups that occur in Africa, Western Eurasia and Eastern Eurasia were selected and combined into two multiplex genotyping assays. Each one consisting of a PCR step and a SNaPShot step. Then for support of our detective haplogroups by SNaPShot system, D-Loop region was sequenced in some samples. : In this province Western Eurasian haplogroups were predominant. Haplogroup U and H (23%, 22%) and then T, J and U8b (11%, 10% and 7%) had the most frequency. Eastern Eurasian haplogroups were present at a lower frequency of 5% (C, D, R9, M and N).

Keywords: mtDNA, SNP, Haplogroup, Isfahan province

P1021

Circulating Tumor BRAF Mutation and Personalized Thyroid Cancer Treatment

Fatemeh Khatami[1] ، Ramin Heshmat[2] ، Seyed Mohammad Tavangar[3] ، Bagher Larijani[4]

1) Chronic Disease Research Center, Endocrinology and Metabolism Population Science Institute, Tehran University of Medical Sciences, Tehran, IRAN : fatemehkhatami1978@gmail.com
2) Chronic Disease Research Center, Endocrinology and Metabolism Population Science Institute, Tehran University of Medical Sciences, Tehran, IRAN
3) Department of Pathology, Doctor Shariati Hospital, Tehran University of Medical Sciences, Iran
4) Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences , Iran

Abstract:
Common medical treatments have some difficulties for cancer therapy in a desire way because of resistance to current therapeutics. Personalized cancer therapy aims to understand the unique properties and dynamics of each patient's cancer in order to provide the most rational and appropriate therapy. It is still under the debate that circulating tumor markers will take the place of standard tissue biopsy or will support it to guide us to the more effective interventions?
According to American Cancer Society 62,450 people diagnosed with thyroid cancer in 2015 and 1950 deaths will result from the disease. In spite of good prognosis of differentiated thyroid carcinoma (DTC), about five to ten percent of patients will develop metastasis and fail to
respond to radioactive iodine (RAI), and other traditional therapies. The lack of effective
therapies for DTC, resistant to radioiodine and traditional therapies is now being overcome by the development of targeted novel compounds.
The published result related to a phase II clinical study in Philadelphia illustrated treating metastatic thyroid cancer patients with the targeted therapy Vemurafenib to establish the activity of Vemurafenib in patients with BRAFV600E-positive papillary thyroid. The large-scale drug screening that incorporates genomic and gene expression data is another breakthrough to identify drug response biomarkers that could inform optimal application of cancer drugs. It is a common
knowledge that a small piece of a tumor receiving after tissue biopsy doesn't represent the whole tumor, let alone metastases. Liquid biopsy, which is a diagnostic concept, opens a new
perspective for real time monitoring of cancer open a new perspective for tumor evaluation.
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 as a non-invasive and cost effective solution to identify reliable biomarkers for measuring tumor growth, metastasis and response to treatments. Liquid biopsies could be used to guide cancer treatment strategy and perhaps even screen for tumors that are not yet visible on imaging. Take advances in molecular genetic technology into consideration,
evaluation and characterization of circulating tumor markers can be the best alternative for realtime tumor tracking. In the near future tissue biopsy will be replaced by liquid biopsy and now is the exact time to focus on CTCs and ctDNA as a circulating tumor biomarker specifically in personalization of cancer treatment.

Keywords:
BRAF mutation, Thyroid Cancer, Personalized Medicine

P1023

Diagnostic value of RASSF1A gene hypermethylation in differential diagnosis of benign and malignant thyroid tumors

Gholamabbas Dinarvand
Faculty member of Abadan School of Medical Sciences, Abadan, Iran. : ab55di@gmail.com

Abstract:
Introduction: Fine Needle Aspiration (FNA) is the best method for diagnosis of thyroid tumors, but it use only for about 20% of cases, the test results is reported as suspicious or intermediate. The aim of this study was to evaluate the RASSF1A gene hypermethylation as a Sensitive and Specific Molecular Test in Differential Diagnostic between Malignant and Benign Thyroid Tumors.
method :To investigate hypermethylation of DNA after bisulfite treatment and PCR, enzyme digestion products are placed under. The measured concentration band in polyacrylamide gel (using software ImageJ) calculation of the quantity of methylation abnormalities. Further, the statistical analysis was used to determine the sensitivity and specificity of this test.
Results: Quantitative evaluation of the RASSF1A gene hypermethylation 8 out of 25 samples malignant tumors from benign distinguish.
Conclusion: The RASSF1A gene promoter hyper methylation has 92% sensitivity 100% specificity.
Keywords:
tumor marker, RASSF1A gene hyper-methylation, papillary thyroid carcinoma
alleles and dietary patterns on odds of general obesity, body fat percent, waist circumference, BMI, WHtR and hs-Crp.

Keywords:
Cardiovascular Diseases, nutritional genomics, Dietary pattern, 9p21, Obesity

P1026

Low amount of extra virgin olive oil in maternal diet positively influences on bone formation markers in offspring

Seyedeh neda Mousavi[1] ، Farzad Shidfar[2] ، Fariba Koohdani[3]

1) Department of Biochemistry and Nutrition, School of Medicine, Zanjan University of Medical Sciences, Zanjan, Iran neda.mousavi@zums.ac.ir
2) Department of Nutrition, School of Public Health, Iran University ofMedical Sciences, Tehran, Iran
3) Department of Cellular and Molecular Nutrition, School of Nutritional Sciences and Dietetic, Tehran University of MEdical Sciences, Tehran, Iran

Abstract:
Background: Osteoporosis is a serious world health problem with economic implications, and it is characterized by enhanced bone fragility and increased fracture risk. These problems arise as a result of low bone mass and micro-architectural deterioration of bone tissue. Evidence has shown that environmental factors may act early in development (in utero and early postnatal life), interacting with the genome to produce a persistent influence on postnatal skeletal development. Therefore, it is important to develop new preventive approaches for reducing the incidence of osteoporosis. Then, the effects of low and high amounts of extra virgin olive oil (EVOO) in maternal diet were assessed on bone formation and resorption markers of offspring.
Material and Methods: Virgin female C57BL/6 mice were received 16% of calorie as soybean oil [LFS] and EVOO [LFO] or 45% of calorie as soybean oil [HFS] and EVOO [HFO] from the time of vaginal plug confirmation until the offspring was weand.
Results: Gene expression of Runx2, Alk.ph, COLI, OPG and OPG/RANK-L ratio were significantly higher in the offspring born from LFO than LFS and LFO than HFO-fed mothers ($p<0.001$). PPARγ2 gene expression was up-regulated in the HFO, as well as LSO than LFO group ($p<0.001$ and $p=0.02$, respectively). Serum OPG/RANK-L ratio was significantly higher in in the LFO than HFO group ($p=0.04$).
Conclusion: Low amount of EVOO in maternal diet leads to increase in bone formation and decrease in bone resorption markers in female mice offspring at adolescence.

Keywords:
Osteoblastogenesis; dietary oil; fetal programming; gestation; lactation

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P1028

Linkage between cancer and life style

Ghazaleh Arabzadeh
nourdanesh : ghazaleharabzadeh11@gmail.com

Abstract:
AIM & INTRODUCTION:
Cancer is seen in all countries whether developed or developing countries. It should be noticed cancer is a disease which both Genetic and Environmental factors are affecting.
In fact, cancer is not a unique disease but a collection of different cells that arise in a similar way. This uncontrolled cell growth path is making a group of diseases and now we call it cancer.
Environmental factor plays a major role in its creation and if a person has a family history of certain cancers still there is hope to comply environmental factors and avoid getting cancer.
Most of cancers have a large number of gene alterations that are created by external factors and only small portion of cancers created by internal gene deviations.
The first thing to accept is the fact that fully one hundred percent certain lifestyle away from cancer there But if they can make decisions that increased risk, strongly influenced and limited.
Cancer is a disease of lifestyle! Living place, work, habits and occupational exposures are important while we talk about Life Style. Each cancer has own risk factor.
After cardiovascular diseases, cancer is the second leading cause of death in developed countries and is the third leading cause of death in developing countries.
Cancer is cause of 12% of all deaths reasons around the world. Cancer killed the people even more than tuberculosis, malaria and HIV.
About 100 types of known cancer are existed and only some of them are solely genetic problem. In this review, some of cancers which are associated more with lifestyle will be explained in details.
MATERIAL & METHOD:
review of 50 researches which published since 2011 till 2016 from.

Keywords:
cancer, life style, risk factors

P1029

The Appropriate Scent for each Person, According to Traditional Persian Medicine

Amir mohammad Jaladat[1] ، Fatemeh Atarzadeh[2] ، Zeinab Nasiri[2] ، Parisa Ghoreishi[2] ، Ayda Hosseinkhani[2]

1) Department of Traditional Medicine, School of Traditional Medicine, Research Center for Traditional Medicine and History of Medicine, Essence of Parsyian Wisdom Institute, Traditional Medicine and Medicinal Plant Incubator, Shiraz University of Medical Sciences Shiraz, Iran.
2) Medicine and Medical History Research Center Shiraz University of Medical Sciences, Shiraz, Iran hoseinkhan@sums.ac.ir

Abstract:
Aim:
Today the concept of personalized healthcare is highlighted in the health policies. Traditional systems of medicine often have the same approach. In Traditional Persian Medicine (TPM) although human beings are mainly categorized into 4 groups and according to a humoral aspect but the physician should see each person as a unique individual. In this study, we aimed to review the categorization and features of suitable scents according to TPM for each category of people.

Methods
In this qualitative study, recommended scents, their categorization, indications, and precautions were extracted from reliable sources of TPM, including Canon of Medicine, Exir-e-azam, Makhzan-al-advieh, and Ghrabadin-e-salehi.

Results
Scents play an important role in preventive and therapeutic approach of TPM. They can affect the nervous system and other associated organs, including digestive, cardiovascular, and reproductive systems. They are divided into two main categories of hot and cold, which can excite or sedate affected organs, respectively. We found 26 aromas recommended by TPM for health maintenance or cure in different people. The appropriate scent can help balancing the functions of specific systems.

Conclusions

According to TPM, a scent is appropriate for a person when it is selected in accordance to the physical and psychological functions and reactions.

Keywords:
Scent, Person, Traditional Persian Medicine

P1030

The impact of genomics on personalized medicine in Familial hypercholesterolemia

Najmeh Ahangari[1] ، Hamidreza Rahimi[2] ، Majid Ghayour Mobarhan[2] ، Alireza Pasdar[2]

1) Department of new sciences and technologies, faculty of medicine, Mashhad university of medical sciences
2) Department of new sciences and technologies, faculty of medicine, Mashhad university of medical sciences a.pasdar@ac.uk

Abstract:
Familial hypercholesterolemia (FH) is the most common inherited form of high cholesterol which is characterized by severely elevated serum LDL cholesterol levels. Increased amount of LDL results in production of atherosclerotic plaque in the coronary arteries and proximal aorta at an early age, leading to an early onset of cardiovascular disorders. The aim of our study is to review recent genomics related techniques and their impact on personalized medicine and management of individuals with FH. There are a number of indicative criteria for FH. Among these, molecular diagnosis of FH through identification of a heterozygote or homozygote individuals for pathogenic variants in one of the three genes known to be associated with FH consists of APOB, LDLR, and PCSK9, is available. Since about 20-40% of cases remained as unknown genetic cause, recent techniques such as genome wide association studies (GWAS), exome sequencing, and newly exome chip studies can be helpful to find novel genes with effects on LDL cholesterol. These findings may have a significant impact on personalized medicine, pharmacogenomics and management of FH patients. Such new perspectives will likely require a standard shift toward further integrated and comprehensive approaches for better prevention and treatment of FH in both individuals and the population as a whole.

Keywords:
Familial hypercholesterolemia, personalized medicine, genomics

P1031

A Gene and microRNAs Expression Profile of CD4 T cells in allergic rhinitis Using Microarray Technology

Leila Akbari kharaji[1] ، Somayeh Reiisi[2]

1) B.Sc genetic student, Department of Genetics, Faculty of Basic Sciences, University of Shahrekord, Shahrekord, Iran
2) Assistant professor, Department of Genetics, Faculty of Basic Sciences, University of Shahrekord, Shahrekord, Iran s.reiisi@yahoo.com

Abstract:
Introduction:Allergic rhinitis (AR) is an inflammatory and heterogeneous syndrome of the upper airway. While, the causative pathogenesis of AR has been broadly studied, it still has been remained unknown yet. Imbalance between Th1 and Th2 immune response results in inducing allergen-specific immunoglobulin (Ig). Beside environmental agent, genetic factors have animportant role affecting progress, severity and treatment of AR. Several candidate genes have been identified but genes and microRNAs (miRNAs) associated with AR in patients still need in-depth study.

Methods: Gene expression data (GSE51392) of sixAR patients were downloaded from Gene Expression Omnibus. After evaluate differentially expressed genes based onExpression Console software (Affymetrix) and FlexArray software (conditions: $P < 0.05$ andlog2 fold change (FC) >2.0), pathway and functional enrichment evaluates were accomplished using the online software DAVID (criterion: $P < 0.05$). The protein-protein interaction networks of AR were created based on the online server STRING and visualized through Cytoscape.

Results:A total of 206genes and 32 miRNAswere identified. Subsequent, 6 functions and 1 pathway were evaluated by up-regulated genes, while 3 functions were enriched by down-regulated genes.In addition, miRNA-gene regulatory networks were constructed. IL17RB was the hub-gene of interaction networks, andmiR-181b1, miR- 15b, miR-142, miR-194, and miR-26bwere up-regulated. ICOS, IL-5, IL12RG, CD3D, and SNORD57 might participate in progress in AR patients, and SLC6A14 and SLC31A1 might be targeted by miR-181b1, miR- 15b, miR-142, miR-194, and miR-26b.

Conclusions:The identified genes and miRNAs might offer a theoretical basis for understanding AR and it's pathogenesis in patients

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Keywords:
Gene expression,MicroRNA, allergic rhinitis, Microarray Technology

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P1032

Biomarkers investigation for presbycusis as a very common human impairment and a future disaster.

Masoumeh Falah[1] ، Mohammad Farhadi[2] ، Seyed Kamran Kamrava[2] ، Maryam Balali[2] ، Saeid Mahmoudian[2] ، Massoud Houshmand[3]

1) ENT and Head & neck Research Center and Department, Iran University of Medical Sciences :
2) ENT and Head &amp; neck Research Center and Department, Iran University of Medical Sciences
3) Department of Medical Genetics, National Institute for Genetic Engineering and Biotechnology housh62@yahoo.com

Abstract:
Presbycusis or Age-related hearing impairment (ARHI) is the most frequent sensory disorder in the elderly. It affects more than half of all persons by age seventy-five years. ARHI has profound economic and social health impacts moreover, the increasing elderly population makes ARHI as an important issue for future generations. Presbycusis is an irreversible symmetrical progressive loss of hearing sensitivity during the lifespan. It has an insidious onset without clinical manifestation so detected by the routine test after losing or damaging to inner ear cells and neurons. Presbycusis counted as an untreatable impairment, since these inner ear structures lose the ability of regeneration.

Mitochondria by producing reactive oxygen species or inducing apoptotic genes is one of most prominent organelles in presbycusis progression. The present study focused on mitochondrial function in order to find the per-diagnostic biomarker for this common impairment. For obtaining this goal the relative mitochondrial DNA (mtDNA) copy number and control region variation compared between presbycusis and healthy subjects. All participants selected by an otolaryngologist after ENT examination, audiology investigation. The proportion of mtDNA to nuclear DNA calculated by quantitative real-time PCR, and variations in the mtDNA control region were investigated by PCR and sequencing. Results indicated that mtDNA copy number were decreased in presbycusis subjects compared with healthy subjects. The frequencies of the variants, 16223 C>T, 16311 T>C, 16249 T>C, and 15954 A>C, were significantly different between presbycusis and control subjects too. The statistically significant difference copy number and control region variation of mtDNA in ARHI patients and controls is in agreement with previous experimental evidence and supports the role of mitochondria in the intracellular mechanism underlying ARHI development. Moreover, this study showed that mitochondrial investigation will enable to establish biomarkers helping to identify individuals at risk for developing presbycusis and to develop screening approaches for pre-diagnosis.

Keywords:
Presbycusis, Age-related hearing impairment (ARHI), Pre-diagnostic, Biomarker

P1033

Bioinformatics analysis to predict and identification target genes for up-regulated microRNAsas promising biomarkers in allergic rhinitis

Maryam Hosseini[1] ، Somayeh Reiisi[2]
1) B.Sc genetic student, Department of Genetics, Faculty of Basic Sciences, University of Shahrekord, Shahrekord, Iran
2) Assistant professor, Department of Genetics, Faculty of Basic Sciences, University of Shahrekord, Shahrekord, Iran s.reiisi@yahoo.com

Abstract:
Introduction: MicroRNAs (miRNAs) are a group of small noncoding RNA that can play important roles as regulators in biological processes comprising the development, inflammation and immune response. Because of the numerous of possible interactions between a single mir and target genes, bioinformatics prediction are very valuable to simplify the procedure for selecting putative target genes.Allergic rhinitis (AR) is a usual disorder in airway. The pathogenesis of AR is unknown but immune deregulation is involved in AR. Evidence displayed that miRNAs are important in regulatory inflammatory processes and they are considered satisfactory biomarkers. Nevertheless, whether miRNAs were involved in chronic allergic airway disease remains largely unknown. Therefore this study aims to investigate putative target genes and interaction networks where they are involved in AR.
Methods:The original data set GSE51392 was received from the Gene Expression Omnibus, and then thedifferentially expressed miRNAsbetweenpatients with seasonal allergic rhinitisin two levels of baseline and allergen challenge were identified using the FlexArraysoftware. Their target genes were selected from four (Tagetscan, miRWalk, miRDB, DIANAmt) miRNA databases. Then, functional analysis was accomplished for the target genes using by construction of a miRNAs target gene network.
Results:In this study, described four miRs (miR-425, miR-146a, miR-133a, and miR-135) whichindicated to be differentially expressed in patients with seasonal allergic rhinitis. The miRs were exposed to the most used predictions software and 26 predicted target genes were recognized. Then, enrichment analysis was performed revealing substantialgroups, comprising role in regulation of receptor protein in interleukin (IL-1RA, IL-13RA, IL-18 and IL-33) signaling pathwayand regulation of TGF-beta signaling pathway. A network construction was generated and links between the selected miRs and the predicted targets.
Conclusions: In this study, we merged miRNA expression analysis with a bioinformatics-based workflow. Some genes, pathways and interactions, putatively involved in ARdevelopment, were identified.

Keywords:
MicroRNA, allergic rhinitis, target prediction, biomarker

P1034

New methods for diagnosis of in malaria-prone areas

Mohammadreza Foroutani[1] ، hannan Kashfi[2]
1) Department of Nursing, Larestan School of Medical Science , Larestan.Iran. : larres@sums.ac.ir
2) Department of Nursing, Larestan School of Medical Science , Larestan.Iran.

Abstract:
Malaria is still considered a problem in many parts of Africa and the Middle East. A feature of the disease that has made it a health problem is its diagnostic problems. Achieving an accurate and efficient, yet affordable and cheap, method will reduce malaria risks. Taking a Blood Smear from the person suspected of having the disease and its microscopic examination after staining it with Wright-Giemsa stain, is the simplest and most accurate laboratory test for diagnosing the disease and determining the Plasmodium type. This is thus the most widely used test. In cases where the number of parasites in the blood is low or the patient is receiving a drug therapy, blood smear method is not effective. In addition, in evaluation of methods for controlling and eradicating Malaria where carriers of Plasmodium are followed up, blood smear method will not be accurate and serological methods should be used. In particular, indirect haemagglutination and fluorescent antibody methods are mostly used in malaria epidemiology and control studies. For diagnosis of Malaria in early stages in people who have recently been infected and have clinical signs of the disease, serological methods are not needed because the parasite is found in blood samples. In addition, in people who have repeated malaria infections or live in malaria-endemic areas, positive serology test does not indicate the infection. In malaria-prone areas, presence of some parasites like Babesia in peripheral blood smears may be diagnosed incorrectly as Plasmodium falciparum.
Today, scientists use light magnet technology (MOT) where magnetic properties are used for detection of Haemozoin, a residue of the malaria parasite in the blood. This new method is preferred to previous methods for malaria testing because of more accurate identification of samples containing little parasite. Using the method, practitioners can diagnose malaria in less than a minute.

Keywords:
methods,malaria,diagnosis

P1035

Using Personalized Medicine for Controlling Herpes: A new paradigm for an old disease

Kaveh Haratian

Department of Microbiology and Immunology, Alborz University of Medical Sciences, Karaj - Iran : kevinharatian@gmail.com

Abstract:

Every person has a unique variation of the human genome. Although most of the variation between individuals has no effect on health, an individual health stems from genetic background with behaviors and influences from the environment. One way that biological variation manifests itself is responsiveness to infections such as virals. In the meantime, herpes virus infections have enormous effects on almost every parts of the body. Herpes never goes away. Rather, the virus retreats to specific nerve roots, where it can be dormant for long periods of time. They even can be easily resulted in a drastic cancer. When it re-emerges, it travels up the same nerve root and causes lesions, usually in the same area as before. Stress and changes in immune function are known factors in determining re-emergence, but it may occur for no apparent reason. Many people have antibodies to HSV-1. This means that they have been exposed, but may have never had a cold sore (or they may have and it went away). For HSV-2, that number is lesser but even high particularly in Iran. As we know the frequency of recurrence of herpetic lesions is different between individuals. Besides, there is a meaningful difference between those individual infected reactively with herpes viruses that overtake by some kind of cancers afterwards and the others who have a less reactive infection. Due to the latency phenomenon of these viruses, it is proposed that this could be a real personal issue for every individual. On the other hand, the persons with a specific genetic makeup may have less severity, reactivity and therefore less probability for sliding to a cancer while the others are different. The aim of current projects should be mainly focused on the related interventional genes which may have prominent effects of the herpes virus latency in various people.

Keywords:

Herpesvirus, HSV-1, HSV-2, Personalized medicine, Latency, Cancer

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P1036

Selecting the Most Immunogenic Fragments on an Antigenic Protein for Designing DNA Vaccine Using Different Algorithms

Roksaneh Sayadi[1] ، Mohsen Mobini-Dehkordi[2] ، Mostafa Shakhsi-Niaei[2] ، Amin Nematollahi[3]

1) Division of Genetics, Department of Basic Science, University of Shahre-Kord, Shahre-Kord, I.R. Iran.
2) Division of Genetcis, Department of Basic Science, University of Shahrekord, I.R. Iran : r.sayadi@std.kashanu.ac.ir
3) Department of Food Hygiene and Quality Control, Faculty of Veterinary Medicine, University of Shahrekord, Shahrekord, I.R.Iran

Abstract:

Approaching novel techniques in delivering vaccines, DNA vaccines are the most interesting devices, which are the head of the 3rd generation of vaccination methods. Lack of requirement of purifying and downstream separation and expression made these vaccines more useful than subunit and peptide vaccines.

However, DNA vaccines utilize endogenous pathways requiring B cells and other APCs to present their immunogen epitopes to CD4+ T helper cells for inducing humoral immune responses. Hence, MHC II epitope determination is a critical issue in designing endogenous DNA vaccines.

Once, DNA vaccine reaches into the cell cytoplasm, it will express antigen protein.

In the following research, a DNA Vaccine is designed against an antigenic glycoprotein of a rhabdovirus family to generate immunity before challenging wild virus. According to the delivery method used for this research, endosomal proteases have been considered to cut down antigen peptide bond into shorter MHC II epitope peptides. The pattern of cleavage of antigen can be predicted by protease databases and servers including endosomal specific proteases cleavage cut site patterns. In this research, both endosomal proteases pattern and MHC II binding epitopes (Linear and Conformational) have been predicted for designing an efficient protective DNA vaccine against viral diseases caused by Rhabdoviridae family.

In order to linear MHC II epitope prediction, Propred[1], IEDB[2] and NetMHCII[3] servers were used while selecting scores above specified thresholds. Likewise, conformational MHC II epitopes have been analyzed with Discotope IEDB[4] server on the 3D structure of peptide sequence chains. On the other hand, specific proteases-mediated peptide cleavage pattern has been studied with PepCleave CD4+[5], and ExPasy Peptide-Cutter[6] servers.

Also, predicted MHC binding epitopes were examined with SYFPEITHI[7] to determine epitope-MHC II binding affinity. Hence, gathered data shows the best-predicted epitopes located on the desired sequence which should be involved in designing DNA vaccine as insert fragments.

Eventually, collected data obtained from different servers have been caparisoned and the most immunogen fragments have been selected for designing efficient DNA vaccine.

Keywords:

Epitope Prediction, Antigen, CD4+, MHC II, DNA Vaccine

P1037

Prevention of Albinism in an Iranian non-consanguineous family with pseudo dominant inheritance

Roshanak Jazayeri[1] ، Seyyed Hosseinali Saberi[2]

1) Alborz University of Medical Sciences : drj_51@yahoo.com
2) Karaj Welfare Organization, Karaj, Iran & National Institute of Genetic Engineering and Biotechnology, Tehran, Iran

Abstract:
Oculocutaneous albinism type 1 is characterized by hypopigmentation of the skin and hair and the distinctive ocular changes found in all types of the albinism, including: nystagmus; reduced iris pigment with iris translucency; reduced retinal pigment with visualization of the choroidal blood vessels on ophthalmoscopic examination; foveal hypoplasia with substantial reduction in visual acuity; and misrouting of the optic nerve fiber radiations at the chiasm, resulting in strabismus. OCA1 is inherited in autosomal recessive manner. This study was designed to find the genetic defect in a 30 years-old affected female, having non-consanguineous parents, who was married with an apparently normal non-consanguineous male, and they wanted to know about recurrence of this disorder in their children. Sanger Sequencing of the TYR gene was performed for the affected individual. She was homozygote for a pathogenic variant in TYR gene (c.996G>A, p.M332I), and her parents were determined heterozygote for that mutation. Sanger Sequencing of the TYR gene was also performed for her husband. Accidently, he was heterozygote for another mutation in TYR gene (p. Arg402Gln). According to his wife, there is 50% possibility of inferring compound heterozygosity to each fetus. This 50% risk, resembles a pseudo-dominant inheritance in their children. Knowing these two mutations, they can use preimplantation genetic diagnosis (PGD) to assure that the embryos implanted are not affected, or use prenatal diagnosis. Genetic counseling and carrier detection is also recommended for all high-risk individuals in this family.

Keywords:
Oculocutaneous albinism, pseudo dominant inheritance, TYR gene, Sanger sequencing, PGD, Iran

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P1038

Survey of Interleukin 10 Gene Promoter Polymorphisms at Position -592(A/C) and -1082 (A/G) in Obese Individuals with Type 2 Diabetes in north west of Iran

Farzin Ferdousi[1] ، Amir Hossein Taromchi[2] ، Abdolreza Esmaeilzadeh[3]

1) Department of Genetic,Biology Research Center,Zanjan Branch,Islamic Azad University,Zanjan,Iran
2) Department of Biotechnology and Nanotechnology, Zanjan University of Medical Sciences, Zanjan, Iran : taromchi@zums.ac.ir
3) Department of Immonology, Zanjan University of Medical Sciences, Zanjan, Iran

Abstract:
Backgrounds and Objectives: lots of genes are associated with the risk of developing diabetes. Overweight and obesity are common risk factors for type 2 diabetes (T2D) and most of the time body composition controlled by genetic factors. There are plenty of evidence to suggest that inflammatory reactions have a significant role in the incidence of these complications. Interleukin 10 is known as one of the most important anti-inflammatory cytokines. Thus, the present study was conducted to investigate the relationship between Interleukin 10 gene polymorphisms -592 A/C and -1082 A/G and susceptibility to get T2D and obesity.
Materials and Methods: In this study, 75 obese patients with T2D, 75 non-obese patients with T2D, 75 obese patients without T2D and 75 healthy controls were studied. DNA extraction was carried out and then the genotype in -592 A/C and -1082A/G positions was determined using PCR-RFLP and chi squared test (X2) was used as statistical methods for data analysis.
Results: The frequency of CC and AC genotype in -592A/C position in obese patients with T2D and non-obese patients with T2D had more importance than non-diabetic patients ($p<0.05$). Also the frequency of AA genotype in -1082A/G position in obese patients with T2D was significantly more than other subjects ($p<0.05$) .
Conclusion: Higher frequency of C allele in -592A/C position can be considered as a factor for T2D. Also the presence of an A allele next to C allele at the position of -592A/C could be predisposing of obesity in patients with T2D. Fewer frequency of haplotype AA/AA can be considered as a predisposing factor for obesity and T2D. Understanding the basis of this heterogeneity provides an opportunity for personalizing prevention and treatment strategies according to individual patient clinical and molecular characteristics.

Keywords:
Type 2 diabetes, obesity, polymorphism, Interleukin 10

P1039

The impact of genetic alterations and gene expression of FSH receptor on ovarian response of infertile women to gonadotropins

Dr Zeinab Ghezelayagh[1] ، Shabnam Zari Moradi[2] ، Mehdi Totonchi[2] ، Poopak Eftekhari Yazdi[3] ، Tahereh Madani[4] ، Hamid Gourabi[1] ، Anahita Mohseni meybodi[5]

1) Department of Genetics, Reproductive Biomedicine Research Center, Royan Institute for Reproductive Biomedicine, The Academic Center for Education, Culture and Research (ACECR), Tehran, Iran
2) Department of Genetics, Reproductive Biomedicine Research Center, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran
3) Department of Embryology, Reproductive Biomedicine Research Center, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran.
4) Department of Endocrinology and Female Infertility, Reproductive Biomedicine Research Center, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran
5) Department of Genetics, Reproductive Biomedicine Research Center, Royan Institute for Reproductive Biomedicine, The Academic Center for Education, Culture and Research (ACECR), Tehran, Iran : anahitamohseni@gmail.com

Abstract:
Poor ovarian response (POR) is an infertility disorder in which women's ovaries do not response to gonadotropins properly. Any deficiency in the genes of hormones in hypothalamic-pituitary-gonadal pathway and their receptors could be the etiology for the progression of the disease. Throughout folliculogenesis, FSH receptor starts a signaling cascade in the granulosa cells after its activation by FSH. Inactivating of this receptor may arrest follicle maturation and therefore adversely effects on ovarian response. The aim of this study was to investigate the association between any alterations in FSH receptor gene with ovarian response to gonadotropins, in order to find a potential predictor for ovarian response of each infertile woman to those gonadotropins. In a case control study comprised of 60 POR and 80 fertile Iranian women, the presence of 566C>T, 1555C>A and 1043C>G mutations and 919G>A, 1572C>G, 1993A>G and -29G>A polymorphisms of the FSHR gene were analyzed by PCR-Sequencing methods. The mRNA expression of FSHR gene was also studied in granulosa cells of 20 POR and normal ovarian response patients by real time-PCR. Although the common 919G>A and -29G>A polymorphisms were seen, no other variants were detected. Different genotypes of -29G>A and 919G>A polymorphisms were seen in the mentioned groups, which statistically significant differences were seen in both polymorphisms when comparing the control group with POR patients. The other above mentioned FSHR gene variants, are not frequent in Iranian POR patients; thus, studying other allelic variants in a larger Iranian population is suggested. A decrease in the mRNA expression of POR patients compared to the control group was also observed but it was not statistically significant (P value ≥ 0.05). Accordingly, -29G>A and 919G>A polymorphisms in the FSHR gene might be associated with poor response to gonadotropins but they might not have an effect at the FSHR expression level.

Keywords:
FSH receptor, Genetic alterations, Ovarian response, Gonadotropins, female Infertility

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P1040

Crocin increases mitochondrial biogenesis in the Striatum rats with cholestasis

Mohammadreza Eteqadi[1] ، Mohammad Nasehi[2] ، saeed hesami takallou[3]

1) Department of Biology, Faculty of science, : eti_mr@yahoo.com
2) Department of Biology, Faculty of modern medical science,
3) Department of Biology, Faculty of science,

Abstract:
Introduction : Oxidative Stress and particularly the increased mitochondrial reactive oxygen species (ROS) production that occurs in cholestasis and links oxidative stress to the development of neurological diseases. Cholestasis effects on striatum and striatum is center of movement learning in the mind. The mitochondrial numbers and the expression of Proliferator-activated receptor Gamma Coactivator-1α (PGC-1α) and Mitochondrial Transcription Factor A (Tfam) are decrease during cholestasis. PGC-1α is the master regulator of mitochondrial biogenesis and function. Tfam is essential for human mtDNA transcription. It is also a key regulator of mtDNA copy number. Attenuation Of PGC-1α expression levels results in increased mitochondrial biogenesis including increased mitochondrial mass, protein import complexes, mitochondrial respiratory and fatty acid oxidation. The objective of this study was to investigate the protective effect of crocin against defects in striatum due to cholestasis in male Wistar rat. Materials and methods : Adult Male wistar rats weighing 200- 250g were randomly divided into five groups (eight rats in each group) which include: Group 1: Normal-control (non operation) . Group 2: Sham-control(underwent laparotomy without bile duct ligation). Group 3: BDL- control (underwent laparotomy with bile duct ligation) and all of three groups weren't received drug. Group 4:Sham- crocin and Group 5:BDL- crocin were treated with Crocin. Rats were injected with a daily dose of crocin (30 mg/kg IP) for 30 days. Striatum homogenates were obtained For Real Time PCR examination. Results: The results showed that the mean change in PGC-1α and Tfam expression of BDL- crocin group. There is a significant difference ($p<0.05$) as compared with BDL- control. Interventions were Improved mitochondrial biogenesis in the Striatum of Cholestatic male wistar rats.
Conclusion:
The present findings provide evidence that crocin by blockade of ROS generation and biogenesis improved may have beneficial effects in the mitochondrial dysfunction. Therefore it can be a therapeutic strategy of neurodegenerative diseases such as Alzheimer and Parkinson.

Keywords:
crocin,striatum,cholestasis,PGC-1α, mitochondrial biogenesis,Tfam

P1041

the prevalence of cyp1a2*1c polymorphism in different ethnic of iranian population

Malihe Khiabani[1] ، Zahra Rezakazemi[2] ، Maryam Banasaz[3] ، Masoud Houshmand[4]

1) Department of biology, Damghan Branch, Islamic Azad University, Damghan, Iran.
2) Department of biology, Damghan Branch, Islamic Azad University, Damghan, Iran.
3) Taban clinic, Tehran, Iran
4) Medical Genetic Department, National Institute of Genetic Engineering and Biotechnology (NIGEB), Tehran, Iran
massoudh@nigbe.ac.ir

Abstract:

Abstract; Background: Human CYP1A2 is one of the major CYPs in human liver and metabolizes a variety of clinically important drugs and caffeine (e.g., clozapine, tacrine, tizanidine, and theophylline) and caffeine. Its activity can be influenced by factors such as sex, age, and smoking. The single nucleotide polymorphism (SNP) rs762551A.C, which has also been studied for its modifying effect on cardiovascular disease, has been reported to alter enzyme activity. The allele was located on 15q24.1 locus. CYP1A2*1C polymorphism is decreased the effect of drugs. We investigated the prevalence of the CYP1A2*1C in an Iranian population of different ethnicities, including Azari , Lure , Fars , Kurd , and Caspian (mazani /Gilaki) , in comparison to the frequency of the CYP1A2*1C in the other population.

Material and method: In this study we were analyzed 300 blood samples of healthy individuals in an Iranian population. The present study was conducted to explore the allelic and genotypic frequencies of CYP1A2 gene polymorphisms, CYP1A2*1C (−3860 G>A) among 300 Iranian volunteers. The CYP1A2 polymorphisms (CYP1A2*1C) were genotyped by the PCR-RFLP (Restriction Fragment Length Polymorphism) method.

Result: The G/C, G/A and A/A allelic frequencies of CYP1A2*1C were 9%, 79%, and 12% respectively. Additionally, the frequency of the homozygote(G/C) variant of CYP1A2*1C was high in the lure , Turk , Fars and low in the Kurd , Caspian ethnicities

conclusion :these result suggest that the predication of the CYP1A2*1C allele is required in drug research and routine treatment ,where the information would be helpful for clinical optimize therapy or identify persons at risk of adverse drug reaction before clinical trials. In addition the ethnicities of Iran that have the polymorphism are the lure ,Turk ,Caspian, Fars and Kurds.

Keywords:
pharmacogenetic,polymorphism,ethnic,cyp1a2*1c,iran
Noninvasive, Quantification

P1043

Exosomes as tumour markers for personalized diagnostics

Somayeh Keshtkar[1] ، negar azarpira[2] ، Mohammad Hossein Ghahremani[3]

1) Department of Molecular Medicine, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences
2) Transplant Research Center, Shiraz University of Medical Sciences : negarazarpira@yahoo.com
3) Department of Molecular Medicine, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences

Abstract:

Exosomes, membrane vesicles of 40_100 nm in diameter, are derived from endosomes in various cells and contain a cargo that include miRNA, mRNA, and proteins. The bioactive molecules specifically packed into exosomes can be transferred into recipient cells changing their biological properties, by which tumour cells continuously modify their surrounding microenvironment and distant target cells favouring cancer metastasis. It has been suspected for a long time that exosomes participate in the whole process of tumour metastasis. Since these exosomes are easily accessible and capable of representing their parental cells, exosomes draw much attention as a promising biomarker for tumour screening, diagnosis and prognosis. In the mean time, cancer researchers are finding biomarkers for utilize in personalized medicine. In personalized medicine, the customized treatment depends on information about the molecular characteristics of the cancer signature, especially the personalized diagnostics. Although traditional biomarkers have been widely and maturely utilized in personalized medicine, their inherent limitations cannot be ignored. First, the most common method to detect pharmacogenomically relevant sequences is fluorescence in situ hybridization, which depends on the sample from biopsy. Secondly, tissue biopsy, the best method of diagnosis, is invasive and dangerous, and is unable to be applied to repeated diagnosis. Thirdly, the low specificity of serum biomarkers in present clinical diagnosis may contribute to a low efficiency of diagnosis. While exosomes ,compared with traditional biomarkers, possess great potential as cancer biomarkers in personalized medicine. Firstly, exosomes can travel across the endothelium into the circulation allowing serum detection. Secondly, exosomes are akin to vessels enriched with much information about the parental cells, and the cargoes in exosomes are protected by the phospholipid bilayer from degradation by proteinases and nucleases. Consequently, biomarkers at a relatively low expression are much easier to be detected through isolating exosomes. Thirdly, analysing the fraction of exosomes can effectively weaken the serum matrix effect and reduce the dynamic range. Fourthly, exosomes are constituently secreted by various cells and the number of exosomes increases obviously in the serum of cancer patients. Accordingly, it is reasonable to assume that the representativeness of exosomes is better than fine needle biopsy, which is of great meaning for the accuracy of personalized diagnostics. Even though the isolation of exosomes is a troubling issue, exosomes have the potential to be used in clinical practice in the near future as the field rapidly expands.

Keywords:
exosome ; personalized diagnostics; cancer biomarkers

P1044

Increase of JAK2 D620K variant and reduction of JAK2 V617F variant and associated lack of D661Y & Y640F variants in STAT3 gene in women with miscarriage.

Parisa Azimi[1] ، Faramarz Vejdandoust[2] ، Hanieh Noferesti[2] ، Vahdie Salimi[3] ، Leyla Akbari[4] ، Masoud Houshmand[5]

1) Medical Biotechnology Research Center, Ashkezar Branch, Islamic Azad University, Ashkezar, Yazd, Iran
2) Medical Biotechnology Research Center, Ashkezar Branch, Islamic Azad University, Ashkezar, Yazd, Iran.
3) Department of Medical Genetics, National Institute of Genetic Engineering and Biotechnology(NIGEB),Tehran, Iran
4) Taban Clinic, Tehran, Iran
5) Department of Medical Genetics, National Institute of Genetic Engineering and Biotechnology, Tehran, Iran: housh62@yahoo.com

Abstract:
Objectives:
Recurrent miscarriage (RM) is the occurrence of repeated pregnancies that end in miscarriage of the fetus before 20 weeks of gestation. Spontaneous abortion occurs in 15-20% of clinically recognized gestations. Considering the significant proliferative functions of JAK2 and STAT3roles in signal transduction and transcription activation, The JAK2 gene provides instructions for making a protein that promotes the growth and division (proliferation) of cells and The STAT3 gene provide instructions for making proteins that are part of essential chemical signaling pathways within cells. In the immune system, the STAT3 protein transmits signals for the maturation of immune system cells. we decided to develop diagnostic polymerase chain reaction (PCR)-based assay to investigate the correlations between miscarriage in Iranian women and JAK2 V617F/C618W/D620K, STAT3 Y640F /D661Y/T632I/S636F/V637M variants.
Methods:
DNA was extracted from blood samples of 24 unrelated Iranian women with three or more unexplained pregnancy losses occurring in the first trimester as well as Forty eight healthy subjects as control group. Genomic DNA was used to detect somatic mutations in JAK2 and STAT3 genes. The exon14, 3´-UTR region of JAK2 for variants V617Fand exon 21 and 3´-UTR region of STAT3 for variants Y640F/D661Y were amplified by PCR. The PCR products were detected by capillary electrophoresis (CE) and subsequently extracted for sequencing
Results:
JAK2 V617F mutation was identified in 6 (28.4%) of 48control. All variants were confirmed by sequencing. Sensitivity studies showed JAK2 V617F ($P < 0.05$) was associated with decrease IRM (idiopathic recurrent miscarriage) risk in Iranian women and STAT3 Y640F ($P > 0.05$) and D661Y ($P > 0.05$) variants were not associated with RM.
Conclusions:
Our phenotype-genotypic association analysis indicated that there was insufficient evidence to demonstrate an association betweenJAK2 D620K, V617F variants and the risk of RM. D620K variation increase RM risk But V617Fvariation decreases RM risk in patients with three or more miscarriages. Our analysis indicates no association between STAT3 D661Y& Y640F variants and recurrent miscarriage. Overall our PCR based assay facilitates fora rapid, accurate screening for JAK2 V617F and STAT3 Y640F and D661Y variations in recurrent miscarriage, hence reducing labor and improving turnaround time

Keywords:
JAK2,V617F,STAT3,Y640F,D661Y,Miscarriage
A, mir-10a, RT-qPCR

P1046

Evalition Expression of mir-338-3p in Chronic Lymphocytic Leukemia Patients and Healthy People

Arman Akbarpour[1] ، Mansoor Salehi[2] ، Parisa Mohammadinejad[3]

1) Department of Basic Sciences, Islamic Azad University of Shahrekord Branch, Shahrekord, Iran
2) Department of Genetics and Molecular Biology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran u8002010@hotmail.com
3) Biology Dept., Shahr e Kord Branch, Islamic Azad University, Shahr e Kord, I.R. of Iran

Abstract:
Background: microRNAs (miRNAs) are short (20-24 nt) non-coding RNAs that are involved in post-transcriptional regulation of gene expression in multicellular organisms by affecting both the stability and translation of mRNAs. Chronic lymphocytic leukemia (CLL) is characterized by an accumulation of mature CD5+ B cells that are dependent on micro environmental support, and genetic mutations. The aim of the present study was to compare the expression level of mir-338-3p in normal and neoplastic samples from CLL patients by RT-qPCR.
Methods: In the present case-control study, 15 blood samples from patients with CLL and 15 blood samples from healthy group under the direct supervision of a pathologist specialist due to clinical presentation and laboratory findings were collected. After extracting RNA from normal and tumor blood samples, cDNA synthesis method according to the protocol and RT-qPCR was performed. mir-338-3p expression level was calculated using ΔΔCT. All data were analyzed using SPSS software.
Results: The results of RT-qPCR indicated that miR-338-3p down-regulation was significantly correlated with CLL cancer clinic pathological features. Expression level of mir-338-3p was 25.68% and 74.32% in CLL patients and healthy group respectively (p value=0.001).
Conclusion: Due to the previous reports, mir-338-3p act as tumor suppressor in CLL, which could be used as biomarker for CLL diagnosis. In this study we propose that miR-338-3p is a potential diagnostic marker and therapeutic target of CLL.

Keywords:
CLL, microRNA, mir-338-3p, RT-qPCR

P1047

Human microbiome as a future approach to personalized medicine

Hanieh-sadat Ejtahed[1] ، Shirin Hasani-Ranjbar[2] ، Bagher Larijani[3]

1) Obesity and Eating Habits Research Center, Endocrinology and Metabolism Molecular -Cellular Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran
2) Obesity and Eating Habits Research Center, Endocrinology and Metabolism Molecular -Cellular Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.
3) Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran : larijanib@sina.tums.ac.ir

Abstract:
Individuals have different responses to different therapeutic agents which is the major problem in clinical practice. Huge amounts of time and money have been invested in looking for the sources of these variabilities. Human microbiome, the bacterial ecosystem residing in every human body which contributes 100 times more genes than the human genome, may be the true source of various responses. Since studies have shown that dysbiosis which results in alterations in both structural and functional profiles of the human microbiota is major contributors to the pathogenesis of immune, infectious and metabolic disorders, modulation of microbiota could be effective in personalized medicine. The term gut pharmacomicrobiomics implies the effect of the gut microbiome on pharmacokinetic and pharmacodynamic processes through the secretion of drug structure-modifying enzymes, secretion of metabolits interfering with drug metabolism, modification of intestinal and liver enzymes, and modulation of human metabolic genes expression. We can imagine a future that routinely analyzing the microbiome allows us to predict individualized responses to different foods and drugs. Microbiome analyzing of individuals may be added to future routine personalized medicine protocols after comparing the costs and benefits of this technology. Improved understanding of the human microbiome could lead to the development of novel therapeutic strategies for different diseases. Potential therapeutic agents such as personalized probiotic and prebiotic supplements, dietary interventions and fecal microbiota transplantation that can be used to reshape the gut microbiome represent a reasonable strategy to enter the era of personalized medicine.

Keywords:
Gut microbiome, pharmacomicrobiomics, personalized medicine

P1048

Pederin as a potential antitumor compound: a review of Pederins antitumor activity with focus on molecular mechanism

Hadi Bamehr[1] ، Zeinab Darvish[2]

1) Hamadan University of Medical Scinces : hbamehr@yahoo.com
2) Hamadan University of Medical Scinces

Abstract:
Pederin is a non-protein toxin with polyketide structure extracted from Paederus and marine sponges. Paederus belong to Staphylinidae family (a large group of beetles,with 600 species) distributed mostly in temperate and tropical agricultural habitats.

Hemolymph of Paederus has pederin that cause dermatit linearis on human skins. Pederin produced by uncultured bacterial symbionts that closet relationship to Pseudomonas. Pederin induce inhibition of DNA. This compound has antiviral and antitumor activity.

Purified form of pederin is a crystalline amide which is soluble in alcohol and water. Pederin is synthesized by a mega-synthases named polyketide synthases (PKSs) /nonribosomal peptide synthetases (NRPSs) involved in the biosynthesis of bacterial complex polyketides.

The gene cluster involved pederin biosynthesis consisting of 18 putative ped genes distributed on three distinct genome regions, ped LMNOPQR, ped IJK and ped ABCDEFGH.

Polyketide chain units are provided by malonyl-CoA or simple derivatives, which are connected by decarboxylative Claisen-type condensations.

The Members of the pederin family including Onnamide A ,theopederin B, and mycalamide A. mycalamide A induces apoptosis by unknown mechanism . Onnamide A and theopederin B induces the PAI-1 gene expression and p38 kinase and JNK activation but not active Smad2/3. Cytotoxicity and antitumor activity of onnamide A and theopederin B are related to activation of p38 kinase and JNK.

However, these compounds unlike the anisomycin which impair peptidyl transferase activity are ribotoxic stress inducers by translocation impair mechanisem. therefore study of this compound because of their biological activity as a candidate for cancer therapy is important. in this review, we focus on the latest data about metabolism, synthesis, and function of pederin agent.

Keywords:
Pederin,toxin,antitumor compound

P1050

Research Gap in Genetic Studies in Diabetes Mellitus in Iran

Fatemeh Bandarian
Diabetes Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, fbandarian@tums.ac.ir

Abstract:

Background: Diabetes mellitus (DM) is the most common metabolic disorder worldwide. The aim was to report characteristics of genetic studies in DM in Iran and to identify knowledge gap in genetics of diabetes in Iran.

Methods: All publications of Iranian authors in national and international journals up to 2015 were included. Comprehensive search was performed in PubMed, Web of Science, SCOPUS, SID, IranMedex and Magiran using “Diabetes mellitus” and “Iran*” keywords and their combination. Our search obtained 25589 documents. The obtained documents were categorized into eleven groups of complications, comorbidity, management, psychology, nutrition, physical activity, genetics, basic sciences, prevention, education and gestational diabetes mellitus (GDM).

In each group after exclusion of unrelated documents and duplications, documents were categorized based on the WHO and Australian National Health and Medical Research Council (NHMRC) criteria, study design and subject area.

Results: After screening, 293 documents remained. The trend of publications was increasing and reached peak in 2013. Case-control was the most common method used in the documents. Most of the studies were association study with case-control design while there was no genome wide association study (GWAS) and there was only one pharmacogenomics 2 study. Genetic risk factors for DM and its complications were the most common topics in the obtained documents followed by DM management.

Conclusion: The most of genetic studies in diabetes in Iran are association studies about genetic risk factors of diabetes and GWAS and pharmacogenomic studies are rare or absent. This may indicate low priority of personalized medicine in the field of diabetes in Iran.

Keywords:
Diabetes mellitus, Genetics, Research gap

P1051

Circulating Cell-Free Nucleic Acids as Potential Biomarkers for Sarcopenia: A step toward personalized medicine

Gita Shafiee[1] ، Ramin Heshmat[2] ، Bagher Larijani[3]
1) Chronic Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran. : gshafiee.endocrine@gmail.com
2) Chronic Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.
3) Endocrinology & Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.

Abstract:

Sarcopenia,a multifactorial geriatric syndrome, is characterized by age-related decline in muscle mass and function. There are multiple intrinsic (biological changes, inflammatory states; etc.) and extrinsic (decreased activity, malnutrition; etc.) factors that participate in the development of sarcopenia .

Given the relatively high prevalence and related-outcome of the disease, correct diagnosis, screening, monitoring and treatment of sarcopenia are needed in clinical practice as well as for the conductance of beneficial interventions. In this regard, the global quantitative data from both genetic, biomarkers and body composition could provide a standardized and international comparable readout for successful care. Although, several biological markers have been found to be associated with age-related skeletal muscle decline, but they are not specific to muscle mass and function.Therefore, a good biomarker for sarcopenia must be specifically for muscle changes, accessible, reliable, non-invasive and cost effective. The biomarker could show specific biological processes of sarcopenia to understand specific therapy as a step toward personalized medicine. Recent advances in technologies provide an extraordinary capacity to characterize the genetic alterations and pathways in diseases comprehensively and make it possible to develop therapies, prevention and screening based on the genetic makeup of each disease.

Circulating cell- free nucleic acids (ccfNA) in various body fluids have been explored as a novel biomarker in a variety of clinical conditions. The first studies concerning the detection of circulating cell free DNA (cf-DNA)was found in various cancers, metastasis and recurrence of tumor. Both apoptosis and necrosis are as the source of the cf-DNA and so, elevated cf-DNA levels have been observed in other conditions such as cardiovascular diseases, sepsis, and trauma. In the recent years, much attention and effort have been put into studies of other circulating nucleic acids, including circulating RNA, microRNA, mitochondrial DNA, mitochondria RNA than cf-DNA. In addition to assessing the quantities of circulating cf-DNA, qualitative features, such as the cf-DNA methylation level, mutations and fragment size have been offered to be useful diagnostic and prognostic markers in various diseases. Given that sarcopenia is accompanied with increased inflammation, apoptosis and necrosis mediate skeletal muscle fiber loss in age-related mitochondrial enzymatic abnormalities; it represents an amenable condition for which to assess cell free nucleic acids as a candidate biomarker.

In conclusion, with development and advances in molecular genetic technology, now is the exact time to focus on ccfNA as a biomarker to access the best therapeutic policy of sarcopenia in personalized medicine and also, to distinguish early stage of sarcopenia without loss of physical or functional independence that might represent a valuable opportunity to carry out interventions to reduce the progress of sarcopenia and prevent physical disability.

Keywords:
Sarcopenia, Circulating Cell-Free Nucleic Acids , Biomarkers

P1052

Personalized Medicine in Cancer

bahar naghavi gargari
shahid beheshti university of medical sciences : bnaghavi@sbmu.ac.ir

Abstract:
Introduction Cancer has important effects on individuals and society. Personalized medicine is used to learn about a person's genetic makeup and how their tumor grows. Using this data, doctors hope to find prevention, screening, and treatment strategies that may be more effective. They also want to find treatments that cause fewer side effects than the standard options. Content Before personalized medicine, most patients with a specific type and stage of cancer received the same treatment. However, it became clear that some treatments worked better for some patients, than for others. The growth in the field of genetics has led researchers to find genetic differences in people and their tumors. Personalized cancer treatment is now an active part of the treatment plan or as part of a clinical trial. Creating a personalized cancer screening and treatment plan includes: • Determining the chances that a person will develop cancer and selecting screening strategies to lower the risk • Matching patients with treatments that are more likely to be more effective and cause fewer side effects • Predicting the risk of recurrence, which is the return of cancer • Some examples of personalized medicine strategies for cancer include the following: • Targeted treatments , Pharmacogenomics. • With our increased knowledge of the human genome, physicians can analyze a patient's genetic makeup—especially with careful consideration to the tumor cells, which can be just as genetically unique—and individualize therapy to treat specifically that patient and that tumor. Conclusion • Personalized medicine aims to have treatments tailored specifically to the patients' individual needs based on their genetic information with the goal of improving outcomes and reducing adverse reactions. • So, treating cancer cannot be classified with a standard approach. • Personalized medicine and genetic characterization of tumours can also help to direct the development of novel drugs.

Keywords:
cancer, personalized medicine

P1053

Evaluation Study of SRA Long non-coding RNA in Breast Cancer Patient and Healthy People

Asghar Arshi[1] ، Dr Milad Khoramian Ghahfarokhi[2] ، Fatemeh Sadat Sharifi[3] ، Mina Dehghani Samani[4] ، Sara Ostovari[5]

1) Young Researchers and Elite Club, Shahrekord Branch, Islamic Azad University, Shahrekord, Iran : asghararshi@yahoo.com
2) Department of Pathobiology, School of Veterinary Medicine, University of Shiraz, Shiraz, Iran
3) Biotechnology Research Center, School of Basic Sciences, Islamic Azad University of Shahrekord Branch, Shahrekord, Iran
4) Young Researchers and Elite Club, Shahrekord Branch, Islamic Azad University, Shahrekord, Iran
5) Department of Microbiology, Jahrom Branch, Islamic Azad University, Jahrom, Iran

Abstract:
Background: Breast cancer entails 10% of all cancers in the world. Among all types of cancers, 30 percent of women are infected with breast cancer. Non-coding of long RNA (lncRNA) is a new group of known genes in the human genome transcribed from large parts of the genome of eukaryotes and play an important role in the regulation of different biological processes. The aim of the present study was to compare the expression level of SRA lncRNA in normal and neoplastic samples from breast cancer patients by RT-qPCR. Methods: In the present case-control study, 40 samples from patients with breast cancer tumor and 40 patients from non-tumor under the direct supervision of a pathologist specialist due to clinical presentation and laboratory findings were collected. After extracting RNA from normal and tumor tissues, cDNA synthesis method according to the protocol and RT-qPCR was performed by SYBR®Premix Ex TaqTM II kit. LncRNA expression levels of SRA gene was calculated using ΔΔCT. Data were analyzed using t-test. Results: The results of Real Time Reverse transcription-PCR indicated that the mean relative expression levels of SRA lncRNA gene in tumor samples compared to normal was overexpressed. This variation gene expression of SRA lncRNA related to about 1.5 times in tumor samples compared to healthy group. Conclusion: Due to the previous reports, this lncRNAs act as tumor suppressor in breast cancer and had differential expression in tumor and normal tissues, which could be used as biomarker for cancer diagnosis. Moreover, expression of these lncRNAs in different breast cancer subtypes and patient with other blood raises the importance of this molecules as a biomarker for cancer diagnosis and prognosis.

Keywords:
Breast cancer, LncRNA, SRA, RT-qPCR

P1054

Life style in personalized medicine

bahar naghavi gargari

shahid beheshti university of medical sciences : bnaghavi@sbmu.ac.ir

Abstract:

Topic : Life style in personalized medicine Authors : *BaharNaghavi Gargari Affiliation : ShahidBeheshti University of Medical Sciences Email : bnaghavi@sbmu.ac.ir Introduction It has been estimated that over 80% of health care spending is directly related to the treatment of conditions rooted in poor lifestyle choices. Chronic diseases such as hypertension, heart disease, stroke, type 2 diabetes, obesity, osteoporosis, and many types of cancer are among the most common, costly and preventable of all health conditions. Dysinger states it succinctly that lifestyle medicine is “the application of simple, natural healing approaches to chronic disease and prevention.” Content Egger refers to lifestyle medicine as “the application of environmental, behavioural, medical and motivational principles to the management of lifestyle-related health problems in a clinical setting include the identification of genetic variants and/or functional biomarkers for the purpose of designing patient-specific prescriptions for diet, exercise, stress, and environment. It is worthwhile to question whether these standardized public health positioning statements are sufficient to meet the diversity of the average individual, including addressing the multitude of variables such as age, lifecycle, gender, medical history, family history, vitamin and mineral status, ethnic background(s), lifestyle habits, genetics, single nucleotide polymorphisms (SNPs), mutations, and epigenetics. Conclusion Personalized lifestyle medicine can provide solutions to chronic health problems by harnessing innovative and evolving technologies based on recent discoveries in genomics, epigenetics, systems biology, life and behavioral sciences, and diagnostics and clinical medicine. Personalized lifestyle medicine may provide a novel means of addressing a health of patient by empowering them with information they need to regain control of their health.In conjunction with being a compelling solution to the chronic disease epidemic and allowing the patient to have control of their health, lifestyle medicine therapies have been shown to be cost effective. Keywords : lifestyle, personalized medicine, epigenetics.

Keywords:
lifestyle, personalized medicine, epigenetics

P1056

Competition of HOTAIR LncRNA in Breast Cancer using RT-qPCR

Fatemeh Sadat Sharifi[1] ، Milad Khoramian Ghahfarokhi[2] ، Asghar Arshi[3] ، Sara Ostovari[4]

1) Biotechnology Research Center, School of Basic Sciences, Islamic Azad University of Shahrekord Branch, Sharekord, Iran
fatemeh.sharifi12@yahoo.com
2) Department of Pathobiology, School of Veterinary Medicine, University of Shiraz, Shiraz, Iran
3) Young Researchers and Elite Club, Shahrekord Branch, Islamic Azad University, Shahrekord, Iran
4) Department of Microbiology, Jahrom Branch, Islamic Azad University, Jahrom, Iran

Abstract:

Background: Breast cancer is the most common invasive cancer in females worldwide. It accounts for 16% of all female cancers and 22.9% of invasive cancers in women. 18.2% of all cancer deaths worldwide, including both males and females, are from breast cancer. The aim of this study was to compare the expression level of HOTAIR lncRNA in normal and neoplastic samples from breast cancer patients by RT-qPCR. Methods: In the present case-control study, 40 samples from patients with breast cancer tumor and 40 patients from non-tumor under the direct supervision of a pathologist specialist due to clinical presentation and laboratory findings were collected. After extracting RNA from normal and tumor tissues, cDNA synthesis method according to the protocol and RT-qPCR was performed by SYBR®Premix Ex TaqTM II kit. LncRNA expression levels of genes HOTAIR was calculated using ΔΔCT. Data were analyzed using t-test. Results: The results of Real Time Reverse transcription-PCR indicated that the mean relative expression levels of HOTAIR lncRNA gene in tumor samples compared to normal was overexpressed. This variation gene expression of HOTAIR lncRNA related to about 3.2 times in tumor samples compared to healthy group. Conclusion: Due to the previous reports, this lncRNAs act as tumor suppressor in breast cancer and had differential expression in tumor and normal tissues, which could be used as biomarker for cancer diagnosis. Moreover, expression of these lncRNAs in different breast cancer subtypes and patient with other blood raises the importance of this molecules as a biomarker for cancer diagnosis and prognosis.

Keywords:
Breast cancer, LncRNA, HOTAIR, RT-qPCR

P1057

Common low-penetrance risk variants associated with breast cancer in Persian women

Hamidreza Agha heydarali naghash[1] ، Ali Salehzadeh[2] ، Ashkan Alborzi[3] ، Shima Forouzan[3] ، Ali Hajizadeh[3] ، somayeh Saeidi[3] ، Behrouz Mohammadi[3] ، Bahareh Abbasi[4] ، Nafiseh Ansarinejad[5] ، Massoud Houshmand[4]

1) Karaj Branch, Islamic Azad University,Karaj,Iran
2) Department of Biology, Rasht Branch, Islamic Azad University, Rasht, Iran
3) Islamshahr Branch, Islamic Azad University, Islamshahr, Iran
4) National Institute of Genetic Engineering and Biotechnology (NIGEB),Tehran,Iran : massoudh@nigeb.ac.ir
5) Iran University of Medical Sciences, Tehran,Iran

Abstract:

Breast cancer is a disease caused by a complex combination of genetic and environmental factors.

Several genes are known to be associated with increased susceptibility to breast cancer , including BRCA1 (Breast cancer 1 gene), BRCA2 (Breast cancer 2 gene), ATM (ataxia-telangiectasia mutated gene) etc., but only about 5% of breast cancer incidence can be explained by these high-penetrance mutations.Therefore, the identification of low-penetrance genes/loci may have a significant impact on breast cancer risk estimation.

Single nucleotide polymorphisms (SNPs) lead to genetic differences in breast cancer susceptibility among women from different ethnicities. In unselected breast cancer patients, genome-wide association studies have identified low penetrance, high frequency SNPs that are associated with breast cancer risk.

A recent multi-stage genome-wide scan for associations has identified five low-penetrance loci that are strongly associated with breast cancer in populations of diverse ethnicity.

Four of them contain plausible causative genes FGFR2 (fibroblast growth receptor 2), TNRC9 (Trinucleotide repeat-containing 9), MAP3K1 (mitogen-activated protein kinase 3 K1), and LSP1 (lymphocyte-specific protein 1).
In this study, the associations between FGFR2 (rs2981582, rs1219648),MAP3K1(rs889312),TOX3 (rs3803662, rs8051542,rs12443621,rs3104746,rs4784227) and LSP1 (rs3817198) polymorphisms and breast cancer risk will validate in our Persian population.

Keywords:
Breast cancer , SNP, FGFR2 ,MAP3K1 ,LSP1

P1059

Genetic variants at 5p12 (rs4415084 T/C and rs10941679 A/G) and risk of breast cancer in Persian women

Hamidreza Agha heydarali naghash[1] ، Ali Salehzadeh[2] ، Bahareh Abbasi[3] ، Nafiseh Ansarinejad[4] ، Massoud Houshmand[4]

1) Karaj Branch, Islamic Azad University,Karaj,Iran : hamidnaghash@yahoo.com
2) Department of Biology, Rasht Branch, Islamic Azad University, Rasht, Iran
3) National Institute of Genetic Engineering and Biotechnology (NIGEB),Tehran,Iran
4) Iran University of Medical Sciences, Tehran,Iran massoudh@nigeb.ac.ir

Abstract:

Breast cancer (BC) is one of the most commonly occurring epithelial malignancies in women, with an estimated 1 million new cases and over 400,000 deaths annually worldwide. Despite
much investigation, the causes are not yet fully understood. Accumulated evidence suggests that multiple genetic and environmental factors, as well as the interplay between these factors,
determine the phenotype.
Single nucleotide polymorphisms (SNPs) lead to genetic differences in breast cancer (BC) susceptibility among women from different ethnicities. The present study aimed at investigating the involvement of SNPs at chromosome 5p12.
A genome-wide association study, conducted among women of European ancestry, has identified two single-nucleotide polymorphisms (SNPs) rs4415084 (T/C) and rs10941679 (A/G) at chromosome 5p12 were associated with risk of breast cancer, suggesting that genetic variants in this region may have a role in the development of breast cancer.
The single nucleotide polymorphism 5p12-rs10941679 has been found to be associated with risk of breast cancer, particularly estrogen receptor (ER)-positive disease.Another study direct by Thomas et al.9 confirmed the single-nucleotide polymorphism.
(SNP) rs4415084 might affect breast cancer risk in the European population. Both rs4415084 and rs10941679 conferred significantly greater risks of ER-positive breast cancer than of ER-negative tumors.The biological mechanism through which genetic variations in 5p12 influences BC risk remains unclear.

To investigate the associations between SNPs at 5p12 and risk of breast cancer in the Persian women, we will conduct in 5p12 polymorphisms (rs4415084 and rs10941679) using a genotype these SNPs with a case–control study in the Iranian population.

Keywords:
Breast cancer ,5p12,SNP,genetic variations

P1061

Carriers of SMA with apparently normal MLPA result: Co-existence of deletion /duplication

Zohreh Sharifi[1] ، Hanieh Noferesti[2] ، Sara Amini[3] ، Sormeh Pourtavakoli[3] ، Maryam Abiri[4] ، Sirus Zeinali[5]

1) Kawsar Human Genetics-Department of Genetics, Tehran Medical Sciences Branch, Islamic Azad University, Tehran, Iran
2) Kawsar Human Genetics Research Center (KHGRC), Tehran, Islamic Republic of Iran,
3) Dr Zeinali's Medical Genetics Lab, Tehran, Islamic Republic of Iran
4) Department of Medical Genetics, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran-Dr Zeinali's Medical Genetics Lab, Tehran, Islamic Republic of Iran
5) Department of Molecular Medicine, Biotech Research Center, Pasteur Institute of Iran, Tehran, Islamic Republic of Iran,Kawsar Human Genetics Research Center (KHGRC), Tehran, Islamic Republic of Iran : sirouszeinali@yahoo.com

Abstract:

Spinal Muscular Atrophy (SMA) is the second most common autosomal recessive genetic disorder with a 1:50 carrier frequency. Deletion /duplication changes in SMN gene are common features in SMA patients. MLPA (Multiplex Ligation-dependent Probe Amplification) is a robust method for investigation of copy number changes because it not only deals with investigating the SMN1 gene but also adjacent genes such as NIPE, GTFH2 and SMN2.

Patients with definite diagnosis of SMA were referred to Dr. Zeinali's Medical Genetics laboratory. Genetic testing of possible deletion/ duplication was performed with MLPA kit (P021, MRC-Holland) based on manufacture protocol.

Analysis of data in 80 probands revealed 5 unrelated cases with homozygous deletion of SMN1gene. Further investigation of their parents revealed a heterozygous deletion in one parent and a normal MLPA result in another (i.e. two copy of SMN1 gene). The results were unexpected findings in an autosomal recessive disorder. Paternity and/or maternity were tested and confirmed.

Further analysis of the grandparents showed that the parents inherited both deletion/ duplication from one of their parents. So they have 2 copies of SMN1 genes in a chromosome (dup) and no copy on the other one.

Due to high carrier frequency of SMA in highly consanguineous population as Iran, co-existence of del/dup must be highly considered. It seems that performing genetic testing of the only in patients is not sufficient and investigation of the parents is also necessary to have reliable results especially for next pregnancies.

Keywords:

Spinal Muscular Atrophy (SMA), Multiplex Ligation-dependent Probe Amplification (MLPA), deletion (del), duplication (dup)

P1062

Frequency of compound heterozygote PAH mutations in Iranian first cousin marriages

Hanieh Noferesti[1] ، Zohreh Sharifi[1] ، Tina Shirzad[1] ، Marziyeh Mojbafan[1] ، Maryam Abiri[2] ، Sirus Zeinali[3]

1) Kawsar Human Genetics Research Center (KHGRC),Tehran,Iran
2) Department of Medical Genetics, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
3) Kawsar Human Genetics Research Center (KHGRC),Tehran,Iran : zeinalipasteur@yahoo.com

Abstract:

Phenylketonuria (PKU) is one of the most common in born error of metabolism of amino acid catabolism with autosomal recessive inheritance. Mainly the disease causation is located in the phenylalanine hydroxylase (PAH) gene. The gene is involved in breaking down of phenylalanine. PKU is mostly a curable disorder, so is crucial in patient management and can prevent disease consequences. Untreated individuals show different levels of mental and physical retardation. Genetic testing is not only necessary to confirm the clinical diagnosis but also helps prenatal diagnosis (PND) and preimplantation genetic diagnosis (PGD) for at risk families. Iran is a country with 38.4% consanguineous marriages. So, it is expected to have higher rate of autosomal recessive disorder.

National newborn screening program of PKU has been in practice since 2007 in Iran. 4200 patients with clinical diagnosis of PKU were referred to Dr.Zeinali's medical genetic laboratory since 2012.Direct sequencing of the PAH gene was performed using specific primers amplifying exons and the exon-intron boundaries in the affected children and results were confirmed by segregation analysis of the mutation(s) in the family.

Initial investigation of the pedigrees revealed 403 cases with first cousin marriages. Among them, 19 patients were found to have a compound heterozygote mutation (4.7%). Totally 38 different types of mutations were found. Most of them were recurrent point mutations and rarely small deletions. So genetic testing confirmed the clinical diagnosis of PKU.

According to the inheritance pattern of the disease and the close consanguinity of the parents, it is expected that just homozygote mutations can justify the disease causation. However, it seems that due to the Iranian population, it is possible to see compound heterozygous mutations even in first cousin marriages.

Keywords:

Phenylketonuria (PKU),metabolism,prenatal diagnosis (PND) ,preimplantation genetic diagnosis (PGD)

P1063

Possible role of genetic variant inTLR4 (rs4986790) in protection against toxoplasmosis

Dr Elnaz Asghari[1] ، Hamidreza Agha heydarali naghash[2] ، Parviz Shayan[3] ، Seyed Shapoor Reza Shojaei[1] ، Massoud Houshmand[4]

1) Islamic Azad University,Karaj
2) Karaj Branch, Islamic Azad University,Karaj,Iran : hamidnaghash@yahoo.com
3) Faculty of Veterinary Medicine, Tehran University,Tehran,Iran
4) National Institute of Genetic Engineering and Biotechnology (NIGEB),Tehran,Iran

Abstract:

Toll-like receptors (TLRs) are highly conservedtransmembrane protein receptors that mediate innateimmunity for hostTLR is a major arm of the innate immune system in sensing pathogen associatedmolecular patterns (PAMP's) and activates the immune system to contain the infections.

TLR/MyD88 signaling has been reportedas the key pathway in a non-specific antimicrobial responseagainst T. gondiiThere are currently 10known human TLRs, each of them contributing tospecific recognition of particular pathogen-associatedmolecular patterns.

As one member of the TLRsfamily, TLR4 widely expresses on macrophages,monocytes,cardiomyocytes,airway epithelial,adipose tissue, skeletal muscle and vascular endothelialand smooth muscle cells.TLR4 plays a key role in theprocess of the innate immune response, and activatesthe inflammatory cell via the NF-κB pathway byinducing the expression of a variety of cytokines andother molecules crucial to immune responses.

The glycosylphosphatidylinositol(GPI) of T. gondii was demonstrated to trigger TLR4 signaling
Pathways.In inflammatory monocytes, T. gondii infectioninduced the production of interferon (IFN)-β throughTLR4 and MyD88 signaling.

The purpose of this investigation will the determinationof the distribution of genotypes at single nucleotide-polymorphism (SNP) of the toll-like receptor 4 (TLR4)in humans infected with Toxoplasma gondii and the identificationof genetic changes predisposing to infection. development.

Considering the role of TLR molecules in the developmentof T. gondii infection, as well as TLR genetic changes, we will decideto describe in this report theprevalence rates of the genotypeand alleles at the TLR4896 A>G SNP (rs4986790) in women infected with T. gondii in IRAN and comparethem to the prevalence rates observed in women uninfected controls.

Keywords:
TLR4 ,SNP,GPI,Toxoplasma gondii

P1064

Genetic variants in LSP1(rs3817198) and MAP3K1(rs889312) are associated with the risk of breast cancer in Iranian population

Dr Behrouz Mohammadi[1] ، Mojgan Hoseini[2] ، Hamidreza Agha heydarali naghash[3] ، Massoud Houshmand[4] ، Bahareh Abbasi[4] ، Nafiseh Ansarinejad[5]

1) Islamic Azad University, islamshahr
2) Islamshahr Branch, Islamic Azad University, Islamshahr, Iran
3) Karaj Branch, Islamic Azad University,Karaj,Iran : hamidnaghash@yahoo.com
4) National Institute of Genetic Engineering and Biotechnology (NIGEB),Tehran,Iran
5) Iran University of Medical Sciences, Tehran,Iran

Abstract:

Breast cancer arises as a result of multiple somatic molecular events that can be genetic or epigenetic. Breast cancer is a polygenic disease and has a component of inheritance due to low-penetrance and common genetic variants.
Single nucleotide polymorphisms (SNPs) lead to genetic differences in breast cancer susceptibility among women from different ethnicities. The present study aimed at investigating the association of SNPs of two genes, MAP3K1 (mitogen-activated protein kinase kinase kinase1) and LSP1 (lymphocyte-specific protein 1) with risk of breast cancer in Persian women.
One of these genes, lymphocyte-specific protein 1 (LSP1), is located on chromosome 11p15.5. It encodes an F-actin bundling cytoskeletal protein expressed in hematopoietic and endothelial cells.
The association between the LSP1 rs3817198 T > C polymorphism and breast cancer risk has been widely investigated, but remains controversial.
This SNP seemed to play a more prominent role in high-risk cases. To date, many studies have evaluated the potential role of LSP1 genotypes in breast cancer development and the risk modification of the effect by the rs3817198T/C polymorphism of this gene. rs3817198 showed strong associations with ER-positive than ER-negative tumors in populations of European ancestry.

The MAP3K1 gene, encodes a serine/threonine protein kinase that activates the ERK, JNK and NF-Kb pathways.
Garcia-Closas et al. have found that MAP3K1 variants were relevant in estrogen receptor (ER)-positive tumors to a greater degree than in ER-negative tumors. The rs889312-C allele showed to be a risk factor for the development of breast cancer in European and Asian ancestry populations,but not in Africans.
It is possible that a low-risk allele not only influences the chance of developing breast cancer but also influences tumour characteristics such as invasiveness.
We will evaluate the associations among MAP3K1 rs889312-C allele and LSP1 rs3817198 T > C polymorphism with breast cancer risk in breast cancer cases and controls in IRAN.

Keywords:
Breast cancer,MAP3K1 ,LSP1 ,SNP,

P1065

Association of genetic variant (rs4784227) at TOX3 gene with the risk of breast cancer in Iranian population

Dr Ali Hajizadeh[1] ، Mojgan Hoseini[2] ، Hamidreza Agha heydarali naghash[3] ، Massoud Houshmand[4]
1) Islamic Azad University, islamshahr
2) Islamshahr Branch, Islamic Azad University, Islamshahr, Iran
3) Karaj Branch, Islamic Azad University,Karaj,Iran : hamidnaghash@yahoo.com
4) National Institute of Genetic Engineering and Biotechnology (NIGEB),Tehran,Iran

Abstract:
Breast cancer is one of the most common malignancies, ranking first in incidence and second in mortality for all cancers diagnosed among women in worldwide. Genetic factors play an important role in the etiology of breast cancer.
TOX3, a gene of uncertain function containing a tri-nucleotide repeat motif, encodes a
putative high-mobility-group (HMG) box motif nuclear protein, suggesting that it might act as a
transcription factor that may be involved in calcium-dependent transcription. Its protein expression has been suggested to predict breast cancer metastasis to bone. Recent studies has provided strong in vitro evidence implicating TOX3 rs4784227 as a functional variant for breast cancers in Asian women.

SNP rs4784227 is located 18.4 kb upstream of the TOX3 gene and in the evolutionarily-conserved region of intron of the LOC643714 gene. Although in European Americans rs4784227 is in strong linkage disequilibrium (LD) with one of the previously-reported SNPs, rs3803602, the positive association of rs4784227 with breast cancer remained after adjusting for previously-reported SNPs.

In vitro experiments showed that risk allele T reduced luciferase activity and altered DNA-protein binding patterns. These results implicate rs4784227 as a functional genetic risk variant for breast cancer, and this SNP may explain, at least partially, the association of breast cancer with other SNPs identified in 16q12.1.

Jirong Long et al. identified SNP rs4784227 as highly significantly associated with breast cancer in both Asians (per allele OR= 1.25, 95% CI = 1.20–1.31, P = 3.2610225) and European Americans (per allele OR= 1.19, 95% CI =1.09–1.31, P =1.361024). SNP rs4784227 is located at 16q12.1, a region reported previously to harbor breast cancer genetic risk variants among European descendents.

In this breast cancer case–control study of Persian women, we investigate the associations of one candidate SNP of TOX3 (rs4784227) and risk of sporadic breast cancer in IRAN.

We will genotype one polymorphism (rs4784227 with the risk T allele) of the TOX3 gene using TETRA ARMS-PCR to determine whether previously identified breast cancer susceptibility allele are associate with sporadic breast cancer in the Iranian population.

Keywords:
Breast cancer , TOX3, 16q12.1,SNP

P1066

Risk-Association of Two SNPs in TOX3/ LOC643714 (RS3803662 and RS12443621) With Breast Cancer in IRAN

Dr Ashkan Alborzi[1] ، Shima Forouzan[2] ، Mojgan Hoseini[2] ، Hamidreza Agha heydarali naghash[3] ، Massoud Houshmand[4] ، Bahareh Abbasi[4] ، Nafiseh Ansarinejad[5]
1) Islamic Azad University, islamshahr
2) Islamshahr Branch, Islamic Azad University, Islamshahr, Iran
3) Karaj Branch, Islamic Azad University,Karaj,Iran : hamidnaghash@yahoo.com
4) National Institute of Genetic Engineering and Biotechnology (NIGEB),Tehran,Iran
5) Iran University of Medical Sciences, Tehran,Iran

Abstract:
Breast cancer is recognized as one of the most common malignancies in women worldwide. The TOX3 gene was one of the first breast cancer regions to be identified through studies in populations of European and East Asian origin. Evidence on the role of TOX3 as a breast cancer susceptibility gene has been contradictory.

It is a gene located at chromosome 16q12, of uncertain function, and a newly described risk factor for breast cancer. TOX3 contains a putative high-mobility group box motif, suggesting its potential to play the role of transcription factor. It has been implicated in breast cancer metastasis of the bone.

Easton et al. observed that SNPs rs3803662 and rs12443621, yielded convincing evidence of association with increased risk of breast cancer.

SNP rs3803662 lies 8 kb upstream of TOX3, and SNP rs12443621 is located in an linkage disequilibrium (LD) block containing the 59 end of TOX3. TOX3 rs3803662 was observed to be associated with an increased risk of breast cancer in both BRCA1 and BRCA2-mutation carriers. SNP rs12443621 was identified to increase breast cancer risk by Easton et al. and was in strong LD with SNP rs3803662 in the TOX3 gene.

Studies showed that rs3803662C/T in TOX3 on 16q12 was associated with increased estrogen receptor (ER) positive breast cancer risk, especially in ER positive breast cancer.

In this breast cancer case–control study of Persian women, we investigate the associations of two candidate SNPs of TOX3 (rs3803662C/T and rs12443621A/G), and risk of sporadic breast cancer in IRAN.

We will genotype two polymorphisms (rs3803662C/T and rs12443621A/G) of the TOX3 gene using TETRA PRIMER ARMS-PCR to determine whether previously identified breast cancer susceptibility alleles are associated with sporadic breast cancer in the Iranian population.

Keywords:
Breast cancer ,TOX3 ,16q12,SNP

P1067

The importance of cell culture as a new approach in personalized drug therapy of oral cancer

Neda sadat Gohari[1] ، Meysam Ganjibakhsh[2]

1) Iranian Biological Resource Center
2) Human and Animal cell Bank, Iranian Biological Resource Center (IBRC), ACECR, Tehran : meysam_ganjy@yahoo.com

Abstract:
Background: Oral cancer is considered to be one of the most prevelant in neck and head cancers. Oral Squamous Cell Carcinoma (OSCC) consist more than 90% of oral cancers diagnosed. Up to now, evaluation of tumors is done by investigating formalin-fixed, paraffin-embedded and freezed tissue samples, which is basically a snapshot of cells and is not suitable for comprehensive studies. One of the approperiate approaches in treating cancers is use of cell culture in diagnosis and targeted therapy.In this study, the ten cell lines were produced from oral cancer tissues for studies on drug effectiveness

Materials and Methods: After obtaining tissue samples from oral cancer patients, cells were isolated using enzymatic digestion and explant culture. After quality control of cells, characterization and authentication of OSCC cells were determined by STR, karyotyping, species identification, growth, morphology and expression of CD326 and CD133 markers as squamous cell cancer markers.

Results: Cells obtained in this study were epithelial-like and had population doubling time (PDT) 30±2.5 hours. Flowcytometry analysis showed that cells were positive for CD326 and CD133 markers. Also, all cells were negative for mycoplasma, bacteria and fungi contaminations. All cells were banked at Human and Animal Cell bank, Iranian Biological Resource Center.

Conclusion: It can be gathered from the results of this study that the established cell lines would provide an extremely valuable in vitro models for studying carcinogenesis pathways of OSCC in Iranian population and it can be considered as a proper method in personalized drug therapy.

Keywords:
oral cancer, cell culture, characterization, authentication

P1068

Genetic variants in KITLG and BAK1 predisposes to testicular germ cell cancer

Dr Mohammad reza Nasehi[1] ، Hamidreza Agha heydarali naghash[2] ، Massoud Houshmand[3]

1) NOOR DANESH UNIVERSITY
2) Karaj Branch, Islamic Azad University,Karaj,Iran : hamidnaghash@yahoo.com
3) National Institute of Genetic Engineering and Biotechnology (NIGEB),Tehran,Iran

Abstract:
Testicular germ cell tumor (TGCT) is the most common malig nancy in men aged 15–45. There are two major subgroups of TGCT: seminomas (comprising 50% of cases), which resemble the primary germ cells from which they are derived, and non-seminomas (comprising 40% of cases), which display varying degrees of differ entiation, from embryonal carcinoma through to teratoma. About 10% of tumors contain mixed histology. Single nucleotide polymorphisms (SNPs) lead to genetic differences in TGCT susceptibility among men from different ethnicities.
Genome-wide association studies (GWAS) of TGCT have identified eight associated SNPs at six loci, which together account for >11% of the genetic risk of TGCT. These loci reside at 12q21 (encompassing KITLG), 5q31 (SPRY4), 6p21 (BAK1), 5p15 (TERT and CLPTM1L), 12p13 (ATF7IP) and 9p24 (DMRT1).
In the present study, we validate the associations between KITLG and BAK1 in persian population. To find susceptibility loci for TGCT, we selected and identify the genetic variants in candidate genes (KITLG and BAK1) .

KITLG (also known as stem cell factor or steel), which encodes the ligand for the membrane-bound receptor tyrosine kinase KIT. rs995030 is within the 3′ untranslated region of KITLG.

rs210138 on chromosome 6 falls within an intron of BAK1 (BCL2-antagonist/
killer 1), which encodes a protein that promotes apoptosis by binding to and antagonizing
the apoptosis repressor activity of BCL2 and other antiapoptotic proteins.

We will develop a system for detection and study the allele and genotype frequencies of the KITLG (rs995030) and BAK1 (rs210138) genes in patients with TGCT and compare with men
without TGCT.

Keywords:
TGCT,KITLG,BAK1,polymorphism,SNP,VARIANT

P1069

Investigation of variation in D-loop region of Mitochondrial DNA in patients with Psychosis disorders

Faramarz Vejdandoost[1] ، Hanieh Noferesti[2] ، Parisa Azimi[2] ، Leila Akbari[3] ، Mahdieh Salimi[4] ، Masoud Houshmand[4]

1) Medical Biotechnology Research Center, Ashkezar Branch, Islamic Azad University, Ashkezar, Yazd, Iran
2) Medical Biotechnology Research Center, Ashkezar Branch, Islamic Azad University, Ashkezar, Yazd, Iran
3) Taban Clinic, Tehran, Iran
4) Department of Medical Genetics, National Institute of Genetic Engineering and Biotechnology (NIGEB), Tehran, Iran
housh62@yahoo.com

Abstract:
Mitochondrial dysfunctions affect tissues with high energetic demands such as skeletal muscle, cardiac muscle, and the central nervous system. A growing body of evidence suggests that there is mitochondrial dysfunction in schizophrenia and bipolar disorder. The D-loop of mitochondrial-DNA is a major control site for mtDNA expression. This region in different population is varied and contains essential transcription and replication elements and it could be used for detection of mother inheritance, and human evolution. The aim of present study was to analyses the D-loop region polymorphisms in patients with psychiatric disorders.
We analyzed the mutations at D-loop on the mtDNA in patients with psychiatric disorders. In a case-control study, our research on 24 patients and 463 normal people (controls), that all of them from Iranian population (Fars and non-Fars). The PCR-sequencing method was used to detection of variation in HV1 and HV2 regions on D-loop area.
From 51 observed polymorphisms in HV1 region; C16294T, C16292T and C16223T polymorphisms were significantly ($P<0.05$) associated with schizophrenia and bipolar disorder, and it may be a risk factor for psychiatric disorders in Iranian population. Moreover, our data revealed that there are not any associations between polymorphisms in HV2 region and psychiatric disorders; but there was a significant difference ($P<0.05$) in T204C between patient and Fars control group. The result suggests that polymorphisms in HV1 and HV2 in Iranian population can be a risk factor for psychiatric disorders such as schizophrenia and bipolar disorder.

Keywords:
D-loop, polymorphism, HV1, HV2, psychiatric disorders, Iranian

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P1070

The Role of Slit-Robo Signaling as a Therapeutic Target for Cancers

Flora Forouzesh[1] ، Seyed omidreza Mousavi[2]

1) Medical Genomics Research Center, Tehran Medical Sciences Branch, Islamic Azad University, Tehran, Iran : f8forouzesh@gmail.com
2) Tehran Medical Sciences Branch, Islamic Azad University, Tehran, Iran

Abstract:
Introduction & Aim: Slits are secreted proteins that bind to Roundabout (Robo) receptors. Slit-Robo interactions are involved in many pathological cellular processes, including cell cycle, apoptosis, cell adhesion, motility, angiogenesis and invasion, which are important for tumorigenesis, cancer progression and metastasis. The current available data suggest that the Slit-Robo pathway could be a promising target for development of anticancer drugs. The aim of this report is to summarize the studies of the role of Slit-Robo signaling in cancer progression, metastasis and therapeutic potential.
Method: the search was done in electronic databases using the following keywords: Slit-Robo pathway, cancers, anticancer, therapeutic, and personalized medicine.
Results: The current data show that Slit-Robo pathways differentially modulate invasion and migration, which varies according to signaling and type of cancers. On the other hand, in most of the cancer types, Slit-Robo acts as a tumor suppressor, except in some gastrointestinal cancers. The activation or suppression of the Slit-Robo pathway modulates several oncogenic pathways that are associated with the development and progression of cancer. The findings demonstrate the angiogenic function of Slit-Robo signaling indicate the effectiveness of blocking this signaling pathway in treating cancers. It can be translated to the diagnosis, treatment, and prevention of malignant tumors remains to be determined.
Conclusion: Data demonstrated the role of Slit-Robo signaling in tumor angiogenesis and have evaluated the significance of this signaling pathway in the pathogenesis of cancers. Results indicate therapeutic potential of understanding Slit and Robo signaling, and this is likely to remain an active area of investigation. Even though the road to Slits and Robos as potential drug targets or biomarkers of cancers is still long, but the hope is that such a personalized strategy in cancer therapy will replace the conventional one-size-fits-all cytotoxic chemotherapy approach.

Keywords:
Slit-Robo pathway, cancers, anticancer, therapeutic, and personalized medicine.

P1071

Evaluation of Gemcitabine pharmacogenetics effect among the patients affected by pancreatic cancer

Sahar Hasani[1] ، Saeid Morovvati[2]

1) Pharmaceutical sciences branch
2) Molecular Biology Research Center, Baqiyatallah University of Medical Sciences : morovvati@hotmail.com

Abstract:
Gemcitabine is an analog of deoxycytidine with the anticancer effect that is prescribed as a cure for different cancers among Pancreatic cancer that is one of the most aggressive and deadly malignancy cancer. Furthermore, this drug is profitable it can be as well as so toxic. Different genotype variations that are resulted by the polymorphisms of the genes coding the proteins contributing to the enzymatic pathways can affect the expression and function of the proteins that cause various responses in front of the Gemcitabine. One of these proteins is cytidine deaminase (CDA) that its gene is so polymorphic. The clearance of gemcitabine after taken up by the cancer cells driven up by rapid inactivation by CDA to its primary metabolite 2, 2-difluorodeoxyuridine (dFDU). Each of the different polymorphisms in the CDA gene contributes to its protein activity and can change the gemcitabine clearance process consequently. Considering the toxicity of gemcitabine, its accumulation throughout the body can cause severe poisoning even death among the patient. Pharmacogenetics and personal medicine help us to recognize phenotype- genotype correlation with correct recognition of each of the patient genotype and studying the effect of the polymorphisms on the cytidine deaminase protein activity; according to this correlation can prescribe the anti- cancer drug with appropriate dose and condition for each of the patients. With recent description, these proceedings prevent poisoning and patient death as well as can achieve to the best drug response. Studying the genotype- phenotype correlation between the cytidine deaminase gene and its common polymorphisms according to data are collected from other articles heretofore considered as our aim in this article. We are hopeful of reaching to a desirable conclusion by this collective information about gemcitabine Pharmacogenetics.

Keywords:
Gemcitabine. Polymorphisms. Pharmacogenetics. pancreatic cancer.

P1072

Personalized Medicine: From Biomarkers to progress in cancers and genetic disorders testing

Yadallah Dalvand[1] ، Mojtaba Khayam Nekouie[2] ، Atena Fazeli3 ، Majid Sadeghizadeh[2]

1) Medical Genetic Department of Center Infertility and Innovation of Mom. Tehran, Iran : dalvandyadola@yahoo.com
2) Faculty of Biological Science
3) Medical Genetic Department of Center Infertility and Innovation of Mom

Abstract:
In recent years, there has been an amazing increase in the number of use biomarkers in detection of genetic diseases and cancers. There are many papers indexed in PubMed.gov directly related to use of biomarkers. Although many of these papers refer to report clinically useful molecular biomarkers. Improvement in biomarker technology, coupled with the companion clinical diagnostic laboratory tests, continue to advance this field, where individualized and customized treatment suitable for each individual patient define the standard of care

Use of molecular biomarkers has excluded their widespread adoption in treatment. For example in Diabetic kidney disease, when the high risk of progressive renal function loss and end-stage renal disease for patients are important, molecular biomarkers can early identification of a renal risk. Therefor novel biomarkers may aid in improving renal risk stratification and other diseases. In other early detection of cancer can particularly reduce cancer mortality and saves lives.

In this review, focus on the novel biomarkers in renal disease such as primarily concentrating on assay-based multiple/panel biomarkers; proteomics biomarkers and metabolomics biomarkers are most important biomarker in early identification of a renal risk. instance

Cancer biomarkers included a broad range of biochemical compounds, such as nucleic acids, proteins, sugars, small metabolites, and cytogenetic and cytokinetic parameters, as well as entire tumor cells found in the body fluid.

These biomarkers can be used for risk evaluation, diagnosis, prognosis, and for the prediction of treatment efficacy and toxicity and recurrence.

As result, clinical predictions based on molecular biomarkers will be demonstrated on the clinician’s screen during the physician–patient interaction and patient outcomes. This will be an interest for the future identify novel biomarkers that can be used to monitor drug efficacy, generate information about the molecular mechanisms through which drugs exert their effects and provide insight into novel drug targets.

Keywords:
Molecular Biomarkers, Testing, Cancer, Diabetic kidney disease, diagnosis

P1073

An electrochemical nanobiosensor for early detection of breast cancer biomarker miRNA-21, using methylene blue as redox indicator, graphene oxide and polyaniline

Hossain-Ali Rafiee-Pour[1] ، Nafiseh Sharifi[2] ، Sedigheh Falahi[3]

1) Department of Molecular and Cell Biology, Faculty of Chemistry, University of Kashan, Kashan, Iran : rafieepour@kashanu.ac.ir
2) Department of Physics, University of Kashan, Kashan, Iran
3) Institute of Nanoscience and Nanotechnology, University of Kashan, Kashan, Iran

Abstract:

Small noncoding microRNAs (miRNAs) have emerged as ideal noninvasive biomarkers for early-phase cancer detection. In this report, Through combining the advantages of electrochemical methods and nanomaterials with the selectivity of the oligo-hybridization-based biosensors, a novel, label-free and simple electrochemical nanobiosensor for miRNA-21 detection have demonstrated, based on carboxylated graphene oxidized and polyaniline (PANI) modified glassy carbon electrode. The successfully immobilization of the single strand DNA (ss-DNA) probe and hybridization with the target miRNA sequence were confirmed by electrochemical cyclic voltammetry (CV) method. The reduction signals of methylene blue (MB) as a redox indicator, were measured by differential pulse voltammetry (DPV) method, and an increase in the peak current was observed after hybridization. the nanobiosensor showed high Specificity, and was able to discriminate sharply between complementary target miRNA, single-base mismatch, and non-complementary miRNA. Consequently, this strategy will be valuable for sensitive, selective and label-free detection of miRNA. The performance of the assay developed here could satisfy the need for rapid, easy, sensitive and specific early cancer diagnosis in clinical diagnostics.

Keywords:
Early detection, Breast cancer, MicroRNA-21, Electrochemical nanobiosensor, Graphene oxide, Polyaniline

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P1074

A common gene expression signature in three gastrointestinal malignancies: Gastric cancer, Colorectal cancer and Hepatocellular carcinoma

Dr Kaveh Baghaei[1] ، Nazanin Hosseinkhan[2] ، Hamid Asadzadeh aghdaei[1] ، Mohammad reza Zali[3]

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) Research Institute for Gastroenterology and Liver Diseases : hosseinkhan@ut.ac.ir
3) Gastroenterology and Liver Diseases Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract:

Recently traditional histopathologic characterizations of cancers is having been replaced by high throughput molecular based methods which study genome scale gene expressional pattern, copy number variations and epigenetic modifications. According to GLOBOCAN 2012, the incidence and the mortality rate of colorectal, gastric and liver cancers are the highest among the total gastrointestinal cancers. In this study in order to find common genes and pathways simultaneously dysregulated in the colorectal cancer, gastric cancer and hepatocellular carcinoma, we conducted differentially expression analysis between three high quality microarray gene expression datasets. The results showed 23 overlapping differentially expressed genes (DEGs) in three cancers. Inspecting the common inferred regulatory network of these genes in the understudied cancers resulted in the detection of two cases of potential feed forward loops (FFLs) indicating cross-talk between cancers associated pathways. The result of vulnerability test of the common protein protein interaction (PPI) network in the three cancers suggested three candidates which their simultaneous targeting will disintegrate the main parts of the network and consequently are potential options for efficient treatment strategies. In total the results of this study introduces new common potential biomarkers in colorectal cancer, gastric cancer and hepatocellular carcinoma that monitoring their expressional changes in suspicious patients can be helpful in prognosis of these gastrointestinal cancers at early stages .

Keywords:
common expressional pattern, gastrointestinal cancers, regulatory network, PPI network

P1076

Mutation spectrum in Iranian patients affected by Factor VII deficiency

Samaneh Ahmadi[1] ، Marzieh Mojbafan[1] ، Tina Shirzad[1] ، Faezeh Rahiminejad[1] ، Sara Gharib[1] ، Hamideh Bagherian[1] ، Sirous Zeinali[2]

1) Kawsar human genetic research center
2) Kawsar human genetic research center; Department of Molecular Medicine, Biotechnology Research Center, Pasteur Institute of Iran, Tehran, Iran : zeinalipasteur@yahoo.com

Abstract:
Factor VII deficiency is an autosomal recessive disorder caused by lack of protein called factor VII in the blood. It contributes to problems with blood clotting. Factor VII is certainly one of the proteins that lead to blood clotting in the coagulation cascade. It belongs to serine protease enzymes. Factor VII deficiency is a rare bleeding disorder that varies in severity between affected individuals. The signs and symptoms of this condition can begin at any age, although probably the most severe cases are apparent in infancy. However, as much as one-third of individuals with factor VII deficiency never show any sign of this disease The gene for factor VII is located on chromosome 13 (13q34). which encode a vitamin K-dependent factor critical for hemostasis.,. The present study aimed to analyze mutations in Factor VII in Iranian patients
Material and methods: In the present study, mutations in factor VII gene were analyzed in a total of 26 Iranian families referred to Human genetic research center. Informed consent for was obtained and DNA extraction was performed using salting out procedure. All exons and introns boundaries of the factor VII gene were sequenced using Sanger sequencing.

Results: We identified 3 different kinds of mutations including seven missense ,two nonsense , two deletion and an splicing mutations in Iranian patients referred to Human genetic research center.

Conclusion: The obtained results revealed high diversity of mutations in Iranian patients which increas our understanding about etiology of Factor VII deficiency in Iranian population and it could be helpful in genetic counseling and genetic diagnosis of this disease In Iran.

Keywords:
Factor VII deficiency, Iran, sequencing, blood clotting

P1078

Role of Personalized Medicine Approach in Traditional Medicine

Moloud Payab[1] ، Shirin Hasani-Ranjbar[2] ، Bagher Larijani[3]

1) Obesity and Eating Habits Research Center, Endocrinology and Metabolism Molecular -Cellular Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran
2) Obesity and Eating Habits Research Center, Endocrinology and Metabolism Molecular -Cellular Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran : shirihasanir@yahoo.com
3) Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

Abstract:
Personalized medicine means a right diagnosis and treatment at the right time with the right cost provided to a right individual. This therapy reduces the incidence of potential side effects, eliminate invalid treatments, improve the effectiveness of treatment and, ultimately, achieve optimum results in its health. Holistic, space-time dynamics and individual variance are three distinctive characteristics of traditional medicine.This medicine enjoys a holistic approach and is based on individual differences in which the concept of temperaments (Mizaj) is determinant. Like a fingerprint,all people have their own unique temperaments which affect their health condition.Temperament is made up of four basic elements whose interaction with each other, in specific ratios. This ratio can be extremely different.The basic elements are water, fire, soil, and wind. Temperaments are divided into 9 groups: moderate, warm, cold, dry, wet, warm and wet, warm and dry, cold and wet, cold and dry.The health of every individual depends on the maintenance of the temperament in a state of balance and imbalance in body temperament or distemperament that can be a cause of disease in humans. Internal and external factors such as ethnicity, age, gender, types of diet, lifestyle, weather, seasons and location can affect on these temperament. In the meantime, similar to any natural material such as food and beverage, the herbal medicines have their specific temperament. Individuals are needed to be categorized according to their different temperament and receive suitable treatment according to their temperament. A similar disease may have different presentations with different temperaments.Each herbal medicine may show specific response according to each person`s temperament. Therefore, one should also consider the temperament of that specific herbal medicine and compatible herbal medicines need to be prescribed according temperament of each individual patient. Accordingly, the type of medicinal plants and their doses can be different. Traditional medicine can be a main approach to personalized medicine in the future.Other advantages of personalized medicine in traditional medicine will be available to the public and at a lower cost.

Keywords:
Personalized Medicine Traditional Medicine Herbal Medicine

P1089

Involvement of MIR4301 in the DRD2 mediated tumor growth by in-silico analysis

naghmeh gholipour[1] ، ghasem ahangari[1]

1) national institute of genetic engineering and biotechnology (nigeb), tehran, iran : ghah@nigeb.ac.ir

Abstract:

Background: Various types of neoplasms including breast cancer exhibit of different profile changes in both mRNA and micro-RNA expression. The dopamine receptors are dysregulated in various human cancers, but the molecular mechanisms underlying dopamine receptors mediated tumor growth remain unclear. Here we examined the involvement of MIR4301 in the DRD2 mediated tumor growth by in-silico analysis.

Methods: To determine the gene targets of the differentially expressed miRNAs, we used three of the leading miRNA target prediction algorithms: mirwalk2, PicTar, and TargetScan. Mirwalk2 found the miRNA-target genes in the Carcinogenesis pathway and verified by KEGG pathways. KEGG pathway is derived from Kanehisa Lab, Kyoto University, Japan. This analysis is used to determine the position and role of this MIR4301 in controling carcinogenesis pathway. The position and function of genes in a pathway are crucial for recognizing the mechanism of intervention or regulation of MIR4301 in carcinogenesis.

We aligned DRD2 (ENST00000362072) and MIR4301 in NCBI database and found that this MIR located within the DRD2 intronic region. Structural and stability analysis of MIR4301 was conducted by using the online application Mfold.

Results: By using three target prediction tools, 9882 candidate genes were predicted for MIR4301 and all the predicted candidate genes were analyzed by pathways enriched analysis. KEGG and Panther pathways enrichment analysis showed that 36417 endometriosis-related miRNA targets were mainly cancer-related pathways RAS and PI3K pathway.

Conclusions: MIR 4301 is a 65 base-pair long non-coding RNA localized in chromosome 11 (nt: 113450023-113450088). Bioinformatics analysis has showed, DRD2 can be a potential target of MIR4301and suggested the probable effect of this microRNA in the regulation of DRD2 expression.

Keywords:
MIR4301, DRD2, cancer

P1080

Bioinformatics analysis of the Hsa-miR-875-5b upstream promoter region as a tumor suppressor in colorectal carcinoma (CRC)

Hadi Bamehr

Hamadan University of Medical Scinces : hbamehr@yahoo.com

Abstract:

The Expression of miR-875-5p down-regulated significantly in tumor tissues in primary stage of CRC. The anticancer effect of Hsa-miRNA-875-5p (miR-875-5p) has recently been discovered.recently studies have showed that this Mirna not only has an inhibiting role against cell proliferation, invasion, migration but also promoting apoptosis in colorectal carcinoma (CRC) mostly by targeting EGFR oncogene .but putative mechanism of miR-875-5p regulation on colorectal carcinoma (CRC) is unclear.

Method: The promoter region of miR-875-5p was obtained using the Ensemble database .CPG analysis was done using the byEMBOSS spgplot software. Target gene explored by three published algorithms, including Target Scan , Mirwalk, Mirdb ,Micron. Binding sites of transcription factors were predicted by several kinds of software of promoter analysis for promoter region.

Result: In this study we explored the regulation mechanism of microRNA has-mir-875-5b by bioinformatics analysis .The analytical results showed that has-mir-875-5b is an intergenic miRNA. Using the Ensemble database the length of the promoter region of has-mir-875-5b was predicted to be1543 bp. determining the locations and distances of the GC box, CCAAT box detected by using the Neural Network method ,and the location of TATA box was found to be in 537 bp.

No CpG island was found in the has-mir-875-5b promoter region with default parameters (Criteria used: Island sized > 100 bp, GC% > 50.0%, Obs/Exp > 0.6) therefor metilation has probably a poor role for transcription regulation. Seventy five transcription factor binding sites in the promoter region including (p53, E2F, Pea3, c-Jun, HNF-1A/B, c-Myb, RXR-alpha, NF-1, TBP, FOXP3 etc.) were discovered using different type of analytical software such promo algoritm. Coclosion :In this study The predictions of transcription factor binding sites ,cpg island analysis, and target gene of has-mir-875-5b provided significant data for further study of putative regulation mechanisms and they role Involved in CRC.

Keywords:
miR-875-5p,promoter,bioinformatic,colorectal cancer

The collected samples will be used for genomics, proteomics and metabolomics analyses in near future. The identification of patient-specific genome/proteome/metabolom profile may help to develop personalized health monitoring programs and design of individualized interventions

Keywords:
personalized medicine- biobank-risk factor-standard operating protocol, omics

P1082

Positive association of C16069T, T16519C and T152C variants in D-loop of mitochondria with recurrent pregnancy loss in Iranian population

Hanieh Noferesti[1] ، Parisa Azimi[1] ، Faramarz Vejdandoust[1] ، Maryam Abiri[2] ، Leila Akbari[3] ، Mahdieh Salimi[4] ، Masoud Houshmand[5]
1) Medical Biotechnology Research Center, Ashkezar Branch, Islamic Azad University, Ashkezar, Yazd, Iran.
2) Department of Medical Genetics, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
3) Taban Clinic, Tehran, Iran: +989128437235
4) Department of Medical Genetics, National Institute of Genetic Engineering and Biotechnology (NIGEB), Tehran, Iran
5) Department of Medical Genetics, National Institute of Genetic Engineering and Biotechnology (NIGEB), Tehran, Iran
housh62@yahoo.com

Abstract:
Recurrent pregnancy loss (RPL) is traditionally defined as three or more consecutive pregnancy losses before 20 weeks of gestation. In Iran, the incidence of recurrent miscarriage is about 3 to 4% of all pregnancies. Several genetic and non-genetic factors have been found to be associated with RPL. Mitochondria are intracellular organelles that have an important role in ATP production and apoptosis. However, a few studies have been performed to find the association between RPL and mitochondria. The identification of the genetic variants that confer risk for RPL is essential for the detection of individuals at high risk.

In this study, we investigated the association of variations of D-loop with RPL. 24 appropriate cases and 463 female controls from different ethnicities (Fars- Kurds- Lurs-….) were selected. DNA was extracted from blood samples taken from participant. Genotyping were performed using direct sequencing of HV1&HV2 regions .Results was analyzed using SPSS version 15 software.
The comparison of allele and genotype frequencies between cases and controls by Chi-square test revealed the T variant confer risk for the studied individual(C16069T , P-value <0.02)
Our findings, is consistent with a report from the study of the two variants (T16519C, T152C) studied by Seyyed Hassani et al.
According to the high mutation rate in D-loop and a regulatory role of this region, it seems that mutations in this region can disrupt cell survival. Therefore, these variants can be recommended as an additional factor for determining the risk of susceptibility to recurrent pregnancy losses.

Keywords:
Recurrent pregnancy loss(RPL), Mitochondria, D-loop, HV1, HV2

P1083

Cyp2c8 GENE POLYMORPHISM AT POSITION cyp2c8 2 805 (A → T) IN HEALTHY POPULATION OF WEST MAZANDARAN PROVINCE

Sarvenaz Sadeghi[1] ، Somayeh Assadian Narenji[2]
1) Department of Biology, Tonekabon Branch, Islamic Azad University, Tonekabon, Iran
2) Department of Biology, Tonekabon Branch, Islamic Azad University, Tonekabon, Iran Assadiansomayeh@hotmail.com

Abstract:
Personalized medicine is a form of medicine that uses information about a persons genes, proteins, and environment to prevent, diagnose and treatment of disease. The exact purpose of showing certain elements in personalized medicine is based on an individual analysis of genomic and biological factors and lifestyle person When you choose the right medication at the right time with the disease s treatment However, such tests can test applications in personalized medicine point out that CYP2C8 genotype of cytochrome P450 enzymes of the cytochrome P450 family plays an important role in the metabolism of a variety of exogenous and endogenous compounds and drugs .this study aimed to investigate common polymorphisms in gene cyp2c8a in healthy population of west Mazandaran province to determine the polymorphism of this gene in the population studied. A total of 200 unrelated healthy volunteers living in Tonekabon, Ramsar during the period January to March 94 were referred to the laboratory. 5 mL of peripheral blood was taken from each subject and DNA was extracted using phenol-chloroform method and the PCR-RPLP method for determining the genotype of the polymorphism CYP2C8 2 805 (A → T) was used. The frequencies of genotypes AA, AT, TT, respectively, 85%, 7.5%, 7.5%, respectively $P \leq 0.05$)) based on the results obtained in this study, among the 200 samples analyzed, the highest genotype is homozygous AA. The results of this study to understand the distribution polymorphism 805 (A → T) of the genes CYP2C8 2. Results also can help predict the risk of diseases such as cancer, cardiovascular disease, hypertension and parasites, and Falciparum drug metabolism and drug benefit in this population.

Keywords:
personalized medicine, cytochrome P450, CYP2C8 2, polymorphism, cancer

P1084

Pharmacogenomics and Treatment of common diseases

Atena Fazeli [1] ، Yadallah Dalvand[2] ، Amir Rezaghlizadeh[3] ، Mojtaba Khayam Nekouei[4]
1) Azad university of Damghan : atena.fazeli91@gmail.com
2) Molecular Genetic Department School of Biological Science Tarbiat Modares University. Tehran, Iran.
3) Patology Department of Baghiyyatollah-Azam Hospital, Tehran. Iran.
4) Faculty of Biological Science. Tarbiat Modares University. Tehran, Iran.

Abstract:
Pharmacogenomics has been widely recognized as fundamental steps toward personalized medicine. The clinical utility and applications of pharmacogenomics is at present particularly evident in some therapeutic areas. For example, anticancer drugs, psychotropic, and anticoagulants, instead of the old fall. The following are some of the gains that had been achieved, listed. Among the most common diseases in the world, cardiovascular disease, kidney disease, and diabetic nephropathy. ACE inhibitor treatment is clearly Reno protective. Furthermore, the ACE I/D polymorphism is a useful test to predict the progression of type 1 or type 2 diabetic nephropathy. Angiotensin -converting enzyme (ACE) is an enzyme involved in the renin-angiotensin-aldosterone and kinin-kallikrien pathways involved in blood pressure control. ACE inhibitors are used to treat cardiovascular and renal diseases, including hypertension. The high inter-individual variability in circulating ACE levels is explained, in large part, by the ACE I/D polymorphism. The D allele of the ACE I/D polymorphism is clearly associated with increased risk of diabetic nephropathy. By contrast, the associations of the ACE I/D polymorphism with hypertension and cardiovascular disease have been inconsistent. The ACE I/D polymorphism is a useful test to predict the renoprotective effect of ACE inhibitor or angiotensin receptor blocker treatment in patients with kidney disease. There is currently no evidence to support a role of the ACE I/D polymorphism in predicting future risk of cardiovascular events or blood pressure response to ACE inhibitors in the absence of renal dysfunction.

Among the selected pharmacogenes, two are nuclear hormone receptors, namely VDR and PXR. The role of nuclear receptors in renal diseases has been recently highlighted with an emphasis on carbohydrate metabolism, lipid metabolism, immune response and inflammation.

Keywords:
ACE inhibitors, cardiovascular disease, kidney disease, diabetic nephropathy

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P1085

Personalization of treatment and Investigation of Tumor Response Prediction to Simultaneous Neoadjuvant Chemo-radiation Therapy Using quantitative features derived from MRI images in colorectal Cancer Patients

Nastaran Sadeghi
kermanshah university of medical science. kermanshah.iran nastaran.sadeghi72@gmail.com

Abstract:
Background: Despite many advances in the field of diagnosis and treatment of colorectal cancer has been established as the leading cause of deaths from cancer. This type of cancer is the third cause of cancer and second leading cause of cancer death in developed countries so that 750,000 new cases of colorectal cancer and 350,000 cancer deaths in developing countries in 2015 are estimated. Personalized treatment and proper treatment in terms of characteristics and circumstances of each individual can make a big difference in improving the health of each patient. Needed to personalize the therapy and treatment regimens to achieve acceptable treatment is a quantitative information. The aim of this study was to extract quantitative information from tumor volume of MRI images in patients with colorectal cancer and determine the relationship between extracted image features and patients response to therapy.

Material and Methods: In this study, 54 patients with advanced colorectal cancer were recruited. All patients before initiating Simultaneous Neoadjuvant Chemo-radiation Therapy were imaged in the pelvic area with 1.5 tesla MRI system. Then, under the supervision of oncology patients treated with the standard treatment regimen of Simultaneous Neoadjuvant Chemo-radiation Therapy and 2 weeks after completion of treatment the tumor pathologic samples have been analyzed in the pathology lab for invasive response evaluation. In the final phase features extracted from images of the tumor volume and the relationship between response to treatment and features extracted from MRI images is studied.

Conclusions: features extracted from the target volume images accurately predict the response to treatment in patients with colorectal cancer and compared to the previous factors such as tumor size and length are more accurate.

Keywords:
personalized treatment, Response to treatment, Simultaneous Neoadjuvant Chemo-radiation Therapy, Colorectal

P1086

Association between polymorphism within the susceptibility region 8q24 and breast cancer in a Iranian population

Dr Somayeh Saeedi[1] ، Mojgan Hoseini[2] ، Hamidreza Agha heydarali naghash[3] ، Bahareh Abbasi[4] ، Nafiseh Ansarinejad[5] ، Massoud Houshmand[4]
1) Islamic Azad University, islamshahr
2) Islamshahr Branch, Islamic Azad University, Islamshahr, Iran
3) Karaj Branch, Islamic Azad University,Karaj,Iran : hamidnaghash@yahoo.com
4) National Institute of Genetic Engineering and Biotechnology (NIGEB),Tehran,Iran
5) Iran University of Medical Sciences, Tehran,Iran

Abstract:
Some cancer-associated SNPs are located in chromosomal regions that do not encode genes. One such SNP is rs13281615 at 8q24.21, whose association with breast cancer risk has been
confirmed in a number of studies in different ethnic groups.

The q24 band of chromosome 8 (8q24) is frequently amplified in human cancers including breast cancer, and several SNPs (single nucleotide polymorphisms) at 8q24, including rs13281615, have been identified for their association with cancer risks.

Easton et al. firstly identified a significant association between rs13281615 (8q24.21) and BC risk through a three-staged GWA study in a European population.

Although these risk alleles are located in a "gene desert," accumulating evidence supports the notion that these 8q24 genetic variants may affect MYC oncogene expression by altering its regulation or amplification status. The protooncogene MYC functions as a transcriptional activator. It is involved in a complex regulatory network modulating cell growth, differentiation, apoptosis, and other cellular responses.

At this SNP, the G-allele is the risk allele for breast cancer while the AA genotype has a protective effect (Gong et al., 2013).The GG genotype at SNP rs13281615 was associated with
estrogen receptor (ER) positivity, progesterone receptor (PR) positivity, lower tumor grade, and improved patient survival in previous studies (Garcia-Closas et al., 2008; Broeks et al., 2011), further suggesting a function of this SNP in breast cancer development.

We will genotype one 8q24 SNP (rs13281615) identified from
Recent publications to examine their relationships with BC risk among a
Iranian population.

Keywords:
Breast cancer, SNP,8q24,MYC

P1087

Cell-free fetal nucleic acid markers in maternal circulation

Mahboubeh Ramezan zadeh[1] ، Rasoul Salehi[2]

1) Department of Genetics and Molecular Medicine, School of Medicine, Bushehr University of Medical Sciences, Bushehr 751463341, Iran : mahboob.ra310@gmail.com
2) Department of Genetics and Molecular Biology, School of Medicine, Isfahan University of Medical Sciences, Isfahan 81744-176, Iran

Abstract:
Prenatal diagnosis is a critical issue of gynecological practice. To perform a genetic test in this field, it is necessary to obtain placental or fetal material. This material, currently, is achieved through invasive procedures such as chorionic villus sampling or amniocentesis. These invasive procedures carry 1% risk of miscarriage, and other maternal and fetal complications have been reported to relate to these invasive procedures. In 1997, the presence of cell-free fetal DNA (cff-DNA) in the circulation of pregnant women was reported. Fragmented cff-DNA originates primarily from apoptotic syncytiotrophoblasts. It is detectable as early as 18 days following embryo transfer in in vitro fertilization pregnancy and is soon cleared from maternal circulation after delivery, with a mean half-life of 16 min, so it is a suitable source for noninvasive prenatal diagnosis (NIPD) in pregnancy. Following these reports, a new area of research in the diagnostic field was opened however, there are two problems with cff-DNA for the development of the noninvasive diagnostic test, the small proportion of cff-DNA in maternal plasma as little as ~19%, and coexistence with maternal DNA. The presence of cff-DNA in maternal circulation is accepted universally, and although via the discovery of cff-DNA many potentially clinical applications have been assessed such as fetal rhesus D status, sex-linked disorders, monogenic disorders, aneuploidies, and many pregnancy complications such as preeclampsia and preterm labor. But confirming the presence of cff-DNA in maternal plasma extracts is still a challenge in diagnostic tests. Researchers have applied many methods to differentiate the fetal-derived sequences from that of mother. Six identifier markers include Y-specific sequence, polymorphisms, epigenetic difference, DNA size difference, fetal mRNA, and microRNA.

Keywords:
DNA, marker, pregnancy, prenatal diagnosis, RNA

P1092

Personalized Medicine; New Medical Approach

Maryam Honardoost
Iran University of medical science, Tehran, Iran : marymail79@gmail.com

Abstract:
Personalized medicine is a new concept in disease treatment, which includes determining particular information about an individual patient and then prescribing a treatment that is specific for that patient. Personalized medicine presents an attitude for defining disease subtypes and defining biomarkers that can recognize patients who are most likely to benefit from a particular treatment and other patients who are doubtful to respond or likely to experience side events.

Not every patient with a disease such as cancers, cardiovascular disease, diabetes or even mental disorders will respond the same way to a therapy. Some patients respond to a treatment whereas others do not. The reason may be a genetic propensity to respond or not respond to a medication. The physician must evaluate every patient and then try to guess which treatment will be better. So personalized information about that patient, including information about his/her genotype will help the physician to choose a suitable strategy for preventing, detecting, treating, or monitoring of him/her. This approach would then lead to better results without wasting time on unsuccessful cure.

To sum up, Personalized medicine advantages such as identification of genes and biomarkers which can be used in screening tests and allocation of resources to prevent or detect the high-risk individuals will help to prevent some diseases before the they appear. Furthermore selection of individualized therapies for affected individuals, measurement of circulating biomarkers of disease to monitor the response to prevention or therapy would be helpful in therapy management.

Keywords: personalized medicine,genetics,diagnosis,treatment

P1186

Bioinformatics and Personalized Medicine

Zarrin Minuchehr[1] ، Mohammad Saberi Anvar[2]
1) NIGEB : zarrin.minuchehr@gmail.com
2) National Institute of Genetic Engineering and Biotechnology

Abstract:
Variability is the law of life, with the use of novel genomics technologies large amount of data from various individuals can be derived which is named Big Data. Novel development of computer software and hardware for Biocomputing deciphers the structure and function of genes. Such Big Data can be used to describe the complexity underneath the obstacles of bringing information and hence knowledge from lab to bed. The systematic study of protein-protein interaction networks through systems biology-based analysis has been provided an appropriate strategy to discover candidate proteins and key biological pathways as a major bioinformatics approach in Biomarker discovery. For example, using a comprehensive list of gastric cancer-involved proteins we retrieved interaction information in this mortal disease. Dominant functional theme and centrality parameters including Betweenness, Closeness and Stress of each topological clusters and expressionally active subnetworks in the resulted network were investigated. The results of functional analysis on gene sets showed that neurotrophoin signaling pathway, cell cycle and nucleotide excision possesses the strongest enrichment signals. According to the computed centrality parameters, HNF4A, TAF1, TP53 and AKT1 were the most significant nodes in interaction networks of the engaged proteins in gastric cancer. Introduced pathways and proteins in this study can be applied as diagnostic markers and therapeutic targets in future studies on gastric cancer and other cancers or complex diseases. Bioinformatics has the mission to verify new knowledge in order to detect prevent and hence cure diseases in a specific or personalized manner.

Keywords: Bioinformatics, Gastric Cancer, Biomarker

P1124

The prediction of miR-199a, miR-199b, and miR-30c role in dopaminergic cell death pathways in Parkinson’s disease

Elaheh Yadegari[1] ، Kamran Ghaedi[2]
1) Biology Department, School of Sciences, University of Isfahan, Isfahan, Iran
2) Department of Biology, Division of Cellular and Molecular Biology, Faculty of Sciences, University of Isfahan
kamranghaedi@yahoo.com

Abstract:
MicroRNAs (miRNAs) are endogenous non-coding RNAs that control gene expression at the posttranscriptional level. The role of miRNAs in the maintenance of normal cellular functions and in disease-inducing pathways has been increasingly demonstrated. miRNAs play important roles in neuronal patterning and cell differentiation. miRNAs also have been reported to be involved in neurodegenerative disorders including Parkinson’s disease (PD). PD is the most prevalent movement disorder characterized by selective loss of midbrain dopaminergic neurons. In this study, network-based systems biology tools including Pathway Studio 9.0 and 3Omics were used to identify PD critical molecular players. Utilizing currently available and frequently used computational tools for miRNA target prediction,i.e., PicTar, TargetScan, DIANA-microT, miRanda and miRWalk2.0 databases to predict miRNA-mRNA interaction, we investigated probable interaction of miRNAs and genes that participate in dopaminergic cell death pathways in PD. we have predicted possible role of three miRNAs miR-199a, miR-199b, and miR-30c which could control dopaminergic cell death pathways in PD so possibly effect on PD onset and progression. several therapeutic approaches may be considered for these miRNAs besides of their application as a valuable prognostic or diagnostic biomarkers in PD.

Keywords: MicroRNA, Parkinson’s disease, Dopaminergic neurons

P1126

fMRI role in chronic pain management

Dr Farhad Assarzadegan
SBMU, Imam Hosein Hospital

Abstract:
We think of pain as a symptom, but there are cases where the nervous system develops feedback loops and pain becomes a terrifying disease in itself. It is primarily assessed by means of self-report, an imperfect measure of subjective experience.It is plausible that neurologic signatures (patterns of activity across brain regions) derived from brain imaging could provide direct measures of pain intensity and be used to compare analgesic treatments. Real-time fMRI (rtfMRI) feedback is a potential tool for pain modulation that directly targets the brain with the goal of restoring regulatory function. Numerous studies indicate rtfMRI feedback assisted control over specific brain areas may have applications including mood regulation, language processing, neurorehabilitation in stroke, enhancement of perception and learning, and pain management. We discuss and review published works in which rtfMRI feedback was used to train both healthy controls and chronic pain patients to modulate anterior cingulate cortex (ACC) activation for the purposes of altering pain experience. Both groups improved in their ability to control ACC activation and modulate their pain with rtfMRI feedback training. We additionally review current advances in rtfMRI feedback, such as real-time pattern classification, that bring the technology closer to more comprehensive control over neural function. Finally, remaining methodological questions concerning the further development of rtfMRI feedback and its implications for the future of pain research are also discussed.

Keywords: fMRI, rtfMRI, pain

P1093

Immobilization of glucose oxidase by entrapment within growing polymeric layers of polyacrylamide-grafted silica nanoparticles

Masoud Marivani[1] ، Elham Afjeh dana[2] ، Bita Mehravi[2] ، Khadijeh Ashtari[2]
1) Cellular and Molecular Research Center, Iran University of Medical Sciences, Tehran, Iran. :
2) Department of medical nanotechnology Faculty of Advanced technology in medicine, Iran university of Medical Sciences, Tehran, Iran : ashtaribeh@gmail.com

Abstract:

Glucose oxidase (GOX) plays important role in the development of biosensors, in addition to its widespread applications in food industry. Immobilization of GOX can provide increased resistance to the variations in operational conditions such as pH and temperature. Different approaches have been used to immobilize GOX in nanostructured materials, due to their high surface area. In this work, we report immunization of GOX by the entrapment in surface confined polyacrylamide. GOX was immobilized by entrapping within growing polyacrylamide chains in silica-polyacrylamide core-shell nanoparticles. The core-shell nanoparticles were prepared by the grafting from polymerization of acrylamide on the surface of silica nanoparticles through surface-bound azo initiators. The products were characterized FTIR spectra, thermal analysis, high resolution transmission electron microscopy (HRTEM) and scanning electron microscopy (SEM). The catalytic activity and stability of the immobilized enzyme was compared with free enzyme. It was found that the storage stability study showed that the immobilized GOD retained 50% of its initial activity after 42 days and 60% of the activity was also remained after 16 repeated uses and also 10% initial activity remained after 22 cycles. Considerable enhancements in thermal stabilities were observed for the immobilized GOD at elevated temperatures up to 80 C and the activity of immobilized enzyme was less sensitive to pH changes in solution.

Keywords:
silica nanoparticles, immobilization, core-shell, glucose oxidase

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P1094

Risk of Breast Cancer and Single – Nucleotide Polymorphism 2q35-rs13387042 in Persian women

Dr Ali Hajizadeh[1] ، Mojgan Hoseini[2] ، Hamidreza Agha heydarali naghash[3] ، Bahareh Abbasi[4] ، Nafiseh Ansarinejad[5] ، Massoud Houshmand[4]
1) Islamic Azad University, islamshahr
2) Islamshahr Branch, Islamic Azad University, Islamshahr, Iran
3) Karaj Branch, Islamic Azad University,Karaj,Iran : hamidnaghash@yahoo.com
4) National Institute of Genetic Engineering and Biotechnology (NIGEB),Tehran,Iran
5) Iran University of Medical Sciences, Tehran,Iran

Abstract:

Detection and characterization of the genetic diversity of Disease - associated loci are a major emphasis of current scientific inquiry in cancer. Rapid technological advances have enabled us to explore the increasingly complex genetic architectures and their relationship to cancer.

Single nucleotide polymorphisms (SNPs) lead to genetic differences in breast cancer (BC) susceptibility among women from different ethnicities. Because compared to genetic variants located outside genes, genic variants are frequently judged to be more likely to alter gene function and affect disease risk.
Genome-wide association studies (GWAS) have identified some non-genic breast cancer susceptibility loci. Validation studies showed inconsistent results among different populations.

The rs13387042 polymorphism at chromosome 2q35 has been identified as a new hotspot for breast cancer susceptibility by a recent GWA study.

GWAS have identified 2q35-rs13387042 as a new breast cancer (BC) susceptibility locus in populations of European descent.

Associations between the 2q35- rs13387042 polymorphism and breast cancer have been independently replicated by subsequent studies; however, a proportion of them have produced contrary results. Growing evidence suggests substantial heterogeneity by tumor subtype, defined by hormone receptor status, for association with the polymorphism.

A recent genome-wide association study identified (SNP) 2q35 -rs13387042 as a marker of susceptibility to estrogen receptor (ER) – positive breast cancer.

Roger L. et al. found strong evidence of association between rs13387042 and breast cancer in white women of European origin. Since then, the relationship between 2q35-rs13387042 and breast cancer has been reported in various ethnic groups.
To investigate association with breast cancer among Iranian women, we genotype one nongenic polymorphism 2q35: rs13387042 using ARMS- PCR in BC patients and controls.

Keywords:
Breast cancer, SNP, 2q35, nongenic

P1095

Genetic variants at the TERT- CLPTM1L locus associate with many cancer types

Hamed Nikjou[1] ، Hamidreza Agha heydarali naghash[2] ، Massoud Houshmand[3]

1) Islamic Azad University,Gorgan
2) Karaj Branch, Islamic Azad University,Karaj,Iran : hamidnaghash@yahoo.com
3) National Institute of Genetic Engineering and Biotechnology (NIGEB),Tehran,Iran

Abstract:
Cancer is caused by a complex interplay between genetic and environmental factors. Highly penetrant mutations explain only a small fraction of cancer cases and the majority of genetic cancer risk is thought to be due to the contribution of many common sequence variants of low penetrance. In the past few years (GWA) studies have identified multiple single-nucleotide polymorphisms (SNPs) on chromosome 5, to breast, prostate, colorectal, and bladder cancer susceptibility.

Rafnar et al. have discovered sequence variants in the region of the TERT and CLPTM1L genes that associate with risk of many types of cancer, and assessed the association of rs401681(C)) and rs2736098(A) with the major histological types of cancers.

Rs401681 resides in an LD block that contains the CLPTM1L (cisplatin resistance related protein CRR9p) gene and the 5′ end of the TERT (human telomerase reverse transcriptase) gene. CLPTM1L is a predicted transmembrane protein that is expressed in a range of normal and malignant tissues including skin, lung, breast, ovary and cervix.

Rs2736098 corresponds to A305A in the second exon of the TERT gene while rs401681 is in an intron of the CLPTM1L gene.

In this study, We will test the joint effect of rs401681(C) and rs2736098(A) to find association with 5 cancer types in cancer cases (lung, breast , prostate, colorectal and bladder) and controls in Iranian population.

Keywords:
Cancer, SNP, CLPTM1L ,TERT

P1096

Patient-specific iPS Cells of Autosomal Recessive Hypercholesterolemia as a Platform for Disease Modeling and Personalized Medicine

Parisa Nikasa[1] ، Mehdi Totonchi[2]

1) Department of Molecular Medicine, Faculty of Advanced Biomedical Sciences, Tabriz University of Medical Sciences, Tabriz, Iran. 2. Department of Stem Cells and Developmental Biology, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran.
2) Department of Stem Cells and Developmental Biology, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran. of Medical Sciences, Tehran, Iran. 2. Department of Genetics, Reproductive Biomedicine Research Center, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran : totonchimehdi@gmail.com

Abstract:
Objective: Familial hypercholesterolemia (FH) is a common genetic disorder that results in elevated levels of low-density lipoprotein (LDL) at birth. Mutations in several genes can lead to autosomal dominant forms of FH. Autosomal Recessive Hypercholesterolemia (ARH) is another type of FH which is most closely resembles forms of homozygous FH. Different mutations located in the LDLRAP1 gene can cause ARH. The LDLRAP1 gene encodes the ARH adaptor protein that is required for clathrin mediated endocytosis of LDLR in hepatocytes. Consequently, ARH patients have high LDL concentrations (often >400 mg/dL) and a high risk of coronary heart disease before the age of 30. Treatment options are suboptimal because therapies that work by increasing LDLR levels (eg, statins or bile acid–binding resins) are partially effective and patients often require LDL-apheresis. In this regard, human induced pluripotent stem cell (hiPSC), could be an ideal source for drug screening, toxicology, generation of disease models and eventually cell replacement therapy. This approach can determine the contribution of each individual's genomic variations to cholesterol homeostasis and lipoprotein metabolism which can be valuable to determine efficient therapeutic agents.

Approaches and Results: Clinical and biochemical characterizations on the patient confirmed familial hypercholesterolemia. The Next-Generation Sequencing (NGS) data, identified a novel pathogenic mutation in the ARH gene, confirmed by segregation analysis within the family. Then, patient-derived hiPS cell lines (ARH-hiPSCs) were generated from dermal fibroblasts of the patient and subsequently characterized. Differentiation of the ARH-hiPSCs toward hepatocyte-like cells can represent an ideal in vitro model for this metabolic disorder.

Conclusion: ARH-hiPSCs derived hepatocytes can provide a valuable platform, which is crucial for understanding the pathophysiology and developing therapies for disease. Furthermore, personalized drug selection and dose finding based on genomic sequencing data can prevent cardiovascular disease.

Keywords:
Autosomal Recessive Hypercholesterolemia, Patient-specific iPSC, Personalized Medicine, Disease Modeling

P1097

Evaluation of SUFU expression in gastric adenocarcinoma

Vahideh Mirnia[1] ، Reza Tabaripour[1] ، Novin Nikbakhsh[3] ، Elham Ghadami[3] ، Sadegh Fattahi[3] ، Mohsen Asouri[2] ، Haleh Akhavan- Niaki[3]
1) Department of Biology, Islamic Azad University, Babol, Iran
2) North Research Center of Pasteur Institute, Amol, Iran
3) Department of Genetics, Faculty of Medicine, Babol University of Medical Sciences, Babol, Iran : halehakhavan@yahoo.com

Abstract:
Introduction:
Hedgehog signaling pathway is an important direction in human gastric cancer. SUFU (supper of Fused) is one of the main genes implicated in this pathway, and acts a negative regulator which interacts directly with the GLI family transcription factors. The aim of the present study was to assess SUFU expression levels in patients affected with gastric cancer.
Materials and Methods: Fresh frozen samples from ten patient's tumor and their non-tumoral borders were studied. All patients have undergone surgery in Babol Clinic hospital of Babol between 1394-1395. Total RNA was extracted using Tripure and cDNA was synthesized from total RNA using with specific primers. SUFU mRNA expression was compared to the expression of GAPDH as a house keeping gene by Real-Time PCR.
Results: Down regulation of SUFU was observed in tumoral tissues.
Discussion: These findings suggest that decreased SUFU expression is more frequently in gastric cancer. Therefore, variation in SUFU expression may play a role in gastric cancer development. Further investigation on this gene may provide a new target for therapeutic strategies.

Keywords:
Gastric cancer, SUFU, tumor suppressor, real-time PCR

P1098

The Prevalence of CYP1A2*1k polymorphism in different ethnics of Iranian population

Zahra Rezakazemi[1] ، Malihe Khiabani[2] ، Masoome Rahmani[2] ، Leila Akbari[3] ، Masoud Houshmand[4]
1) Damghanazad university, Damghan, Iran : zahra.kazemi1990@yahoo.com
2) Damghanazad university, Damghan, Iran
3) Taban clinic, Tehran, Iran
4) Medical Genetic Department, National Institute of Genetic Engineering and Biotechnology (NIGEB), Tehran, Iran
massoudh@nigbe.ac.ir

Abstract:
Cytochrome P450 1A2 (CYP1A2), a member of the cytochrome P450 mixed-function oxidase system, is involved in the metabolism of xenobiotics in the body. In humans, the CYP1A2 enzyme is encoded by the CYP1A2 gene, CYP1A2, a hepatic enzyme inducible by smoking, metabolizes various chemical procarcinogens, such as food-derived heterocyclic and aromatic mutagens, N-heterocyclics found in tobacco smoke, and difuranocoumarins, to reactive carcinogens.there are many epidemiological reports examining the role of variant CYP1A2, metabolism of procarcinogens and cancer risk. The enzyme has a significant role in chemical carcinogenesis and is induced by its substrates. CYP1A2*1K, rs762551:C > A plus rs2069526:T > G, and rs12720461:C > T showed decreased metabolism Subjects with CYP1A2*1K hadsignificantly decreased CYP1A2 activity in vivo, and reporter constructs with this haplotype had significantly less inducibility with 2,3,7,8-tetrachlorodibenzo-p-dioxin. CYP1A2*1K polymorphism is decreased the effect of drugs in human ovarian carcinoma cell.
Keywords:
Polymorphism,CYP1A2*1k,Iran,ethnic,pharmacogenetic
CONCLUSIONS: These data suggest that three mentioned properties in gastric cancer stem cells are regulated by common miRNAs, therefore, target these miRNAs or their targets can be helpful to stop tumor growth and metastasis.

Keywords:
Gastric cancer; Bioinformatics; miRNA; Metastasis; Stemness; Drug Resistance

P1100

Polymorphism of Diabetes Mellitus in Iran (A review)

Homa Bazireh[1] ، Reyhaneh Normohamadi[2] ، Roxana Houshmand[2]
1) Department of genetics,Tehran Medical sicences branch,Islamic Azad university,Tehran,Iran : homabazireh@yahoo.com
2) ehran Medical sicences branch,Islamic Azad university,Tehran,Iran

Abstract:
Background and Objective
Diabetes Mellitus(DM) is a common metabolic disorder presenting increased amounts of serum glucose and will cover 5.4% of population by year 2025and in 2012 ,4.8million people died owing to diabetes. In addition, 75% of diabetic patients will be inhabited in developing countries. Similarly, in Iran diabetes is a major health problem. Genetic variation can impact on efficacy and risk of adverse events to commonly used oral agents in diabetes. Pharmacogenetics is the study of genetic polymorphisms affecting responses to drug therapy.
Search Method
Initial searching was conducted using related keywords such as ''Diabetes'' ,''pharmacogenetics of type 2 diabetes (T2D)'' and '' Diabetes mellitus'' and ''polymorphism'' in databases including Pub med and Google scholar. Papers conducted in Iran and published between 2010 and 2016 were collected and reviewed.
Findings
The common rs7903146 (C.T) polymorphism of the TCF7L2 gene has recently been associated with type 2 diabetes (T2D).In that study, the frequency of the homozygous (T/T) variant of rs7903146(C.T) was high in the Fars ethnicity, but low in the Lure, similar to that of ethnic Turk and Kurd. The rs7903146 polymorphism was found with a frequency of 0.37 in the Iranian population, which is higher than the Asian Indians,25 Mexicans,12 Italians,34 Polish. Insulin secretion pathway starts with potassium channels in pancreatic beta cells. KCNJ11 gene encodes ATP-sensitive potassium channel subunits. That study suggests that KCNJ11 (E23K) gene polymorphism is associated with T2DM. Moreover, Several single nucleotide polymorphisms (SNPs) of ABCC8 gene and their interaction are involved in pathogenicity of DM. Additionally, The possession of both MTHFR 677T and 1298C alleles increase the risk of microalbuminuria to 4.3-fold ($p = 0.007$) in T2DM patients. The presence of either MTHFR 677T, 1298C allele is sufficient to increase the risk of macroalbuminuria in T2DM patients. There have been inconsistent reports about SNPs of the adiponectin gene and risk of type 2 diabetes (T2DM) as well. Several single nucleotide polymorphisms (SNPs) of ABCC8 gene and their interaction are involved in pathogenicity of DM.
Conclusion
In conclusion, this review demonstrates the presence of the rs7903146, KCNJ11, MTHFR, adiponectin, and ABCC8 polymorphism in the Iranian population, suggesting susceptibility to T2D and adverse or poor drug responses, which may lead to increase in mortality risk.

Keywords:
pharmacogenetics of type 2 diabetes (T2D); Diabetes mellitus; polymorphism

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P1101

Personalized tumor therapy using patient-derived cancer tissues

Mohammad reza Lornejad[1] ، Christine Schaefer[2]
1) Pioneer Research Anahita
2) Pioneer Research Anahita : chrschaefer9@googlemail.com

Abstract:
Introduction: The number of cancer patients is increasing in Iran and worldwide. This challenge can only be met with the development of more effective and convenient therapies for cancer patients.
Despite advances in the treatment of cancer patients, side effects occur and mortality remains high due to inappropriate therapy or resistance. Heterogeneity is commonplace in all cancer types and at several levels (intrinsic (genetic), epigenetic, positional, and at the population level). The cells of different tumor subpopulations communicate with each other and influence the behavior of other tumor cells. This implicates, each tumor behavior is complex and different and tailored therapies should be administered.
Because cancer can now be sub-classified by its genetics (e.g., melanoma BRAF positive, breast cancer HER2 positive), in some clinics patients with melanoma, or breast cancer are now routinely offered tailored treatments. A targeted cancer therapy can greatly improve the chances of survival. For instance, about 30 percent of breast cancer cases are characterized by overexpression of the human epidermal growth factor receptor 2 (HER2). Antibody treatment (Trastuzumab) can reduce the recurrence of a tumor by 52 percent when used in combination with chemotherapy, in comparison to chemotherapy alone. Thus, identified HER2 overexpressing women will benefit from receiving drugs that target HER2 (Romond et al. 2005). Promising in the clinical setting, is the targeting of the BRAF kinase in melanoma using BRAF kinase inhibitors (e.g. Vemurafenib) (Holderfield et al. 2014). Patient-derived tumor tissues generated from fresh tumor specimens recapitulate the diversity of cancer and reflect histopathology, tumor behavior, and the metastatic properties of the original tumor and in vitro testing of individual tumor responses to anti-cancer drugs might improve personalization of cancer treatment. Effective selection can prevent unnecessary treatment that would mainly result in the unwanted side effects of the therapy.
Objective: Our goal is to establish the first platform for personalized tumor therapy in Iran using patient-derived breast, melanoma and intestinal cancer tissues. They will be analyzed regarding drug screening, biomarker analysis and identification of sensitivity and resistance mechanisms.

Methods: After patient recruitment in cooperation with clinics, tumor tissue units from breast, skin, intestine, obtained after surgery, are cultured. Characteristic properties with regard to response to therapeutics and resistances will be examined. In addition, tumor stem cells, extracellular matrix and vascularization will be investigated.

Keywords:
Personalize, therapy, cancer, tissue, drug, screening

P1102

Association between TERT- CLPTM1L Gene to risk of cancer by rs401681(C) and rs2736098(A) in Iranian population

Hamed Nikjou

National Institute of Genetic Engineering and Biotechnology, Iran-Department of cellular and molecular biology, Islamic University of Azad, Gorgan, Iran : hamednik.hn4@gmail.com

Abstract:
Cancers are considerably caused by a complex interaction between genetic and environmental factors. Highly penetrant mutations explain only a small fraction of cancer cases, while the majority of genetic cancer risk occurs due to contribution of many common sequence variants of low penetrance. It has been shown that two markers rs401681(C) and rs2736098(A) are in linkage disequilibrium (LD) with two genes TERT and CLPTM1L in which variation in the genomic region of the genes are associated with risk of many types of cancer.
The Rs401681 resides in an LD block that contains the CLPTM1L gene and the 5′ end of the gene. The Rs2736098 is, also, linked to TERT-CLPTM1L genes that are causal genes for cancers in malignant tissues. In this study, we are testing the joint effect of rs401681(C) and rs2736098(A) in a population consisted of 100 individuals with different cancer types and 100 healthy individuals as control treatment. Therefore, DNA is extracted for each individual by protocol of kit, then PCR is ran according to the TETRA-ARMS method. Results of PCR are visualized after gel transferring to the Gel Doc to analysis the length of elongated DNA. The initial result shows polymorphic pattern for the used markers between patient and control populations, suggesting a genetic association between the genes and risk of cancer. Furthermore, the two markers might be used for marker assisted selection in order to detect risk of cancers in human populations.

Keywords:
Cancer, SNP, CLPTM1L ,TERT

P1104

Personalized Medicine and cancer therapy

Amir Rezagholizadeh[1] ، Atena Fazeli[2] ، Yadallah Dalvand[2] ، Mojtaba Khayam Nekouei[3] ، kambiz hasrak[4] ، sharareh kamfar[5]
1) Baghiyyatollah al-Azam Hospital : ar_772004@yahoo.com
2) Medical Genetic Department of Center Infertility and Innovation of Mom. Tehran, Iran
3) Faculty of Biological Science. Tarbiat Modares University, Tehran. Iran
4) Baghiyatallah al-Azam Hospital
5) medicine shool hamadan,department genetin and molecular

Abstract:
Cancer is one of the leading causes of death in the world, and more than 14 million new cases and more than 8.2 million cancer related deaths in 2012. After completion of the human genome sequencing project, Significant progress in the human epigenome, proteome, and metabolome seen; One of the main achievements of this project is a better understanding of pharmacogenetics, and the potential for customizing health care for the individual has grown tremendously.
Personalized medicine (PM), can be defined as studying an individual’s distinctive characteristics such as genetic variation, gender, age, family and social history, and environmental exposure in order to tailor a medical treatment regimen to that individual that will provide the most effective care.
With biopsy of cancer tissue, cancer cells gene sequence will be determined and factors that cause normal cells to become mutated cells will be detected.
The discovery of genetic factors predisposes cancer to successful targeting, will eventually lead to a more individualized treatment approach.
Taking advantage of specific biomarkers in cancer cells, one of the best methods of treatment is based on personalized medicine.
Some important things has been done today, can be noted to: early diagnosis and treatment of esophageal cancer with use of miRNA, epidermal growth factor receptor (EGFR) kinase inhibitors resistance mechanisms in lung cancer, innovative antibodies development to immunohistochemical proteins detection, metastatic colorectal cancer treatment by anti–epidermal growth factor (EGFR) monoclonal antibodies, Breast cancer treatment with CYP2D6 inhibitors and prostate cancer treatment with SRD5A2 variations.
To date, significant progress has been made, such as ongoing genomic projects, merging translational medicine with PM, increasing advance toward personal genetic testing, and the observed evolution of conventional medicine to PM. Prevent the occurrence disease and its progression, is the most important goal of PM in the future.

Keywords:
Personalized medicine,cancer,treatment

P1105

Evaluation of Aflibercept effect on VEGF gene expression in CAFs and CAFs/epithelial cells of Oral Squamous Cell Carcinoma

Dr Masoumeh Mirkeshavarz[1] ، Ahmad Nasimian[2] ، Pouyan Aminishakib[3] ، Meysam Ganjibakhsh[2] ، Parvaneh Farzaneh[2] ، Abbas Karimi[4] ، Nazanin Mahdavi[1] ، Fatemeh Kamali[5] ، Mohammad Javad Kharazifard[6] ، Abdolreza Ghamarian[2]

1) Department of Oral and Maxillofacial Pathology, School of Dentistry, Tehran University of Medical Sciences
2) Human and Animal cell Bank, Iranian Biological Resource Center (IBRC), ACECR nnasimiann@gmail.com
3) Department of Oral and Maxillofacial Pathology, School of Dentistry, Tehran University of Medical Sciences : aminishakib@tums.ac.ir
4) Department of Oral and Maxillofacial Surgery, School of Dentistry, Tehran University of Medical Sciences
5) Tumor Bank, Cancer Institute, Tehran University of Medical Sciences
6) School of Dentistry, Tehran University of Medical Sciences

Abstract:

Introduction: Oral cancer is the tenth most common cancer in Iran. The main reason of poor prognosis is early, distant metastasis. Recent investigations show tumor stroma and especially Cancer-Associated Fibroblasts (CAFs) have a considerable role in angiogenesis and consequently tumor progression. In the present study we investigated and compared the anti-angiogenic impact of Aflibercept (Anti-cancer drug) in both CAFs and CAFs/epithelial cells co-culture.

Materials and Methods: After obtaining tissue samples from an oral cancer patient, CAFs and CAFs/epithelial cells were isolated using enzymatic digestion and explant culture. VEGF gene expression were investigated using Real-Time PCR before and after treatment by Aflibercept.

Results: VEGF gene expression was significantly increased in CAFs/epithelial cells co-culture comparing with CAFs. After treatment by Aflibercept, although VEGF gene expression was decreased, it was not significant.

Conclusion: Although Aflibercept may confine oral squamous cell carcinoma progression through decreasing VEGF gene expression, it seems other molecular factors interfere this process.

Keywords:
Oral Squamous Cell Carcinoma; Aflibercept; Carcinoma Associated Fibroblast

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P1106

The future of personalized medicine in cancer therapy

Fatemeh Sanjabi[1] ، Reza Nekouian[2]
1) Faculty of Allied Medicine,Department of Medical Biotechnology,Iran University of Medical Sciences
2) Department of Biotechnology, School of Allied Medicine, Iran University of Medical Sciences (IUMS), Tehran, Iran
reza_nik@unipune.ernet.in

Abstract:

Conventional medicine originated from empirical treatments and gradually evolved to mechanism-based treatments. Improvements in understanding of molecular basis of diseases which is deeply indebted to whole genome sequencing program, forms the genetic medicine. Further improvements in different fields like system biology and pharmacology alongside of genetic medicine builds the basis of personalized medicine. Personalized medicine, enables to tailor specific therapy to each patient by considering the gene makeup and biomarkers which is specific to each person and also predicting the complex nature of drug responses beyond patients with the same disorder. The road to personalized medicine for cancer treatment is not linear as the cancer is enormously complex and heterogeneous but the aim in this mission is measuring some key tumor characteristics which inform the optimum therapy regimen tailored for each given patient to successfully treat their cancer and prevent relapse. Although personalized medicine is young and in its beginning steps but in would be capable of being a tool to detect, manage and prevent diseases in primary stages and this depends on its progress in area such as ongoing genomic project, merging translational medicine with personalized medicine, increasing advance toward personal genetic testing and the observed evolution of conventional medicine to personalized medicine in the future.

Keywords:
personalized medicine,pharmacogenetics,cancer

P1107

Functional application of Personalized Medicine in Cardiovascular Disease

Mahsa Ale-ebrahim
Pharmaceutical Sciences Branch, Islamic Azad University, Tehran, Iran : Mahsa.Alebrahim@Yahoo.com

Abstract:
Cardiovascular diseases (CVDs) accounts for 30% of deaths worldwide, including nearly 40% in high-income countries and about 28% in low- and middle-income countries. There was a remarkable growth in scientific publication on personalized medicine within the past few years in the cardiovascular field. We can classify personalized medicine into comprehensive, genomics, structural and functional fields. Examples of functional factors include endothelial function, exercise testing, and heart rate variability. Endothelial dysfunction is a novel target for CVDs risk reduction and therefore is of great interest to interventionists. The endothelium regulates vascular tone through releasing several vasoactive substances, like nitric oxide. The nitric oxide mediates the protection of the endothelium by limiting the vascular inflammation, vascular smooth muscle proliferation, platelet aggregation, and tissue factor production. Endothelial function can be tested by flow-mediated dilation (FMD) in the brachial artery. The treatment of coronary heart disease reverses endothelial dysfunction, including drugs that modify lipids and reduce blood pressure, along with smoking cessation, physical exercise, and dietary intervention. One of the alternative methods for measuring endothelial function is the noninvasive peripheral arterial tonometry that examines the endothelial dysfunction and can predict late cardiovascular events. The Reactive hyperaemia (RH) response with peripheral arterial tonometry as detected by the RH index is another useful technique for detecting the CVDs and it has been shown to be related to multiple traditional and metabolic risk factors. Also, pulse amplitude tonometry (PAT)-derived measures of arterial stiffness (augmentation index, AI) had strong repeatability. These functional fields of personalized medicine can help cardiologists to diagnosis the endothelial dysfunction and prevention of causing CVDs.

Keywords:
Cardiovascular diseases, personalized medicine, Endothelial function, peripheral arterial tonometry

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P1108

Metabolomics in personalized medicine

Golbarg Mehrpoor
Alborz University of Medical Sciences : golbargmehrpoor@gmail.com

Abstract:
The sequencing of the human genome and other genomes assigns potent protein data sets for making beneficial contributions to medicine and human health issues. Personalized medicine that focuses on molecular diagnostics makes it possible to improve safety, effectiveness and the costs of the treatment based on patient's individual needs. Identification of novel, better biomarkers would allow understanding of the molecular pathways involved in the pathophysiology of the rheumatoid arthritis (RA) and more appropriate selection of the optimal treatments for first-line care. Because multiple genes are involved in the pathogenesis of RA, genome-wide association studies (GWAS) could be a more potent approach for identifying candidate genes. Because the effect size of genetic associations with clinical phenotypes is often small, large populations need to be screened in order to obtain sufficient statistical power for the identification of new disease-causing genetic variants. Metabolomics which is the rapidly evolving field of measuring all endogenous metabolites in a cell or body fluid may contribute to solving this problem. Biochemical measurements of particular intermediate phenotypes on a continuous scale can be expected to provide more details on potentially affected pathways and to be more directly related to the etiology of the disease. Metabolomics delivers its promise of providing access to functionally relevant endpoints in the framework of GWA studies, and thereby opens new avenues for a functional investigation of the role of gene environment interactions in the etiology of complex diseases. The investigation of the genetically determined metabolomics in their biochemical context might help to better understand the pathogenesis of common diseases and gene–environment interactions. These findings could result in a step towards personalized health care and nutrition based on a combination of genotyping and metabolic characterization.

Keywords:
personalized medicine, spectroscopy, metabolomics, rheumatic disease,

P1109

Tailoring right drug with right dose to right patients based on patient's genome, proteome, metabolom makeup

Dr Mohammad Javad Hajipour[1] ، Zohreh Mahmoudi[2] ، Negar Mahmoudi[3] ، Shohreh NaderiMagham[2] ، Nasim Hadian[2] ، Ameneh Kazemi[2] ، Hossein Zokaiee[2] ، Farshad Farzadfar[4]

1) The Persian Gulf Marine Biotechnology Research Center, The Persian Gulf Biomedical Sciences Research Institute, Bushehr University of Medical Sciences, Bushehr, Iran
2) Non-Communicable Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran
3) Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran
4) (Non-Communicable)Diseases Research Center ,Endocrinology and Metabolism Population Sciences Institute,Tehran University of Medical Sciences,Tehran,IRAN : farzadfar3@yahoo.com

Abstract:
It is well recognized that a drug may exert different therapeutic and/or toxic impacts in different individual patients due to distinct genome, proteome, metabolom profile of patients. In recent years, pharmacogenomics, proteomics, metabolomics studies have been concerned with the effects of several genes, proteins, metabolites on particular phenotype, especially when inter-individual variation exists in the response to a particular drug or when adverse drug reactions are known to occur. In order to develop optimal patient-specific therapy, we collected the biological samples (e. g. blood, serum, plasma, buffy coat, urine and DNA) from a total 33000 employees of the Ministry of Health (community health workers/Behvarz) selected from all rural areas of Iran through Behvarz health study (Cohort). These samples were collected, processed and stored in biobank based on the consensus protocols that guarantee the suitability of biological samples for omics analyses (e. g. genomics, epigenomics, proteomics and metabolomics). The behhvarz health study biobank was established for long-term storage (at least twenty years) of biological samples. In addition, a new laboratory information management system (LIMS) software was developed to manage, track, and organize the participant's samples, data, and samples stored in the biobank. A whole experimental approach was performed to measure the blood parameters such as glucose, calcium, creatinine, blood urea nitrogen, Alanine aminotransferase, Alkaline phosphate, low and high density lipoprotein, cardiac c-reactive protein, aspartate aminotransferase, Cholesterol, Triglyceride, urea, phosphate and complete blood count. In addition, the urine parameters including color, appearance, bilirubin, ketone bodies, urobilinogen, ascorbic acid, protein, pH, nitrite, leukocyte and specific gravity were measured using urine test strip. The health and personal condition and lifestyle of all behvarzes were collected and will be tracked for more than 20 years. This approach will provide unique opportunities to determine the biomarkers and risk factors that associate with disease prevalence. The collected samples will be used for omics analyses and therefore, it is possible to develop patient-specific drugs.

Keywords:
pharmacogenomics, Bio bank, behvarz

P1110

Polymorphism Detection of VKORC1 and CYP2C9 Genes in Iranian patients who are under warfarin therapy

Masoumeh Dehghan manshadi[1] ، Omid Aryani[2] ، Vadieh Ghodsinejad[3] ، Arash Kadivari[3] ، Masoud Houshmand[3]

1) National Institue of Genetic Engineering and Biotechnology : masoumehdehghan60@gmail.com
2) Iran University Medical Science Department of Neuroscience Tehran,Iran
3) National Institue of Genetic Engineering and Biotechnology   housh62@yahoo.com

Abstract:
Warfarin (Coumadin) is the most commonly used vitamin K antagonist. It has demonstrated effectiveness for the primary and secondary prevention of venous thromboembolism, for the prevention of systemic embolism in patients with prosthetic heart valves or atrial fibrillation, as an adjunct in the prophylaxis of systemic embolism after myocardial infarction, and for reducing the risk of recurrent myocardial infarction.
Warfarin is metabolized primarily via oxidation in the liver by CYP2C9, and exerts its anticoagulant effect by inhibiting the protein vitamin K epoxide reductase complex, subunit 1 (VKORC1). Three single nucleotide polymorphisms (SNPs), two in the CYP2C9 gene and one in the VKORC1 gene, have been found to play key roles in determining the effect of warfarin therapy on coagulation.
This study investigates the impact of these polymorphisms on 50 patients, referred to our Laboratory for determining the appropriate dose of warfarin. After DNA extraction of whole blood , PCR reverse dot blots technique was used to determine the polymorphism of CYP2C9 gene and VKORC1 gened in collected DNA samples.
VKORC1 G/A was the most common genotype of VKORC1 allele among the study samples,with a rate of 56.2%. In CYP2C9 variant, 22% and 13.8% of subjects carried CYP2C9*1/*2 and CYP2C9*1/*3 genotyping, respectively.
The results showed a significant relationship of the VCORC1 and CYP2C9 polymorphisms with warfarin sensitivity and severe side effects.

Keywords:
CYP2C9 and VKORC1 polymorphisms, Polymerase Change Reaction, Warfarin dose requirements

P1112

Genotyping and expression study of NRG1 in schizophrenic patients have presented biomarkers for negative symptoms

Zahra Sadat Hosseini [1] ، Mohammad Tahmaseb[2] ، Sahel Hemmati[3] ، Arvin Haghighatfard[4] ، Masoud Houshmand[5]

1) Faculty of biological science,kharazmi university,karaj,iran
2) Faculty of biological science,kharazmi university,karaj,iran
3) Pediatric neurohabilitation research center, social welfare and rehabilitation sciences university, Tehran, Iran
4) Department of biology, Tehran North branch, Islamic Azad University, Tehran, Iran
5) Department of Medical Genetics, National Institute of Genetic Engineering and Biotechnology (NIGEB), Tehran, Iran housh62@yahoo.com

Abstract:
Schizophrenia (SCZ) is a complex psychiatric disorder with no clarified etiology or biological diagnosis. Most common symptoms of schizophrenia are positive, negative and cognitive. Neurodevelopmental deficiencies have been suggested as one of the possible reasons of schizophrenia. Neuregulin1 (NRG1) gene-located at 8p12- is an epidermal growth factor which is essential for normal development of central nervous system. NRG1 has several isoforms that could be grouped in six type based on their functions. Type I, II and III of NRG1 are expressed in excitatory and inhibitory neurons, as well as astrocytes and are involved in regulation of neuronal activity.

Prevalence of 13 most common single nucleotide polymorphisms of NRG1 in psychosis along with mRNA level of types I, II and III in this gene were studied in blood samples of 190 Iranian schizophrenic patients and 150 non-psychiatric subjects using quantitative Real time PCR. Also positive and negative symptom scale (PANSS) and brief psychiatric rating scale (BPRS) from patients and Wechsler Adult Intelligence Scale (WAISE) from all subjects were obtained.

Presence of rs2954041, rs3924999 and rs6994992 were significantly associated (p

Results have confirmed role of NRG1 in schizophrenia. Findings showed down regulation of types I, II and III of NRG1 in schizophrenia which were significantly related to lack of emotional and executive functions and could be a marker of low neural activity in schizophrenic brain. In addition rs3924999 have presented as marker for down expression of NRG1 and a potential peripheral marker for negative symptoms of schizophrenia.

Keywords:
NRG1 - schizophrenia - gene expression - rs3924999

P1114

Biobank, Right Drug, Right dose, Right Time

Mansoureh Farhangniya[1] ، Parvaneh Farzaneh[2] ، Mehrnaz Izadpanah[2] ، Seyed Abolhassan Shahzadeh Fazeli[2]

1) Human and Animal Cell Banks, Iranian Biological Resource Center (IBRC), ACECR, Tehran. Iran
2) Human and Animal Cell Banks, Iranian Biological Resource Center (IBRC), ACECR, Tehran. Iran : shfazeli@yahoo.com

Abstract:
Two major formats of biobank; population based and disease oriented biobanks have many subgroups in different categories. The development into personalized medicine is highly depends on the researchable and usable data. Biobanks are the important and necessary tools that be used for available large number of samples with enough information of each person for the aims of personalized medicine. Also biobanks can reinforce personalized medicine by finding and verification of interactions between genetic variability and environmental factors such as life style and phenotype of the persons. For the purpose of establishment human biobank, we collected the blood samples from two formats –population based and people with disease- Iranian ethic groups and people with genetic disease. We completed the questionnaire for demographic and other necessary data. Then certified the cell lines and keeping in nitrogen vapor phase with IBRC code number according to standard protocols. We show considerations in setup a biobank, including compliant and governance, bio-samples, risk factor and related data and informatics. Additionally we carefully designed biobanks for provide critical research and infrastructure support for clinical genetics in the era of personalized medicine.

Keywords:
Biobank, personalized medicine, Iranian biobank, genetic bank

P1115

A Novel iPSC Model of Parkinson’s Disease Based on IFNB-Knockout Mice

Mojtaba Nemati1 ، Adele Taee[2] ، Mahdi Hesaraki[2] ، Shohreh Issazadeh-Navikas[3] ، Hossein Baharvand[2] ، Mehdi Totonchi[2]
1) Royan Institute
2) Royan Institute : totnchimehdi@gmail.com
3) University of Copenhagen

Abstract:
Background:
Parkinson’s disease is an elusive condition causing the loss of dopaminergic neurons in the Substantia Nigra with not much being known about its underlying mechanisms. Despite many efforts to model this disease both in vivo and in vitro, until recently none have been completely successful. We have used cells from the recently developed mouse model based on the knockout of Interferon beta to create induced pluripotent stem cells (iPSCs) which were then differentiated to dopaminergic neurons. After characterizing their Parkinsonian phenotype a novel in vitro model for Parkinson’s disease was developed.
Materials and Methods:
iPSCs were generated from both KO and WT mouse-fibroblasts using retroviral induction of the four Yamanaka factors Oct4, Sox2, KLF4 and C-Myc. The generated iPSCs were characterized using Alkaline phosphatase assay as well as immunofluorescence and qRT-PCR to confirm the expression for pluripotency factors. After characterization these cells were differentiated to dopaminergic neurons using the dual SMAD inhibition method of neural induction. Complete differentiation to functional dopaminergic neurons were assessed using immunofluorescence for Tyrosine Hydroxylase, and GIRK2 and electrophysiological tests (patch clamp). Immunofluorescence imaging using an antibody against phosphorylated Alpha-Synuclein was used to check for Lewy bodies.
Results:
Our results show the aggregation of phosphorylated alpha-synuclein which is the hallmark of Parkinson’s disease in the the KO neurons, as detected using immunofluorescence, but not in the neurons differentiated from WT iPSCs.
Conclusion:
This model is the only model to date which exhibits Lewy body formation in vitro, we have an unprecedented opportunity to study the mechanisms of Parkinson’s disease The setup of this procedure allows individuals identified as being at risk of this disease to be tested using in vitro modeling. If they are found to be susceptible, drug screening can be used to tailor a personalized treatment.

Keywords:
Parkinson’s Disease, IPS model, Disease Modeling, Interferon Beta

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P1118

Genetic variants in dopaminergic pathway were associated with ADHD in Iranian population

Atieh Alizadenik [1] ، Ali Shahbazi[2] ، Arvin Haghighatfard[3] ، Sahel Hemmati[4]
1) Department of biology ,Damghan branch,Islamic Azad university,Damghan,Iran
2) Department of biology ,Damghan branch,Islamic Azad university,Damghan,Iran : arvinland@yahoo.com
3) Department of biology, Tehran North branch, Islamic Azad University, Tehran, Iran
4) Pediatric neurorehabilitation research center, University of social welfare and rehabilitation sciences, Tehran, Iran

Abstract:
Attention deficit hyperactivity disorder (ADHD) is a neurodevelopment behavioral disorder in children with no clarified etiology. ADHD is a disease with high heritability and major genetic bases. Gene expression studies could help to better understand the mechanisms and pathways involved in the disorder as well as development of molecular diagnosis markers. In present study associations between three single nucleotide polymorphisms in dopaminergic pathway with ADHD were assessed. Three SNPs were presented in D2 receptor of dopamine (DRD2), dopamine beta hydroxylase (DBH) and Catechol-O-Methyltransferase (COMT) genes. Blood samples were collected from 150 Iranian ADHD patients and 250 non-psychiatric subjects. DNA was extracted from blood samples and ARMS-PCR was used for evaluation the frequency of three SNPs, rs4680 in COMT, rs1800497 in DRD2 and rs1611115 in DBH, in ADHD patient vs. non-psychiatric children.
Results have been showed that all three SNPs were significantly associated with ADHD.
Findings of present study confirmed association of these SNPs with ADHD in Iranian population. Also support the dopaminergic hypothesis about etiology of ADHD. It seems that rs4680 in COMT, rs1800497 in DRD2 and rs1611115 in DBH may use as prognostic marker for ADHD.

Keywords:
ADHD, COMT, DRD2, DBH

P1120

Nutrigenomics and Personalized Nutrition

Naheed Aryaeian
Department of Nutrition, School of Public Health, Iran University of Medical Sciences,Tehran, Iran. : aryaeian.n@iums.ac.ir

Abstract:
Like drugs, Nutrients have the ability to interact and modulate molecular mechanisms underlying an organism's physiology functions. Awareness of different effects of nutrients according to our genetic construction (Nutrigenetics) and how foods and food constituents (Nutrigenomics) may affect gene expression. It is about how our DNA is transcribed into mRNA and then to proteins and provides a basis for understanding the biological activity of food components. Nutrigenomics is applying the sciences of genomics, transcriptomics, proteomics, and metabolomics to human nutrition in order to understand the relationship between nutrition and health. Part of the approach of nutrigenomics involves finding markers of the early phase of diet related diseases; this is the phase at which intervention with nutrition can return the patient to health. Nutrigenomics has been associated with the idea of personalized nutrition based on genotype. While there is hope that nutrigenomics will ultimately enable such personalized dietary advice. It can also be seen as research to provide people with methods and tools who are looking for disease preventing and health promoting foods that match their lifestyles, cultures and genetics. As nutrigenomics seeks to understand the effect of different genetic predispositions in the development of such diseases, once a marker has been found and measured in an individual, the extent to which they are susceptible to the development of that disease will be quantified and personalized dietary recommendation can be given for that person. The aims of nutrigenomics also includes being able to demonstrate the effect of bioactive food compounds on health and the effect of health foods on health, which should lead to the development of functional foods that will keep people healthy according to their individual needs. This article discusses relationship between nurtigenomics and personalized diet.

Keywords:
Nutrigenomics, Nutrigenetics, Personalized Nutrition

P1122

First report of an Ethylmalonic encephalopathy (EE) patient in Iran

Vadieh Ghodsinejsd[1] ، Omid Aryani[2] ، Masumeh Dehghan[3] ، arash kadivar[3] ، Parvin Pishva[3] ، Masoud Houshmand[3]
1) Medical genetic center ,national institute of genetic engineering and biotechnology
2) Iran University of Medical Sciences,Tehran, Iran
3) National Institute for Genetic Engineering and Biotechnology(NIGEB), Tehran, Iran : Housh62@yahoo.com

Abstract:
Ethylmalonic encephalopathy (EE) is an autosomal recessive disease of early infancy characterized by progressive encephalopathy, recurrent petechiae, acrocyanosis and chronic diarrhea. EE is caused by mutations in the ETHE1 gene that codes for a mitochondrial protein located into the matrix of the organelle.
EE is characterized by psychomotor regression and generalizedhypotonia, later evolving into spastic tetraparesis, dystonia, and eventually global neurological failure.
Lactic acidosis, high levels of ethylmalonic acid (EMA) in urine, and high levelsof C4 and C5 acylcarnitines in blood are the biochemical hallmarks of this disease.
Symmetrical necrotic lesions in the deep gray matter structures are the main neuropathological features of the disease.
In our patient, laboratory finding and MRI features suggest the diagnosis of EE, therefore PCR- sequencing of ETHE1 gene was performed. Seven sets of primers were designed to amplify the coding regions and exon–intron boundaries of the ETHE1gene using Gene Runner .Sequence analysis showed a homozygous c.1461C>T (p.R487W) mutation in exon 4 of the patient, which was previously reported.

Since the first report of EE by Burlina et al in 1991, 46 other patients and 31 different mutations havebeen reported in the literature. We have described one additional EEpatient;this report broadens the phenotype and genotype of EE in Iran.

Keywords:
key wordsETHE1, encephalopathy, ethylmalonic acid, EMA

P1129

The study of non coding RNA HOXD-AS1 gene expression in women with ovarian cancer

Hadis Karimi saraskanrood[1] ، Mohammad Khalaj-kondori[2]

1) Genetics, Faculty of Science, Science and Research Branch, Islamic Azad University of Tabriz
2) Associate Professor of Molecular Genetics, Department of Animal Sciences, Faculty of Natural Sciences, University of Tabriz
khalaj@tabrizu.ac.ir

Abstract:

The study of non coding RNA HOXD-AS1 gene expression in women with ovarian cancer
Hdis karimi –saraskanrud1,Mohammad Khalaj-kondori2,*
1MSc. of Genetics, Faculty of Science, Science and Research Branch, Islamic Azad University of Tabriz
2Associate Professor of Molecular Genetics, Department of Animal Sciences, Faculty of Natural Sciences, University of Tabriz.
* Corresponding author: Khalaj@tabrizu.ac.ir
Abstract
Background: Ovarian cancer is a neoplasm in women and shows malignant behavior and poor prognosis. Current methods used for its diagnosis and prognosis, are not so useful. Studies have shown that the expression of lncRNA HOXD-AS1 gene is altered in cancers. This study aimed to investigate the expression pattern of HOXD-AS1 gene in ovarian cancer.
Methods: Total RNA was extracted by RNX-Plus solution from tumoral and marginal tissue samples of 30 patients with ovarian cancer, and reverse transcripted by cDNA synthesis kit from TAKARA. Then, the HOXD-AS1 gene expression was measured quantitatively by Real-time PCR.
Results and Discussion: The results revealed HOXD-AS1 gene expression in ovary and showed that its expression in tumoral tissues is altered compared to tumor marginal tissues. So, evaluation of its expression might be helpful in the diagnosis and prognosis of ovarian cancer.
Keywords: ovarian cancer, HOXD-AS1, lncRNA.

Keywords:
ovarian cancer, HOXD-AS1, lncRNA

P1132

Prevalence of post-traumatic stress disorder and associated factors in children with experience of traffic accident in Tehran

Dr Ali Moradi[1] ، Gholamreza Garmaroudi[2]

1) Asadabad health and treatment network, Hamadan University of Medical Sciences, Hamadan, Iran
2) Department of Health Education & Promotion, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
garmaroudi@tums.ac.ir

Abstract:

Introduction: Iran is one of the countries with the highest incidence of accident and mortality associated with road and traffic accidents. Studying the prevalence of acute post- traumatic stress disorder among the victims of traffic accidents, and also the causes and context of this type of disorder, especially in children, can help to clarify most dimensions of psychological complications of these types of accidents in the community.
Method: The current study is a cross-sectional type. The determined sample was divided into classes, based on sex and age groups, by the proportional allocation method. A random selection of samples was made among victims of traffic accidents, who were referred to the hospitals covered by Tehran University of Medical Sciences, during the year 2014. Data for measuring the acute post-traumatic stress disorder in children was collected using a standard questionnaire.
Results: From the study, a total of 450 participants, including 344 (76.4%) males and 106 (23.6%) females, were investigated. The mean and standard deviation of age of participants in the research were 10.90 and 4.04 years, respectively. Based on the results of principal components analysis, 121 (26.9%) and 76 (16.9%) of the studied children have had the symptoms of mild and severe post trauma- stress during the interviews, while 253 (56.2%) had no symptoms of acute post trauma- stress. After removal of the effect of confounding variables, the relationship between the gender, maternal education level, and the location of accident, ethnicity, and the elapsed time after the accident was evaluated with the post trauma-stress, using the logistic regression models. This result was statistically significant.
Conclusion: Given the importance of effect of environmental and socially-economic factors on the incidence of complications caused by injuries and accidents related to children, especially on acute post trauma- stress, it is therefore necessary to carry out further studies on elimination of the economic, environmental, and social risk factors, in order to identify these factors in a more detailed manner.

Keywords:
Accidents, acute stress, children.

P1134

Individualized pharmacotherapy and Alzheimer’s disease: now and future

Bahman Sadeghi
University of Tehran, Institute of Biochemistry and Biophysics (IBB), Tehran, Iran : bahmans1983@yahoo.com

Abstract:
Since even target-engaging drugs have been tested without significant outcome, treatments for Alzheimer’s disease (AD) remain stubbornly elusive. A comprehensive risk profile of a patient with AD indicates vast variation in risk markers that may serve to guide treatment. Datasets including several genetic variants such as well-recognized APOE ε4 alleles which define an individual’s likelihood of developing AD by about a decade compared with the general population are becoming increasingly developed. Personalized pharmacogenetic trials that help in diagnosis and treatment choice are now becoming available for clinical practice. Also, amyloid beta (Aβ) peptide biomarkers in the cerebrospinal fluid of AD patients as well as phosphorylated tau measurements, PET scan of Aβ or tau deposition and volumetric MRI are now available. Meanwhile, the application of Plasma markers including serum cytokines and phospholipids are gaining validity and credibility as diagnostic and predictive methods. A new biomarker is misfolded tau that assumes case-specific stable conformations in vivo and may be amenable to treatment with antibodies that are personalized for the patient’s tau strain. Patient-specific neurons derived from induced pluripotent stem cells offer accessibility to numerous personalized data points such as cellular properties, electrophysiological measurements and transcriptomes. While Individual genetic variation maybe assessed as quantitative trait loci (genomic loci that regulate expression levels of mRNA), it is still extensive and poorly understood. Also, variation of personal lifestyle traits like poor nutrition or being sedentary can add up to the current failure of AD clinical trials. Considering these complications, the expected waiting time for an approved AD medication is estimated to be 260 years of independently and sequentially conducted trials. One way to accelerate this is to consider N-of-1 trials in future, in which a patient is fully assessed for genetic variants and endophenotypes and, based on this profile, a thoughtful treatment approach is defined.

Keywords:
Alzheimer’s disease, Biomarkers, Genetic variants, Tau, Amyloid β, N-of-1 trials

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P1135

Application of digital PCR to clinical diagnostics: The first option toward personalized medicine

Fatemeh Mansouri
urmia university of medical sciences : mansouri1600@hotmail.com

Abstract:
The origins and principles of digital PCR as a new clinical diagnostics based on the ability of absolute quantitation to detect a single molecule of the target genes. This technology is used for detection of DNA, RNA, microRNA and other biomarkers with a limited number of targets and a range of small concentrations. The samples must be diluted and divided into a large number of aliquots so that some aliquots receive one molecule of the target gene. The number of positive aliquots, as performed on thermocycler reflects the abundance of the target genes in the sample and measure flourescence signal after each cycle of PCR. Positive samples have increased fluorescence against negative samples and quanta software measures the number of positive and negative samples per fluorescence. It provides absolute and extremely high resolution for target quantification without the need for a standard curve and makes the correct measurement of very few copies of a target. If the sample is sufficiently dilute, only a few of the aliquots will be positive and each of these positive aliquots can be assumed to have contained only a single target molecule. Digital PCR only detects specific targets DNA or RNA and cannot detect proteins or degraded DNA molecules and adjusted for multiple targets. Although this method is very expensive but is very suited for detection individual biomarkers in cancer with a limited number of targets molecules (DNA, RNA, miRNA) in all biofluid samples, Circulating tumor cells and tumor surrounded by normal cells. Moreover, digital PCR is a robust method for quantifying genome amplification, fetal DNA in maternal blood and copy number variation in formalin fixed paraffin embedded in tumors, cardiovascular disease and diabetes.

Keywords:
Clinical diagnostic, Digital PCR, Biomarker

P1138

Haplotype analysis in three QDPR Iranian patients revealed a possible founder effect

Tina Shirzad[1] ، Marziyeh Mojbafan[2] ، Hamideh Bagherian[2] ، Zohreh Sharifi[2] ، Ameneh Sarhadi[2] ، Rasaneh Yazdani[2] ، Sirous Zeinali[2]
1) Medical Genetics Lab, Kawsar Human Genetics Research Center, Tehran, Iran.
2) Medical Genetics Lab, Kawsar Human Genetics Research Center, Tehran, Iran : zeinalipasteur@yahoo.com

Abstract:

Hyperphenylalaninemia is a condition characterized by elevated level of phenylalanine in the blood which is results from deficiency in phenylalanine metabolic pathway. Any defects in the PAH gene that constructs Phenylalanine hydroxylase, as the main enzyme in Phenylalanine breaking down process, leads to phenylketonuria. Five other essential genes also contribute in these pathways which are called PTS, PCBD1, GCH1, SPR and QDPR can cause hyperphenylalanemia too.

In the present study co-segregation of this disease was investigated by six sets of short tandem repeat (STR) markers linked to the PAH and other mentioned genes. Here we have ruled out PAH deficiency in 3 families based on the clinical and biochemical examinations. haplotype analysis of these families were performed using five multiplex sets of STR markers linked to genes responsible for BH4 deficiency such as GCH1, PCBD1, PTS, QDPR and SRP. Autozygosity mapping followed by Sanger sequencing has led us to the causative mutation. In silico analysis of the observed mutation was performed by on line softwares such as Polyphen-2, Hope project and mutation taster. Autozygosity mapping showed same haplotypes in affected members in the mentioned families. Sanger sequencing revealed a same missense mutation which is located in exon 5 in all affected members. According to the mentioned softwares, this mutation is a damaging one.

The mutation was occurred in an almost conserved residue which can disturb protein function, therefore it can be concluded that the mutation is a disease causing one.

Observing same mutation with same haplotype suggested a founder mutation in QDPR gene in Iranian patients. More sample size is needed to confirm our results.

Keywords:
Hyperphenylalaninemia, QDPR, autozygosity mapping,Iran

P1141

Analysis of TRBP2 Gene Expression in Ovarian Cancer Patients

Hossein Moharamzadeh[1] ، Saeid Ghorbian[2] ، Ali Dastranj Tabrizi[3]
1) Tabriz university of medical sciences
2) Department of Molecular Biology, Ahar Branch, Islamic Azad University, Ahar, Iran : ghorbian20@yahoo.com
3) Pathology Laboratory, Alzahra Hospital, South Artesh Aven., Tabriz, Iran.

Abstract:

Introduction: Human trans-activation response (TAR) RNA binding protein 2 (TRBP2), a known molecular partner of the miRNA processing enzyme Dicer, which involved in RNA interference and microRNA pathways. Aberrant expression of TRBP2 is reported in several human cancers. Our aim was to assess the prognostic role of TRBP2 in ovarian cancer patients.

Methods: TARBP2 mRNA expression levels were analyzed in 41 specimens, including 17high grade carcinoma and 13 normal ovarian tissue (from healthy woman) by quantitative real-time reverse transcriptase polymerase chain reaction.

Results: The results of the study showed that there was no significant difference in the TARBP2 expression levels between normal ovarian tissue and tumoral tissue and also between different of tumoral grades ($P > 0.05$).

Conclusions: In this study, the correlation between TRBP2 gene expression were not detected in ovarian cancer. Our findings suggest that TRBP2 is not an important prognostic marker in ovarian cancer and further investigation of other genes involved in this pathway is recommended.

Keywords:
TRBP2, ovarian cancer, microRNA, Gene Expression, Grade

P1143

The prevalence of SLCO1B1 in different ethnics of Iranian population and its relation with dtstin induced myopathy

Sahar Sarajian[1] ، masoud houshmand[2]

1) Department of cell & molecular sciences,Technology faculty, pharmaceutical sciences branch,Islamic azad university ,Tehran,Iran
2) ,national institute of genetic engineering and biotechnology,Tehran,Tehran : housh62@yahoo.com

Abstract:
Background and purpose:The relation between SLCO1B1 gene polymorphism and statin induced myopathy has been reported.SLCO1B1 gene encodes an organic anion transporter polypeptide transmembrane which facilitate the uptake of statin in hepatocyte membrane.rs4149056 polymorphism in the mentioned gene,increases the risk of statin induced myopathy.the aim of this study was to identify the prevalence of SLCO1B1 in different ethnics of Iranian population.

Material and methods:Frequencies of rs4149056 polymorphism in SLCO1B1 gene in 300 healthy Iranian subjects in five different ethnis groups by using Tetra ARMS-PCR. Also by using Real time PCR and sequencing as control.
.
Results:There is no significant difference between Iranian ethnic groups ,($p > 0.05$) approximately 5/6 % of Iranian showed mutant homozygote allelic type (CC), 14/48% heterozygote (TC) and 74/29% wild type (TT). but in comparision with Brazil,france,China,Japan,Russian/Sakha,Czech,Africa,the homozygote C-allele type,which causes more increased risk of statin-induced myopathy ,was found significantly more often in Iranian population.

Conclusion:Findings showed that there is no significant difference between Iranian ethnic groups which.Indicates that statin-therapy can be almost similar for every groups in Iranian population.Also the presence of SLCO1B1 C-allele in Iran forces us to be more careful in statin drug prescription,according to higher risk of statin-induced myopathy. These data would be useful in programming and classificating individual, for prescribing appropriate statin.

Keywords:
rs4149056,SLCO1B1 polymorphism , Statin induced myopathy

P1144

Mir-21 Expression before and after Chemotherapy in New Cases of Breast Cancer in Women

Homa Baghbani [1] ، Hosseinali Sasan[2] ، Reza Kazemi Nezhad[1] ، Mohamad Reza Hajari[1]

1) Department of Genetics, Faculty of Sciences Shahid Chamran University of Ahvaz, Ahvaz, Iran : h.baghbani70@gmail.com
2) Department of Biology, Faculty of Science Shahid Bahonar University of Kerman, Kerman, Iran

Abstract:
Abstract Background: Cancer is the second leading cause of death, after cardiovascular diseases worldwide. Breast cancer is the most common known cancer in women with incidence rate of annually 7000 in Iran. MicroRNAs are a group of non-coding RNAs with 20-25 nucleotides length. These molecules play important roles in biological processes such as differentiation, proliferation and apoptosis by post transcriptional regulation of genes. Mir-21 was known as the first microRNA oncogene with the high expression in patients. In this study the level of expression of mir-21 gene was evaluated in new cases of women breast cancer before and after chemotherapy. Materials and Methods: 5 ml of blood was sampled from 40 affected women with age between around 35 to 60 years using of K3-EDTA 6 ml sterile tubes. Plasma was isolated from all blood 40 samples and stored at −80°C.Total RNAs was extracted by RNXplus procedures. PolyA segment was added in 3´ region RNA using of poly(A) polymerase enzyme and cDNA was synthesized using of Fermentas kit. In the last stage expression of mir-21 gene was detected via Real-time PCR experiments. Then, the real time data was analyzed by Rest software. Results: Results showed the significant decrease in expression of mir-21 gene after chemotherapy in compare to non-treatment women. Conclusion: By results of this study it can be suggested that chemotherapy causes decrease in mir-21 expression. Therefore, all drugs decreasing the expression of Mir genes could be used as affective way to treatment cancers.

Keywords:
Breast cancer, Women, MicroRNA, Mir-21, Chemotherapy, Real time

P1145

Study of MDR1 C1236T Polymorphism in patients with Breast Cancer and Relationship with Response to Treatment in Women

Athareh Pabarja[1] ، hosseinali sasan[2]

1) Department of genetics , Faculty of Sciences Shahid Bahonar University of Kerman : At.pabarja@yahoo.com
2) Department of genetics , Faculty of Sciences Shahid Bahonar University of Kerman

Abstract:

Background: Multidrug resistance is the main cause of unsuccessful chemotherapy. The most important reason of drug resistance is ATP dependent pumps such as MDR1 gene that extrude drugs from the cell. MDR1 gene encodes p-glycoprotein (P-gp), a transmembrane glycoprotein that transports many hydrophobic substrates and anti-cancer drugs out of the cell. This geneis highly polymorphic and it seems that these polymorphisms influence the gene expression and response to treatment. The aim of this study was to investigate MDR1 gene C1236T polymorphism and its association with response to treatment in patients with breast cancer.

Materials & Methods: A number of 50 patients and 50 control persons were selected in city of Kerman. 5 ml of blood was sampled from everybody and immediately kept in -80° C until use. DNA samples were extracted by standard salting out extraction method. Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) was used for the detection of 1236T single nucleotide polymorphism. Results were analyzed by SPSS software using Chi-square test and P value < 0/05 was considered statistically significant.

Results: The results showed that CC, CT and TT genotype frequencies in breast cancer patients as 16%, 32%and 52%, respectively. In the control group, frequencies of genotypes were found as 10% for CC, 36% for CT and 48% for TT. Also the results showed that CC, CT and TT genotype frequencies in responder to treatment as 10/81%, 24/32% and 64/86% , respectively. In the non-responder patients to treatment, these values were found as 30/76% for CC, 53/84% for CT and 15/38% for TT.

Conclusion: There was no significant difference in frequencies of C1236T polymorphism between patients and control group (p = 0/317). Also this results showed that there was significant difference frequencies of C1236T polymorphism between responders and non- responders (p = 0/004).

Keywords: Breast Cancer, Polymorphism, Multi Drug Resistance, PCR-RFLP.

Keywords:
Breast Cancer, Polymorphism, Multi Drug Resistance, PCR-RFLP

P1146

An indirect measure of cancer susceptibility to radiation in Iranian breast cancer patients with different ethnicity

Mahdieh Salimi

1) Department of Medical Genetics, Institute of Medical Biotechnology, National Institute of Genetic Engineering and Biotechnology (NIGEB) : shaghayeghit@yahoo.com

Abstract:

BACKGROUND:

Breast cancer is the leading cancer among Iranian women. Iran has citizens from diverse ethnic groups. Candidate genes for increased breast cancer risk are those involved in DNA damage repair pathways, and mutations in these genes are characterized by increased chromosomal radiosensitivity. To investigate the in vitro chromosomal radiosensitivity of patients with breast cancer and the possible influence of ethnicity and clinical parameters on it, the micronucleus assay was used in the present and absent of bleomycin as a radiomimetic agent.

METHODS:

Chromosomal radiosensitivity was analysed with the micronucleus assay using lymphocytes of breast cancer patients and healthy individuals of different ethnic groups. DNA damages expressed as micronuclei are scored specifically in once-divided binucleated cells arrested at cytokinesis in this technique. The micronucleus is an established biomarker for genomic instability indicating chromosome breakage and/or whole chromosome loss. Lymphocytes were treated with defined doses of bleomycin, and micronuclei (MN) were scored in 1000 binucleated cells in each sample. These MN frequencies were correlated with the ethnicity and clinical parameters of the breast cancer patients.

RESULTS:

MN values were higher in breast cancer patients than in healthy controls in all ethnicity groups. The lower MN frequency was observed in triple negative (ER-, PR-, HER2-) breast cancer groups that indicate the radioresistance in this group.

CONCLUSION:

Iranian breast cancer patients have elevated chromosomal radiosensitivity compared with healthy controls. Triple negatives also influences chromosomal radioresistance. Our results indicated that genomic instability consideration that expressed as MN in blood could be used as personal risk assessment and radiotherapy response prediction in breast cancer.

Keywords:
genomic instability, Micronucleus assay, Breast cancer, Radisensitivity

P1148

Naringenin impacts on SkBr3 and BT-474 human breast cancer cells: A systematic review

Farnaz Parvaresh [1] ، Zahra Akbarzade[1]
1) Food Security Research Center, Isfahan University of Medical Sciences, Isfahan, Iran : fparvaresh1@gmail.com

Abstract:
Background: Top cancer in woman throughout worldwide is breast cancer. Recently, natural remedies such as Naringenin (Nar) - a kind of flavonoids which it can be found in oranges grapefruits and tomatoes- seem to be interesting that might play a useful role in chemoprevention because of possesses pleiotropic molecular mechanisms of action on breast cancer cells.
Objective: We performed a PRISMA-directed systematic review to investigate the effects of Naringenin on some human breast cancer cells (SkBr3 and BT-474). Cytotoxicity, tumor size, apoptosis and estrogenic properties were assessed as primary outcomes.
Methods: The systematic search without restriction was conducted in the electronic databases including PubMed, Scopus, Google scholar, Cochrane Library before Dec 2016.
Results: Initially, 6137 articles were identified. After screening title and abstract, 21studies were selected for text appraisal. Finally, 4 articles which met the inclusion criteria were evaluated. Based on the evaluation, Nar at different concentration can inhibit both cell proliferation and tumor growth. Also it can induce apoptosis.
Conclusion: Due to anticancer properties of Nar, some probably mechanisms that provide these effects are inducing alteration in, caspase and aromatase enzymes, and suppression of oestrogen signal transduction pathways. However, more investigations will be necessary in future to decide whether Nar consumption is recommendable as a part of breast cancer control. Also designing some clinical trials are needed to determine the optimal dose for therapeutic use.

Keywords:
Naringenin, breast cancer cells, systematic review

P1149

Survey of interaction between macronutrients with selected CETP gene polymorphism in relation with metabolic syndrome

Zohreh Esfandiar[1] ، Parvin Mirmiran[1]
1) Shahid beheshti University of Medical Sciences : parvin.mirmiran@gmail.com

Abstract:
Background: Metabolic syndrom is (MetS) is a complex disorder that is linked to cardiovascular disease and type 2 diabetes. The interaction between genetic and environmental factors, especially diet is the main causes of MetS And we may be able to annul unfavorable effect of genetic changes by altering dietary intake.
Aims: to examine the interaction between CETP polymorphisms and macronutrient intake in relation to MetS and its componenets.
Methods: In this matched nested case-control study, MetS subjects and controls were selected from of the Tehran Lipid and Glucose Study. Dietary intakes were assessed using semi-quantitative food frequency questionnaire. Anthropometric measurements and biochemical assays were conducted. Single Nucleotide Polymorphism CETP rs3764261, rs5882 were genotyped by the conventional polymerase chain reaction and restriction fragment length polymorphism.
Results: A significant interaction between calory density and rs3764261, rs5882 polymorphisms associated with the risk of MetS, high blood pressure and high triglyceride was observed (Pi
The risk of metabolic syndrome in carriers of the A (rs3764261) allele decreases by increasing omega-3 fatty acid intake (P trend=0.04). Total fat intake has a significant interaction with rs5882 polymorphism associated with low HDL-C (Pi= 0.02). The ORs of high triglyceride increase significantly in fourth quartiles of total fat and omega3 fatty acid in the CC homozygote, in fourth quartiles of MUFA and trance fatty acid in the A allele carriers of rs63764261 and in fourth quartiles of trance fatty acid in the G allele carriers of and rs5882, compared to first quartiles (P trend<0.05).
Conclusion: In the present study the interaction between CETP: rs3764261, rs5882 polymorphisms and the intake of macronutrients in relation to MetS was not significant.
There was a significant associations between the rs3764261 CETP SNP and concentration of HDL-C, although there was not a significant interrelation between rs3764261 polymorphism and intake of macronutrients in relation to HDL-C concentration. An interaction between fats intake and rs5882 genotype associated with HDL-C levels was observed
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Keywords:
polymorphism, CETP, gene, diet

P1150

Check increasing the expression of Ki67 cell proliferation in the hippocampus gene brain ischemia reperfusion model rats brain after pretreatment with iron oxide nanoparticles

Niloofar Sadeghi mazdeh[1] ، Leila Pishkar[2] ، Mojtaba Falahati[3]

1) Department of Biology,IslamshahrBranch,Islamic Azad University,Islamshahr,I ran
2) Department of Biology,IslamshahrBranch,Islamic Azad University,Islamshahr,Iran : leilapishkar@gmail.com
3) Department of Nanotechnology,Faculty of Advance Sience and Technology,Islamic Azad University of Pharmaceutical Sciences(IAUPS),Tehran,Iran

Abstract:
Ischemia-reperfusion brain increasing in the developing world need access to efficient treatment procedures based on the waste Baztrmymy shows. Increased rate of proliferation and migration of endogenous neural stem cells after injury neurological damage to the central nervous system is the most important goal of regenerative medicine. It was found that neural stem cells in certain brain regions such as the hippocampus brain actively and Zyrbtny zone (SVZ) in the end there are mammals. Evidence show that iron oxide nanoparticles can induce cell cycle, cell proliferation induced by increasing the routes in some cells have shown. The purpose expansion of the study of gene expression Ki67 cell proliferation in the hippocampal brain ischemia reperfusion model rats brain after pretreatment with iron oxide nanoparticles. In this study, after induction of ischemia / reperfusion in rats and the treatment of brain 5 mg / kg and 10 mg / kg Ki67 expression levels of genes involved in cell proliferation in the hippocampus area of the brain in real time-PCR using animals Was investigated. Analysis of gene expression in the SVZ brain Ki67 animals in different groups represent appropriate and can be pre-treated with iron oxide nanoparticles dose-dependent increase in the expression of Ki67 was SVZ Accordingly, it was found that pretreatment of animals with a dose groups 10 mg / kg of iron oxide nanoparticles significantly (P-value<0.05) leads to increased expression of Ki67 antigen in cells in rats under ischemia reperfusion brain SGZ area in throughput. The results of this study seem to be pre-treated with iron oxide nanoparticles in cells by increasing the expression of Ki67 be appropriate SVZ area Enhance the proliferation of stem cells / progenitor neural ischemia reperfusion model in rats having brain.

Keywords:
key words gene expression of cell proliferation Ki67, area SVZ, ischemia reperfusion model rats brain, pretreatment, iron oxide nanoparticles

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P1151

The study of the expression of Bax and Bcl-2 genes in the liver and kidneys of rats after chronic administration of different doses of iron oxide nanoparticles.

Sanaz Homayoun hamedani[1] ، Leila Pishkar[2] ، Mojtaba Falahati[3]

1) Biology,IslamshahrBranch,Islamic Azad University,Islamshahr,iran
2) Department of Biology,IslamshahrBranch,Islamic Azad University,Islamshahr,iran : leilapishkar@gmail.com
3) Department of Nanotechnology,Faculty of Advance Sience and Technology,Islamic Azad University of Pharmaceutical Sciences(IAUPS),Tehran,Iran

Abstract:
With the arrival of nanotechnology in the medical field and increasing the use of these compounds in the treatment and diagnosis of a wide range of diseases, understanding the behavior of nanoparticles in different organs interact with living organisms is critical. Iron oxide nanoparticles are used extensively in the area of diagnosis and treatment of many diseases used. Many studies, including iron nanoparticles oxide nanoparticles on healthy, low-power-induced toxicity introduce Tissue body, but a careful examination of the molecular toxicity of these nanoparticles on the liver and head as the most important organ of interacting with iron oxide nanoparticles are required. In this study, 40 male rats Wistar divided into 4 groups of study as control group, animals treated with 10 mg / kg particles of iron oxide for a week, the animals treated with 20 mg / kg of iron nanoparticles oxide for a week and the animals treated with 40 mg / kg of iron oxide nanoparticles were used for a week. The liver and kidneys of animals at day 7 after initiation of injection were extracted under sterile conditions and then the expression of Bax and Bcl-2 genes using real time-PCR in the tissues were measured. More than a dose of 5 mg (PV <0.05), respectively. Bax gene expression also increased at all doses 20 and 40 mg (P-V <0.01) significantly more of the dose of 5 mg (P-V <0.05), respectively. The results of this study suggest that the chronic use of high doses of iron oxide nanoparticles can induce cell death process in the liver and all living beings possess.

Keywords:
Chronic, iron oxide nanoparticles, Bax and Bci-2, hepatic and renal toxicity, rat

P1152

The effect of pre-treated with nanoparticles of iron oxide (Fe2O3) to reduce the level of NF-kB gene expression in rats model brain Ischemia-reperfusion.

Farnaz Jalili[1] ، Leila Pishkar[2] ، Mojtaba Falahati[3]

1) Biology,IslamshahrBranch,IslamicUniversity,Islamshahr,Iran
2) Department of Biology,IslamshahrBranch,Islamic Azad University,Islamshahr,iran leilapishkar@gmail.com
3) Department of Nanotechnology,Faculty of Advance Sience and Technology,Islamic Azad University of Pharmaceutical Sciences(IAUPS),Tehran,Iran

Abstract:

Studies the role of NF-kB signaling pathway in the development of nerve cell death caused by ischemia reperfusion, as well as the development of inflammation in nerve tissue after a brain injury is. In this regard, the nanoparticles of iron oxide (Fe2O3) protect neurons in the central nervous tissue against oxidative stress has been proved. The aim of this study was to investigate the effect of pre-treatment of Fe2O3 nanoparticles on NF-kB gene expression is reduced.

During the study, 40 Wistar albino rats were randomly divided into four groups, control group pretreated with doses mg / kg 5 and mg / kg 10 respectively. Animals pre-treated and control groups underwent common carotid artery occlusion for 20 minutes with cerebral ischemia and reperfusion was established by re-opening the arteries. were treated only by saline. 48 hours after induction of ischemia - reperfusion in brain tissue, animal euthanasia and animal brain hippocampus tissue was extracted and the expression of NF-kB was evaluated using the Real time- PCR techniques.

The results of the study showed was that relative gene expression NF-kB in the context of the hippocampus of animals in both dose 5 mg / kg and 10 mg / kg significantly compared to the control group decreased (P-V

doses of relationship (P-V <0.05).

The results of the survey demonstrate the genomics was that pretreatment of Fe2O3 nanoparticles significantly to the performance factor NF-κB as a key factor NF-κB signaling pathway involved in controlling brain tissue of mice ischemia-reperfusion Injury been brain.

Keywords:
Pretreatment, iron oxide nanoparticles, NF-kB, cerebral ischemia reperfusion, rats.

P1153

Systematic review: The role of Naringenin (Trihydroxyflavanone) on MCF-7 and BT- 483 Human Breast cancer cells

Zahra Akbarzadeh[1] ، Farnaz Parvaresh[1] ، Maryam Miraghajani[2]

1) Department of Community Nutrition, School of Nutrition and Food Science, Isfahan University of Medical Sciences, Isfahan, Iran
2) Food Security Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

Abstract:

Background: Breast cancer is a major public health problem in women. Recently, natural treatments such as Naringenin (Nar) - a kind of flavonoids which it can be found in oranges, grapefruits and tomatoes- seem to be interesting. Nar can play a useful role in chemoprevention because it has pleiotropic effects on breast cancer cells. Methods: We performed a PRISMA-directed systematic review to investigate the effects of Naringenin on MCF-7 and BT- 483 human breast cancer cells. Primary outcomes were including: estrogenic properties, tumor size, cytotoxicity and apoptosis. The systematic search without restriction was conducted in the electronic databases including Cochrane Library, PubMed, Scopus and Google scholar before Oct 2016. Results: Initially, 739 articles were identified. After screening title and abstract, 37 studies were selected for text appraisal. Finally, 6 articles which met the inclusion criteria were evaluated. Cell proliferation and tumor growth can be prevented by Nar with different concentration. Also it can induce apoptosis. Conclusion: Probably mechanisms that provide anticancer properties of Nar are inducing alteration in caspase, aromatase enzymes and interdiction of oestrogen signal transduction pathways. So Nar may be used as food supplement or a potential therapeutic compound for breast cancer. It seems for determining the optimal dose, more investigations will be necessary in future.

Keywords:
Naringenin, breast cancer cells, MCF-7, BT- 483, systematic review

P1154

Mir-21 Expression in New Cases of Breast Cancer in Stage 3 and Stage 2

Homa Baghbani [1] ، Hosseinali Sasan[2] ، Reza Kazemi Nezhad[1] ، Mohmad Reza Hajari[1]
1) Department of Genetics, Faculty of Sciences Shahid Chamran University of Ahvaz, Ahvaz, Iran : h.baghbani70@gmail.com
2) Department of Biology, Faculty of Science Shahid Bahonar University of Kerman, Kerman, Iran

Abstract:
Abstract Background: Cancer is the second leading cause of death, after cardiovascular diseases worldwide. Breast cancer is the most diagnosed non-skin cancer and the second leading cause of cancer death in women in the USA. MicroRNAs are small RNA molecules that play critical roles in many different cellular processes such as differentiation, proliferation, and apoptosis by post transcriptional regulation of genes. Hence, aberrant microRNA expression is common in a variety of disorders, including cancer. It is well established that miR-21 expression promotes proliferation and invasiveness of breast cancer cells. MiR-21 is considered a key oncogene miRNA in carcinogenesis since its expression is consistently high in a wide range of cancers including Breast cancer. In this study the level of expression of mir-21 gene was evaluated in new cases of women breast cancer in stage 3 and stage 2. Materials and Methods: 5 ml of blood was sampled from 40 affected women with age between around 35 to 60 years using of K3-EDTA 6 ml sterile tubes. Plasma was isolated from all blood 40 samples and stored at −80°C.Total RNAs was extracted by RNXplus procedures. PolyA segment was added in 3′ region RNA using of poly(A) polymerase enzyme and cDNA was synthesized using of Fermentas kit. In the last stage expression of mir-21 gene was detected via Real time PCR experiments. Then, the real time data was analyzed by Rest software. Results: the results show that changes of expression of mir-21 gene in breast cancer in grade 3 than grade 2 is not significant. Conclusion: By results of this study it can be suggested that whit Development breast cancer expression of mir-21 Dose not change much.

Keywords:
Breast cancer, Women, Stage, MicroRNA, Mir-21, Real time

P1155

Study of MDR1 C3435T Polymorphism in patients with Breast Cancer in Women

Athareh Pabarja[1] ، Hosseinali Sasan[2]
1) Department of genetics , Faculty of Sciences Shahid Bahonar University of Kerman : At.pabarja@yahoo.com
2) Department of genetics , Faculty of Sciences Shahid Bahonar University of Kerman

Abstract:
Study of MDR1 C3435T Polymorphism in patients with Breast Cancer in Women

Athareh Pabarja1, Hosseinali Sasan1, Behjat Kalantarikhandani2,

1 Department of genetic, Faculty of Sciences Shahid Bahonar University of Kerman, Kerman, Iran

2 .Department of oncology, Kerman University of Medical Sciences, Kerman, Iran
At.pabarja@ yahoo.com

Abstract
Background: One of the limitations in the treatment of cancer patients with chemotherapy is the development of multidrug resistance (MDR). The multidrug resistance (MDR) 1 gene encodes a 170-kDa membrane transporter called P-glycoprotein, which P-gp is a member of the ABC family of transporters that extrudes various hydrophobic drugs and peptides from the inside to the outside of the plasma membrane by the way of an ATP-dependent cellular efflux mechanism. MDR1 gene polymorphisms could alter the expression level of P-gp and consequently result in drug resistance. The aim of this study was to investigate MDR1 gene C3435T polymorphism.
Materials & Methods: A number of 50 patients and 50 control persons were selected in city of Kerman. 5 ml of blood was sampled from everybody and immediately kept in -80° C until use. DNA samples were extracted by standard salting out extraction method. Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) was used for the detection of C3435T single nucleotide polymorphism. Results were analyzed by SPSS software using Chi-square test and P value $< 0/05$ was considered statistically significant.
Results: The results showed CC, CT and TT genotype frequencies in breast cancer patients as 14%, 56% and 30%, respectively. In the control group, genotype frequencies were found as 22% for CC, 52% for CT and 26% for TT. The C allele frequency was found in 42% and the T allele frequency was found in 58% patients. In control group the C allele frequency was found in 48% and the T allele frequency was found in 52%.
Conclusion: There was no significant difference in genotype frequencies of C3435T polymorphism between patients and control group ($p = 0/373$). Also there was no significant difference in allele frequencies of C3435T polymorphism between patients and control group ($p = 0/420$).

Keywords:
Breast Cancer, Polymorphism, Multi Drug Resistance, PCR-RFLP, C3435T

P1157

Comparison of two molecular methods for detection of EBF1 gene copies number abnormalities in Patients with Acute Lymphoblastic Leukemia

Sahar Mehranfar[1] ، Narges Sozangar[2] ، Farhad Jeddi[2] ، Abbasali Poue feizi[3] ، Sirous Zeinali[4]

1) Tabriz medical university
2) School of advanced medical science,tabriz medical university
3) Hematology & Oncology Research Center, Tabriz Medical Sciences University, Tabriz, Iran.
4) Kawsar Human Genetics Research Center, Kawsar Genomics Center, Tehran, Iran zeinalipasteur@yahoo.com

Abstract:
Background: Despite advances in diagnosis, still need a screening method in patients with acute lymphoblastic leukemia (ALL), yet. Our aim is to evaluate Multiplex Ligation-dependent Probe Amplification (MLPA) method ability for screening patients with ALL.
Material and Methods: Samples were obtained from 45 childhood patients with B-cell ALL. EBF1 gene copy number abnormalities (CANs) were studied by this method and qPCR. In last we confirm our results by sequencing.
Results: From 45 patients with B-ALL, 7 (15%) patients, showed CNAs by MLPA method. 14 (18%) from all mutations, were seen in EBF1 gene and from all these, 3 samples showed changes in exon 10 that were evaluated by qPCR. We used Sanger sequencing as a gold standard method to compare the two methods.
Conclusion: Screening mutations of genes involved in acute leukemia remains a challenge in the diagnostic laboratory. MLPA a rapid and valid method for screening genes mutations.
Key words: acute lymphoblastic leukemia, copy number abnormality, MLPA, qPCR.

Keywords:
acute lymphoblastic leukemia, copy number abnormality, MLPA, qPCR

P1180

genotype-phenotype correlationin in Iranian patients with Kennedy disease

Omid Aryani[1] ، Masoumeh Dehghan[1] ، Vahideh Ghodsinejad[1] ، Masoud Houshmand[1]
1) National Institute of Genetic Engineering and Biotechnology : housh62@yahoo.com

Abstract:
Kennedy (SBMA) is a X-linked recessive rare neurodegenerative disorder which is associated with an unstable expansion of CAG trinucleotide repeat in the first exon of the Androgen receptor on chromosome X and only occur in male. Kennedy cause sit expansion CAG repeat in the nuclear and transcription disorder of target gene. Also three nucleotide expansion CAG in AR causes disruption of molecular chaperon s function and mitochondrial toxicity. it in turn affects apoptosis and degeneration motorneurons .
The main clinical manifestations are muscular weakness, tremor, bulbar signs (dysphonia, dysphagia, …), infertility and gynecomastia
Aim of this study was to fine out the most available method to determine genotype correlation expansion repeats and patients phenotypes
50 patient with a clinical diagnosis of kennedy from un related families and were investigated for the CAG trinucleotide repeat expansion PCR-Sequencing were used to determine the CAG expansion.
In 38 of patients were found expansion in normal range so it could be because of un clear clinical diagnosis.
By using PCR-Sequencing 12 patients were found in long range expansion. In kennedy patients there was an inverse correlation between the size and age of onset of diseases.

Keywords:
Kennedy expansion، CAG reaped، Androgen receptor، investigation genotype-phenotype

P1159

Association of leptin gene A19G and G-2548A polymorphisms with obesity and overweight in an Iranian young population

Elahe Amanloo[1] ، Mohsen Kalantari[2] ، Sanaz Mahmazi[3]

1) Department of Genetics, Faculty of Basic Sciences, Islamic Azad University, Zanjan Branch, Zanjan, Iran
2) Biology Research Centre, Zanjan Branch, Islamic Azad University, Zanjan, Iran
3) Department of Genetics, Biology Research Center, Zanjan Branch, Islamic Azad University, Zanjan, Iran
sanazmahmazi@yahoo.com , sanaz.mahmazi@iauz.ac.ir

Abstract:
Background and Objective: Obesity is the result of increasing general or localized fat in the body that is measured by the body mass index (BMI). If body mass index is equal to or more than 25 kg / m², the person is overweight. With the increase in overweight and obesity in today`s society, the study in this regard is particularly important. Many years ago scientists tended to discover a substance that could control and cure this phenomenon biologically, until 1994 a researcher named Friedman Jeffery discovered a hormone produced from ob gene in America and named it leptin taken from the Greek word Leptos, meaning thin.

Materials and methods: Genomic DNA from peripheral blood samples of 120 normal subjects and 120 overweight individuals (BMI> 25kg / m²) with an average age of 24 years of Zanjan Islamic Azad University students were taken with consent. Genetic studies were conducted in three stages: 1- Extraction, 2-PCR-RFLP and 3- Electrophoresis. The data`s were analyzed in SPSS software.

Results: Statistical analysis of data on A19G polymorphism of leptin gene showed a significant relationship between GG genotype with obesity and overweight ($p = 0.023$). Significant relationship between G-2548A polymorphisms with increasing BMI and obesity was not observed ($p = 0.436$).

Conclusion: This study showed that A19G polymorphisms of leptin gene could be linked with susceptibility to obesity and overweight in the study population, which may be due to a decrease in leptin mRNA translation. Determining individuals` genotype due to lack of leptin or reducing its amount may prevent or treat obesity with the administration of leptin.

Keywords:
Obesity, BMI, polymorphism, leptin

P1160

Association of leptin receptor gene Gln223Arg and lys109Arg polymorphisms with obesity and overweight in an Iranian young population

Fereshteh Farzam[1] ، Javad Nasseryan[2] ، Sanaz Mahmazi[3]

1) Department of Genetics, Faculty of Basic Sciences, Islamic Azad University, Zanjan Branch, Zanjan, Iran
2) Department of Statistical and Mathematics, Faculty of Basic Sciences, Islamic Azad University, Zanjan Branch, Zanjan, Iran
3) Department of Genetics, Biology Research Center, Zanjan Branch, Islamic Azad University, Zanjan, Iran.sanazmahmazi@yahoo.com , sanaz.mahmazi@iauz.ac.ir

Abstract:
Background and Objective: Obesity is an energy imbalance disorder and happens in deficiency of energy intake and consumption. Leptin is an important hormone that regulates energy expenditure. Leptin through its receptors located in the hypothalamus regulates appetite and energy consumption. By understanding genetic base of obesity we could design effective methods for patient`s treatment. The aim of the study was to investigate the associations of leptin receptor gene Lys223Arg and Gln109Arg polymorphisms with Overweight and Obesity.

Materials and Methods: We examined two polymorphisms in 240 subjects consisting of obese, overweight, low weight and normal subjects as controls from Zanjan Islamic Azad university students. For Genotyping we used PCR-RFLP. Statistical analysis was performed using t-test and chi-square to show the significant difference between the groups.

Results: In study of Gln109Arg polymorphism we didn`t investigate significant differences between genotypes and allelic frequencies in our studied groups. In Lys223Arg polymorphism by A-G substitution we find that AG genotype was higher in normal group and AA genotype was higher in obese and overweight groups but there wasn`t significant difference in GG genotype and allelic frequency ($P<0.05$).

Conclusion: Lys223Arg polymorphism of LEPR gene was associated with obesity Gln 223 of leptin receptor gene was located on extra cellular part of receptor and substitution of Glu by Arg in this position may influence leptin signaling. By understanding this polymorphism it might be possible to select a treatment for appetite and energy expenditure control for obesity prevention. AG genotype and existence of Gln and Arg might have protective effect against obesity and overweight.

Keywords:
LEPR, PCR-RFLP, polymorphism, obesity

P1161

Evalition Expression of mir-30-3p in breast cancer

Nasrin Noshadi[1] ، Asghar Arshi[2]
1) Marvdasht Azad Universtiy
2) Young Researchers and Elite Club, Shahrekord Branch, Islamic Azad University, Shahrekord, Iran : asghararshi@yahoo.com

Abstract:
Background: microRNAs are short non-coding RNAs (20-24 nt) that are involved in post-transcriptional regulation of gene expression in multicellular organisms by affecting both the stability and translation of mRNAs. miR-30-3p has been reported to be a tumor suppressor and a promising therapeutic target in cancer. miR-30-3p has been associated with epithelial mesenchymal transition and chemo-resistance in cancer. The aim of this study is to investigate the expression of miR-30-3p, its prognostic roles and its potential targets in breast cancer by RT-qPCR.

Methods: In the present case-control study, 20 tissue samples from patients with breast cancer and 20 tissue samples from healthy group under the direct supervision of a pathologist specialist due to clinical presentation and laboratory findings were collected. After extracting RNA from normal and tumor blood samples, cDNA synthesis method according to the protocol and RT-qPCR was performed. mir-30-3p expression level was calculated using Livak method. All data were analyzed using SPSS software.

Results: The results of RT-qPCR indicated miR-200b was downregulated in breast cancer tissues and its low-expression correlated with poor outcome in breast cancer patients. Expression level of mir-30-3p was 31.24% and 68.76% in breast cancer patients and healthy group respectively (p value=0.001).

Conclusion: Due to the previous reports, mir-30-3p act as tumor suppressor in breast cancer, which could be used as biomarker for breast cancer diagnosis. In this study we propose that miR-30-3p is a potential diagnostic marker and therapeutic target of breast cancer.

Keywords:
breast cancer, microRNA, mir-30-3p, RT-qPCR

P1162

The study of EDA and EDAR mutations in 1 HED persian patient

Atefe Papi[1] ، saeedreza Khatami[1] ، Hamid galledari[1]
1) Shahid chamran university of ahvaz : a.papi1990@yahoo.com

Abstract:
Introduction: Hypohidrotic ectodermal dysplasia (HED(is most common type of ectodermal dysplasia that is the result of faulty ectodermal development lead to ectodermal derivatives defects including sparse hair (hypotrichosis), anodontia or hypodontia and hypohidrosis or anhidrosis. X-linked HED is caused by mutations in Ectodysplasin A (EDA) gene that account for 90% of all HED cases. Whereas mutations in other involved genes, EDA-receptor (EDAR), EDAR-associated death domain (EDARADD) result in autosomal dominant (OMIM: 129490) and autosomal recessive (OMIM: 224900) forms. It was recently shown that some other genes, including TRAF6 and WNT10A, could be involved in causing HED. Material & Methods: we studied 1 family members with 1 affected persons. The proband was A 5 years old boy from healthy Persian parents with Third-degree relatives (cousin) that was referred to the Laboratory. We collected about a 5-mL quantity of blood from each family members. Genomic DNA was extracted .exons and flanking intronic Primer sequences of EDA and EDAR, were designed. Standard PCR were used and products were sequenced.The sequencing results were analyzed with Sequence Scanner Software. Result and conclusion: EDA gene was studied at first, due to high mutation rate in this gene. The EDAR gene was investigated in secondary. No mutation was found in EDA and EDAR genes. Probably some other genes (e.g. WNT10A, TRAF6) was involved in this case. Other genes analysis was not performed.

Keywords:
Hypohidrotic ectodermal dysplasia, EDA, EDAR, EDARADD

P1164

A Mini Review on Hot Topics in Precision Medicine

Maryam Yazdanparast

Experimental Medicine Research Center, Department of Pharmacology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran. : yazdanparast.maryam@gmail.com

Abstract:
Today, there is a consensus that every prescribed medicine behaves distinctly in each body. Therefore, different modelling, meta-data analysis, and various advanced detection techniques are being recruited to reduce the probable side-effects of classic methodology of trial and error; known as "precision medicine". Generally, precision medicine aims to distinguish interpersonal distinctions by studying genetic variations and utilizing precise targeted agents including drugs and markers. Precision medicine, also known as "personalized medicine", have raised promises for many therapeutic and diagnosis objects including cancer treatment, regenerative medicine, diets, etc. Cancer is the most promising target for precision medicine due to the variability in its causes and alarming incidence. Studies are aimed to detect the tumor developing mutations by monitoring the genetic profiles of cancerous cells compared to normal tissues in order to select the optimum chemotherapy and immunotherapy, or specifically target certain cancer markers. Concerning tissue replacement, stem cells have revolutionized the organ transplantation by decreasing the risk of rejection and dependence on matched-donor waiting lists. Regarding the diagnosis, rapid DNA sequencing and analysis tools play as magic gadgets helping doctors to identify the responsible pathogens and decode the relation between individual microbial profiles with complex diseases such as obesity, vascular disease, autism, and preterm birth. Finally, personalized medicine has enabled physicians to perceive the unique response of every individual to different medications providing the possibility of designing costume diets for certain patients such as diabetics. Then, it is indispensable to consider that précised medicine would not obtain its current achievements unless by calling up a colorful variety of disciplines including material science, engineering, 3D printing, molecular biology, and medical engineering, converting it to a multidisciplinary field. In conclusion, precision medicine is a wide open window to a future promising advantages of cutting unnecessary prescription costs, more efficient cures, and less side-effects.

Keywords:
Precised medicine, Cancer, Tissue transplantation, Diet,

P1165

Association of G22A polymorphism of adenosine Deaminas with obesity in an Iranian population

Sepideh Borhan[1] ، Samaneh Sadat Enayati[2] ، Mahsa Mohammad Amoli[2]

1) Obesity and Eating Habits Research Center, Endocrinology and Metabolism Molecular -Cellular Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran
2) Metabolic Disorders Research Center, Endocrinology and Metabolism Molecular -Cellular Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran : amolimm@tums.ac.ir

Abstract:
Obesity is an important clinical and public health challenge and defined as an excess adipose tissue accumulation resulting from an imbalance in energy intake and energy expenditure. It is a forerunner for a variety of other disease such as type-2-diabetes, cardiovascular disease and can be fatal leading to premature death. Obesity is highly heritable and arises from the interplay of multiple genes and environmental factors. Adenosine deaminase, a key enzyme in purine metabolism, regulates extracellular and intracellular concentrations of adenosine by irreversible deamination of adenosine into inosine. ADA, present in all mammalian cells and its primary function in humans is development, differentiation, and maturation of the lymphoid system. ADA is encoded by the polymorphic ADA gene, which is located on chromosome 20q13.11. One of the commonest single nucleotide polymorphisms of ADA gene is the SNP G22A in exon1. This SNP results in the substitution of Asp amino acid (G allele) with Asn (A allele) amino acid in position 8 of the enzyme. The aim of the present study was to investigate the association between SNP G22A in the ADA gene with the obesity.

Keywords:
obesity, adenosine deaminas (ADA), G22A polymprphism

P1166

The study of the expression of apoptotic Bax, Bcl2 cells in the hippocampus following ischemia reperfusion model, pretreatment with nanoparticles of iron oxide in rat brain

Sanli Soltannejad[1] ، Mojtaba Falahati[2] ، Leila Pishkar[3]

1) Biology,IslamshahrBranch,Islamic University,Islamshahr,iran
2) Department of Nanotechnology,Facuity of Advance Sience and Technology,Islamac Azad University of Pharmaceutical Sciences(IAUPS),Tehran,Iran
3) Department of Biology,IslamshahrBranch,Islamic University,Islamshahr,Iran : leilapishkar@gmail.com

Abstract:
Progressive cell death of nerve cells after injury to the central nervous system is known as one of the most destructive factors in nervous system diseases. Ischemia / reperfusion cerebral blood supply to the brain process the sudden loss of blood supply to the brain and then return stroke during different parts of the brain under stress. Return observations have shown that reperfusion or re-perfusion to the brain by increasing the oxygen free radicals, mitochondrial dysfunction of neurons and activation of many signaling pathways involved in cell death key role in the development of neurological complications resulting from ischemia / reperfusion brain hasNanoparticles of iron oxide nanoparticles safely and with minimal cellular toxicity, which is now widely used in MRI-based brain imaging and treatment of diseases have been Bzkhy.

Studies show that the use of appropriate doses of the nanoparticles can restrict the right of free radicals within the cell That seems to have the appropriate power to protect neurons against cell death from ischemia / reperfusion have a brain In this study, the neuroprotective effects of ischemia reperfusion model in rats brain Fe2O3 nanoparticles were studied In this study Alfa' after ischemia / reperfusion brain injury in rats and treated with 5 mg / kg and 10 mg / kg apoptotic Bax and Bcl-2 gene expression using real time-PCR in the hippocampus region of the animals was investigated The results of the study showed that the expression of Bax and Bcl-2 ratio and pre-boarding after ischemia / reperfusion brain using iron oxide nanoparticles resulted in the induction of apoptosis Bax gene expression significantly (P -Value <0.01) than the control group decreased According to the results of the above study seem to be pre-treated with iron oxide nanoparticles with high potential to protect nerve cells in the brainfrom stroke are entitled.

Keywords:
apoptotic genes Bax and Bcl-2, hippocampus, ischemiareperfusion rat model of stroke, pretreatment, Nanvzra iron oxide

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P1168

Neutrigenomics: Future of Health and Disease

Azim Nejatizadeh[1] ، M.R. Noori-Daloii[2]

1) Molecular Medicine Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran : azimnejate@yahoo.com
2) aDepartment of Medical Genetics, Faculty of Medicine, Tehran University of Medical Sciences,Tehran, Iran

Abstract:
Today, the role of food and nutrition in human health and especially prevention of illness is gaining recognition. Micronutrients are essential for optimal human health. Diseases of modern society, such as diabetes, heart disease and cancer have shown to be effected by dietary patterns. Nutrition and genetics both play a significant function in human health as well as the development of chronic diseases. The risk of disease is often associated with genetic polymorphisms, but the effect is dependent on dietary intake and nutritional status. In other words, nutrigenomics describes the scientific approach that integrates nutritional sciences and genomics and incorporates the application of other high-throughput 'omics' technologies such as transcriptomics, proteomics and metabolomics to investigate the effects of nutrition on health. In fact, using the human genome data base as well as that of model organisms, nutrigenomics studies the genomewide effects of food components on gene expression (transcriptomics), the complete collection of proteins at a given nutritional state (proteomics) and the entire metabolite pattern occurring under a defined nutritional condition (metabolomics). Applied wisely, Omics will promote an increased understanding of how nutrition influences metabolic pathways and homeostatic control; how this regulation is disturbed in the early phase of a diet-related disease and to what extent individual sensitizing genotypes contribute to such diseases It is a great potential to improve health by understanding the interaction between nutrients/foods and body physiology, and thus improve dietary prevention and treatment of diseases affecting people in rich as well as poor societies. For the time being, nutrigenomics will definitely discover new, tasty, readily suitable, and more proper foods. There is no doubt that investment in nutrigenomics will advance the role of nutrition in public health.

Keywords:
nutrigenomics; omics; micronutrients; nutrition; genomics

P1169

Study of prevalence (HLA-A*3101) polymorphism association with Carbamazepine medicine prescription in different Iranian ethnicity

Parisa Azimii[1] ، Masood Hooshmand[2]
1) Islamic azad university of pharmaceutical science branch
2) National institute genetic engineering and biotechnology : housh62@yahoo.com

Abstract:

Pharmacogenetics is the study of medicines and their interactions as well as individuals' genotype. Single medicines have different impacts on different people. Some people need greater or lesser doses of medicines in order to achieve a therapeutic effect similar to the ones obtained in others.
Human leukocyte antigen (HLA) is the most polymorphic genetic system in human beings and is also known as major histocompatibility complex (MHC). Modulation of the immune response is the key role of HLA molecule. Human MHC has been mapped on the short arm of chromosome 6 (6p21). Human HLA has a total of 120 loci and 554 allele and covers about 1/3000 of the entire human genome.
HLA is a unique tool to study the genetic relationships between different populations. A strong signal in the MHC region is identified using a few SNPs (Single nucleotide polymorphism) around the HLA-A area.

HLA-A * 31: 01 is common allele on the HLA genes this is known as the most common genetic markers for prediction of hypersensitivity to carbamazepine. This medicine is used to treat epilepsy and bipolar disorders and leads to mild to severe allergies, as well as death in some cases.
It is proved that the HLA-A * 31: 01 allele causes hypersensitivity to carbamazepine and is also used to predict the occurrence of hypersensitivity to carbamazepine. A Significant correlation has been observed between the HLA-A * 31: 01 allele and carbamazepine hypersensitivity syndrome (HSS) and maculopapular Eczema (MPE).
A Definite Background on the relationship between rs1061205 and HLA-A * 3101 allele has already been observed. The present study is an attempt to investigate the presence or absence of HLA-A * 31: 01 allele among all the Iranian 10 ethnic groups(300 person), as a response with high resolution.

Keywords:
pharmacognetic , hla , carbamazepin , polymorphism

P1170

Over expression of MMP9 gene in peripheral blood of schizophrenic patients

Mahsa Dashtbani[1] ، Arvin Haghighatfard[2] ، Hossein Abaspour[1]
1) Department of Biology, Damghan Branch, Islamic Azad University, Damghan, Iran
2) Department of Biology ,Tehran North Branch,Islamic Azad university,Tehran,Iran

Abstract:

Schizophrenia (SCZ) is a complex psychiatric disorder with one percent prevalence in world population and severs positive, negative and cognitive symptoms. Matrix metallopeptidase 9 (MMP-9) or gelatinase B (GELB) located in 20q11 belong to the zinc-metalloproteinases family which are involved in the degradation of the extracellular matrix. Previous studies were reported involvement of MMP9 over expression with etiology of multiple sclerosis and metastatic tumors.

mRNA level of MMP9 gene have been studied in peripheral blood of 50 Iranian schizophrenic patients and 50 non-psychiatric subjects by using quantitative Real time PCR. Also positive and negative symptom scale (PANSS) from patients and Wechsler Adult Intelligence Scale (WAISE) from all subjects were obtained.

Significant over expression of MMP9 was detected in SCZ vs. non-psychiatrics. Correlations were found between over expression of MMP9 and higher scores of positive symptoms in PANSS. No significant correlation was found between gene expression and WAISE results.

Findings were suggested MMP9 involvement in etiology of schizophrenia. It seems that metalloproteinase deregulation may lead to neuronal dysfunction which in turn increases the positive symptoms in schizophrenic patients.

Keywords:
MMP9 -schizophrenia - gene expression

P1171

Epigenetics role on male reproduction

Roya Askarian
Medical Biochemistry : royaaskarian@gmail.com

Abstract:
The correlation between epigenetics and human reproduction represents a very interesting field of study, mainly due to the possible transgenerational effects related to epigenetic modifications of male and female gametes. The main epigenetic mechanisms of gene expression regulation are represented by DNA methylation, histone modifications, and small, non-coding RNAs. In the present review, we focused our attention to the role played by epigenetics on male reproduction, evidencing at least four different levels at which sperm epigenetic modifications could affect reproduction: (1) spermatogenesis failure(impairment of male fertility due to alterations in sperm number and morphology), (2) embryo development; (3) outcome of assisted reproduction technique (ART) protocols, mainly as concerning genomic imprinting; and (4) long-term effects during the offspring lifetime. Recent studies have demonstrated the presence of unique consensus DNA sequence motifs, zinc finger motifs, and G-quadruplex sequences in transgenerational DMR in sperm, which, by the interaction of molecular factors, could induce alterations of the chromatin structure and accessibility of proteins with DNA methyltransferases altering de novo DNA methylation patterns. Several environmental and lifestyle factors (stress, physical activity, alcohol intake, smoke, shift work) are known to affect male and female fertility , and in many cases, they have been shown to influence the occurrence of epigenetic modifications with implications for human diseases. It can be suggested that in the next future, the study of epigenetics and epigenomics will likely represent a crucial step in the diagnostic workup of the infertile male, especially in cases submitted to ART, where it will be necessary to select adequately functional sperm to avoid the epigenetic alteration impact on the procedure. Surprisingly, seminal plasma may affect offspring independently of sperm, by stimulating the production of embryotrophic cytokines and growth factors by the female reproductive tract. The alteration of this process induces abnormal fat deposition and metabolic phenotype in the offspring, particularly in the males.Most importantly, the possibility that paternal lifestyle could affect the health of the offspring during lifetime opens a novel and exacting scenario in the prevention of common, late onset diseases. The environmental agents responsible for epigenetic modifications are also examined, suggesting that the control of paternal lifestyle prior to conception could represent in the next future a novel hot topic in the management of human reproduction.

Keywords:
Male infertility, Gametogenesis, Epigenetics, DNA methylation, Transgenerational effect

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P1172

Therapeutic microRNA-based strategies in heart failure

Roya Askarian
Medical Biochemistry : royaaskarian@gmail.com

Abstract:
Background:MicroRNAs (miRNAs) have been studied intensively since their discovery more than two decades ago, which led to a drastic change in our understanding of regulatory epigenetic processes. MicroRNAs (22 nucleotides in length) are involved in several cell processes by repressing messenger RNA (mRNA) translation mainly via binding at the complementary 3′-untranslated region, thus modulating gene expression at the post-transcriptional level. In cardiac development, miRNAs are needed for the formation of normal, functional heart tissue and a variety of miRNAs have been discovered as important regulators of several phases in cardiac development.

The importance of miRNAs was originally demonstrated in embryonic development by modifications in Dicer, an enzyme involved in miRNA processing. Dicer1 gene targeting in mice resulted in early embryonic death. Furthermore, cardiac-specific deletion of Dicer shortly after embryonic heart formation resulted in cardiac malformations, heart failure and eventually death .Deletion of Dicer in the postnatal myocardium induced cardiac remodelling, increased atrial size, and resulted in early lethality. These results led to an increasing number of studies identifying specific miRNAs associated with several phases of cardiac development.

MicroRNAs (miRNAs) with key roles in cardiac fibrosis and hypertrophy in response to cardiac injury or overload. MiR-1, miR-21, miR-29, and miR-133 are presented with their known targets. The expression of miR-1, miR-29, and miR-133 is downregulated in cardiac tissue in response to cardiac injury or overload, leading to a decreased negative regulation of their mRNA targets. MiR-21 is upregulated in response to cardiac injury or overload, resulting in increased negative regulation of the corresponding targets. Moreover, long-term follow-up studies are necessary to identify any side-effects that may develop after months or years. Furthermore, circulating miRNAs are promising new biomarkers in heart failure for diagnostic and prognostic purposes, and to identify a patient’s response to therapy. Several miRNAs have been related to important mechanisms leading to heart failure, such as hypertrophy and fibrosis. An increasing number of miRNAs and miRNA targets have been reported in heart failure models, increasing our insight into the pathophysiology of this syndrome.

Conclusions:Loss- and gain-of-function experiments revealed an important role for miRNA mimics and antimirs—an interesting development that might broaden the treatment options for patients with heart failure. Together, miRNAs and miRNA-based therapies comprise one of the most innovative advancements of the last years and hold great promise for future clinical application in heart failure.

Keywords:
microRNA, heart failure, miRNA-based therapies

P1173

RNA-interference-mediated silencing of OCT4B1, alters expression profile of several TNF ligand/ receptor transcripts in human tumor cell lines

Mohammad reza Mirzaei[1] ، Gholamhossein Hassanshahi[2] ، Mohammad Kazemi Arababadi[3] ، Mohammad Reza Hajizadeh[2] ، Seyed Javad Mowla[4]

1) Rafsanjan university of medical sciences : mirzaeemr@gmail.com
2) Molecular Medicine Research Center, Rafsanjan University of Medical Sciences, Rafsanjan, Iran.
3) Immunology of Infectious Diseases Research Center, Rafsanjan University of Medical Sciences, Rafsanjan, Iran.
4) Department of Molecular Genetics, Faculty of Biological Sciences, Tarbiat Modares University, Tehran, Iran.

Abstract:
Background and aims: The OCT4B1 as a new discovered variant of OCT4 is expressed in both cancer cell and tissues. This variant with its anti-apoptotic properties aid cancer cells to scape from apoptosis. TNF ligands and receptors are amongst two categories of eleven gene families involved in the apoptosis pathway. Therefore, the aim of the present study was to investigate the effects of OCT4B1 suppression on several transcripts of both TNF ligands and receptors family in some tumor cell lines. Materials and methods: The AGS (gastric adenocarcinoma), 5637 (bladder tumor) and U-87MG (brain tumor) tumor cell lines were transfected with specific OCT4B1 siRNA and , as well as a scrambled sequence and PBS, as controls, using Lipofectamine 2000 comerical kit. The expression of TNF ligand and receptor transcripts were evaluated in parallel with beta-actin (as housekeeping gene) using Real-Time PCR technique. Results: our results indicated that in TNF ligand transcripts family, the mRNA level of TNF transcripts was up-regulated and inversely TNFSF8, TNFSF7, TNFSF10, TNFSF1 and TNFSF6 was down-regulated. We observed also that in TNF receptor transcripts family, six transcripts including, TNFRSF 10A, TNFRSF10B, TNFRSF11B, TNFRSF1A, TNFRSF21 and TNFRSF25 were up-regulated, while TNFRSF9 and CD27 were down-regulated. Conclusions: According to these results, it may be concluded that OCT4B1 suppression can lead to apoptosis in tumor cell lines via up-regulation of several TNF ligand and receptor transcripts. Thus, OCT4B1 suppression effects on TNF and its receptors may be considered as promising target genes in future studies in cancr research and therapy.

Keywords:
OCT4B1 suppression and TNF transcripts expression

P1175

The investigation of rs9939609 in FTO gene variation for identification of obesity predictor marker

Mina Mozafarizadeh[1] ، Masoud Houshmand[2]

1) Nour Danesh Institute of Higher Education
2) National Institute for Genetic Engineering : housh62@yahoo.com

Abstract:
Background and purpose:Obesity is a worldwide health challenges and the negative impact on health And reduces the lifespan and increase the risk of various diseases. Obesity is a medical condition characterized by the accumulation of excess fat in the body defined so that may have adverse effects on body mass index.Fat mass and obesity (FTO) leading to obesity and strongly expressed in the hypothalamus involved in regulation of energy balance and appetite.The aim of this study was to investigate the association between polymorphisms in genes of choice for obesity-related FTO (rs9939609). Methods: In this retrospective study The allelic frequency of markers selected from between 226 and 144 patients with obesity BMI 30 and below BMI 20 to BMI 25-30 and 83 Cases selected with BMI 20-25 TetraArms PCR was used to detect the expression of FTO .Statistical analysis was performed to assess the association between FTO expression and the clinicopathological features Result: Genetic factors play a significant role in the development of obesity Based on this research focused on identifying the genetic factors in the regulation of body weight. In this study a significant association was seen FTO . Body mass index (BMI) were divided into three groups: People with BMI less than 20 had on the people genotype A-A and A-T of RS9939609 were significant.(P = 000 and p = .120). In people who had a BMI between 25-30 were all significant. And those who had a BMI above 30 carries the gene FTO RS9939609 were all significant Conclusion: Our study suggests that FTO expression may have a vital role in the obesity. Which can be prevented by changing the living conditions of obesity in individuals.

Keywords:
obesity , fto , genetic variation

P1179

The role of personalized medicine in fluoropyrimidine-based chemotherapy: Identification of predictive markers in chemotherapy treatment

Mohamad hadi Abasian[1] ، Bahareh Abbasi[2] ، Nafiseh Ansarinejad[3] ، Farshid Fardad[3] ، Tayeb Ramim[4] ، Ali Ardekani[5]

1) National institute of genetic engineering and biotechnology (nigeb)
2) Department of Medical Genetic, Medical Biotechnology Ins., National Institute of Genetic Engineering and iotechnology (NIGEB), Tehran, IR Iran
3) Department of Hematology and Oncology, Hazrat Rasool-e Akram Hospital, Iran University of Medical Sciences, Tehran, IR Iran
4) Cancer Pharmacogenetics Research Group (CPGRG), Iran University of Medical Sciences, Tehran, IR Iran
5) National institute of genetic engineering and biotechnology (nigeb) iranhealth@hotmail.com

Abstract:
Introduction & Aim: The fluoropyrimidine drug 5-fluorouracil (5-FU) and the prodrug capecitabine, have been extensively used for treatment of many types of cancer including colorectal, gastric and head and neck. Approximately 10% of the patients suffer from severe fluoropyrimidine-induced toxicity, like diarrhea, mucositis, myelosuppression and hand-foot syndrome. This may lead to dose reduction and treatment discontinuation. Pharmacogenetics research could be useful for identification of predictive markers in chemotherapy treatment.
Methods: Germline DNA was extracted from 83 cancer patients treated with fluoropyrimidine-based chemotherapy in Hazrat Rasool-e Akram Hospital . In this study, we genotyped three polymorphisms in dihyropyrimidine dehydrogenase gene (rs3918290),(rs67376798),(rs55886062) and two polymorphisms, The variable number of tandem repeat (VNTR) polymorphism (rs45445694) and 6-bp insertion/deletion polymorphism(rs151264360) in thymidylate synthase gene. These genetic markers were correlated with toxicity to treatment. 5-FU-related toxicities such as Anemia, febrile neutropenia, neurotoxicity, vomiting, nausea and mucositis were evaluated according to NCI-CTC criteria version 4.0 .
Results: DPYD gene polymorphisms was not observed in this study. The frequency of the TYMS +6 bp allele was 40.35% and the -6 bp allele was 59.65% in this study. And frequency of VNTR 2R allele was 48.75% and 3R allele was 51.15% .Toxicity grade two diarrhea,mucositis,nausea,vomiting and neurotoxicity are 2.2%,24.1%,15.7%,6% and 51.8%, respectively . Thymidylate synthase ins/del polymorphisms was significantly associated with increased grade three Neurotoxicity (p=0.02) .
Conclusion: A pharmacogenetic approach could be a useful strategy for personalizing chemotherapy in cancer patients. Although rare DPYD polymorphisms was not observed in our study, according to large population studies, DPYD gene polymorphisms could be used as a predictive biomarker for efficacy of fluoropyrimidene-based chemotherapy . This study is currently underway to evaluate the role of thymidylate synthase polymorphisms in Progression-Free Survival, and Overall Survival in cancer patients .

Keywords:
chemotherapy,fluoropyrimidines, 5-fluorouracil,colorectal cancer, gastric cancer , dihydropyrimidine dehydrogenase,pharmacogenetics .

P1193

Whole Exome Sequencing Reveals a Novel Frameshift Deletion in Exon 7 of Wiskott-Aldrich Syndrome Causes Primary Immunodeficiency

Dr Majid Fathi[1] ، Arshad Hoseini[2]
1) Department of Medical Biotechnology, Faculty of Allied Medicine, Iran University of Medical Sciences, Tehran, Iran
2) hoseini.a@iums.ac.ir

Abstract:
Introduction: Emersion of next generation sequencing(NGS) has revolutionized our understanding of molecular basis of different diseases due to its great accuracy, high speed of sequencing and lowering the costs of previous methods. One of the most practical kinds of NGS methods is whole exome sequencing(WES) which sequences all of the exons of a genome as encoders of proteins which their defects are the main reasons of diseases. However, lots of our recent discoveries about novel genes and mutations are due to the data elicited from WES through several studies conducted for mendelian diseases, but some of the exome studies did not reached to the right fatal mutation because of wrong analyzing manners for identifying a variant, so acquisition of a right procedure for assessing data is indispensable.
Methods: In this study we outlined a practical framework to discover the variants cause a primary immunodeficiency as a heterogeneous mendelian disorder. We trimmed the reads based on their quality and merged them to reduce their numbers and also make them longer for better alignment in mapping step. After mapping and variant detection, we tried to filter and annotate variants with data and information from other genome wide associations studies which reduced the variants to less than 10 numbers. The rested variants were scrutinized by checking pathways and clinical manifestation of related disease, aiming to the real causing variant.
Results: We candidate a deletion in gene WAS which makes a frameshift leading its encoded protein to half of its normal size. Our claim was assayed by sanger sequencing of patient and his parents and its outcome verified our x-linked recessive mutation.
Conclusion: In this study we showed that utilizing of appropriate analysis tools can accede us to the exact deleterious mutation. As targeted therapeutics and personalized medicine are becoming increasingly common in diagnosis and treatment, utilizing NGS with appropriate ways of analyzing will smoothen our path to desired goals in this field.

Keywords:
whole exome sequencing, Primary Immunodeficiency, alignment, pathways, targeted therapeutics, personalized medicine

P1181

Investigation of SNPs of CXCL8 and KLRG1 in PBMC OF SLE patients

Fateme Shaabanpour aghamaleki[1] ، Shirin Farivar[2] ، Mohammad Mersad Ghorbani[2]
1) Shahid Beheshti University
2) Shahid Beheshti University : s_farivar@sbu.ac.ir

Abstract:
Background: Systemic lupus erythematosus (SLE), also known as lupus, is an autoimmune disease in which the body's immune system mistakenly attacks healthy tissue. Common symptoms include painful and swollen joints, swollen lymph nodes and a red rash on the face. The cause is not entirely clear. It is believed to involve hormonal, environmental, and genetic factors but genetic factors and SNPs play critical role.

Material and method: Expression profile by array of PBMC of SLE patients were downloaded from GEO website. SLE patient and control were compared with logfc for level of gene expression. Genes were divided into hyperexpression in SLE and hypoexpression in control and vice versa. Then genes with smallest p-value in each group were chosen. All SNPs and variations of genes were identified with UCSC and NCBI webservers. SNPs that related to south Asia were extracted with ExAC. Inaddition, Pathways that related to these genes were identified with reactome and genecard webservers and drugs related to SNPs for these genes were identified.

Results: CXCL8 was highly expressed and KLRG1 was down expressed in SLE patients with smallest p-value. Then some SNPs of these genes that are common in south asia was identified. Most important pathway of KLRG1 was adaptive immune system and it interact with PTPN11 and LYN. Also important pathway of CXCL8 was TLR signaling, this pathway interacts with RELA and CXCR4. Furthermore, some drug such as Simvastatin and ABT was identified that target CXCL8.

Conclusion: Genes and their SNPs are associated with several diseases such as SLE. SNPs can affect protein structure and pathway, but ethnic variations of polymorphisms have very important role in seceptibility of variants for diseases So it is important to detect critical genes and their SNPs in each disease to help drug designing also it can help in personal medicine.

Key word: Genes, SNP, Pathway, Drug.

Keywords:
Genes, SNP, Pathway, Drug

P1195

CRISPR Method and Applications

دکتر لادن یاری
Nigeb : lad_ya@yahoo.com

خلاصه مقاله:
از جمله روش های ویرایش ژنوم CRISPR است که به صورت Crisper تلفظ می شود. این سیستم شامل بخشی از DNA پروکاریوتی است که به صورت تکرارهایی کوتاه قرار گرفته اند. در فاصله هر تکرار قسمتهای کوتاهی از DNA به صورت Spacer DNA ایجاد شده است که نتیجه مواجهه قبلی با باکتریوفاژ ویروسی یا پلاسمید است. این سیستم یک سیستم ایمنی پروکاریوتی است که باعث مقاومت به عناصر ژنتیکی خارجی می شود و شکلی از ایمنی اکتسابی را فراهم می کند. این توالی های فاصله انداز مسئول شناسایی عناصر اگزوژن بوده و مشابه RNAi در سیستم یوکاریوتی عمل می کنند. در حضور Cas که نوکلئاز وابسته به CRISPR است و gRNA شناسایی و برش ژنوم خارجی میسر می شود. این سیستم ویرایش ژنومی قابلیت اصلاح جهش های نقطه ای، حذف و اضافه شده گی های کوچک و درنتیجه بازیابی ژن سالم را در دسته های مختلفی از اختلالات ژنتیکی داراست. به علاوه با امکان اصلاح سلول های بنیادی لایه زایا امید فراوانی به اصلاح نواقص ژنتیکی پیش از تولد هم هست.

واژه های کلیدی:
Cas ، RNAi ، CRISPR ، نوکلئاز، gRNA .

P1010

سرطان ریه، عوامل و راهکارها

Golahmadnejad Arezoo ، Dr Alireza Sehat[1]
arezoo.g.ahmadnejad@gmail.com
1) Research

خلاصه مقاله:
در سالهای اخیر پیشرفت های بدست آمده در زیست شناسی سلولی و ژنتیک مولکولی ما را نسبت به سرطان بصورت قابل توجهی افزایش داده است. تمامی سرطانها بیماری ژنتیکی سلولهای سوماتیک هستند و دلیل اصلی آنها نقص در تقسیم طبیعی سلول و یا از دست رفتن مرگ برنامه ریزی شده سلول است. اما؛ تعدادی از سرطان ها هستند که بر اثر به ارث بردن یک جهش در سلول های رده ی زاینده بوجود می آیند و بصورت یک صفت مندلی به ارث می رسند. دلیل ۹۰ درصد از سرطان های ریه قرار گرفتن در معرض دود دخانیات برای یک مدت طولانی است . درصد ابتلا به سرطان ریه در افرادی که سیگار نمی کشند ٪۱۵ است.

SCLC (Small cell Lung cancer)حدود ٪۲۰ از سرطان های ریه را تشکیل می دهند و Non-Small Cell Lung Cancer (NSCLC) نیز حدود ٪۸۰ را تشکیل می دهند.

این مطالعه ، بر اساس کارهای تحقیقاتی صورت گرفته در عامل ایجاد سرطان (اپی ژنتیک) و مطالعات انجام شده در ارتباط با برخی روش های درمان سرطان (جراحی، غدد لنفاوی مدیاستن، PET اسکن ، نانو فناوری siRNA، RNA) ، به خصوص سرطان ریه می باشد.روشهای درمان باید بگونه ای باشد که برای بیماران تحمل پذیرتر بوده و عوارض کمتری داشته باشد که اغلب این تکنیک ها نیاز به دستگاه های مدرن پزشکی و تجربه کاری بالا دارند.

واژه های کلیدی:
سرطان، ریه، درمان، جراحی، اپی ژنتیک

شناسنامه

صاحب امتیاز:
شرکت دانش بنیان گروه توسعه فناوری پزشکی آمیتیس ژن

سردبیر:
سیده نیره مصلحی

انتشار:
زمستان ۱۳۹۵

طراح و صفحه آرا:
شهاب رزاق

طراح جلد:
شهاب رزاق

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P1119

پزشکی شخصی بر اساس رابطه متقابل روان و ژن

پروفسور سید ضیاءالدین تابعی

Director of the medical ethics department : ethics@sums.ac.ir

خلاصه مقاله:

بر اساس تحقیقات و پیشرفتهای علمی ، روانی ، روحانی نکات زیر امروزه در صدر تحقیقات زیربنایی قرار گرفته است .
۱ـ با تعیین نقشه ژنتیکی انسان (Human gene mapping یا Human genome اثبات شده است که ژن در ایجاد و پیشرفت بیماری های جسمانی نقش در حد ٪۵۰ بیشتر ندارد و مطالعاتی که بخصوص در سال های اخیر به همکاری جامعه شناسان و متخصصین ژنتیک به عمل آمده و توصیه علمی آن یعنی اثر اراده و روان انسان بر ژنتیک از طریق دانش epi genetic به اثبات رسیده است لذا مسئله Personalized Medicine باید شامل تمام ابعاد هویتی انسان باشد که شامل روح که خود را در انسان به صورت Cognition(شناخت) وIntention (اراده) نمود می یابد شخصیت روانی فرد را شکل می دهد و این مجموعه روحانی ، روانی ارتباط دوجانبه با دستگاه ژنتیکی انسان دارد لذا اگر بخواهیم پزشکی شخصی را جامع الاطراف کنیم باید به این تحقیقات گوشۀ چشمی داشته باشیم . اولین کنگره در مورد خود شخص انسان از روح تا مغز در یک کنگره عظیم در آکادمی علوم Newyork برگزار شده است بطور جامع مورد کنکاش قرار گرفته است .
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۱ـ پروفایل ژنی
۲ـ پروفایل شخصیتی (روحی و روانی)
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۴ـ پروفایل بیوشیمیایی و ایمنولوژی

واژه های کلیدی:
پروفایل ژنی، پروفایل شخصیتی، رابطه روان و ژن

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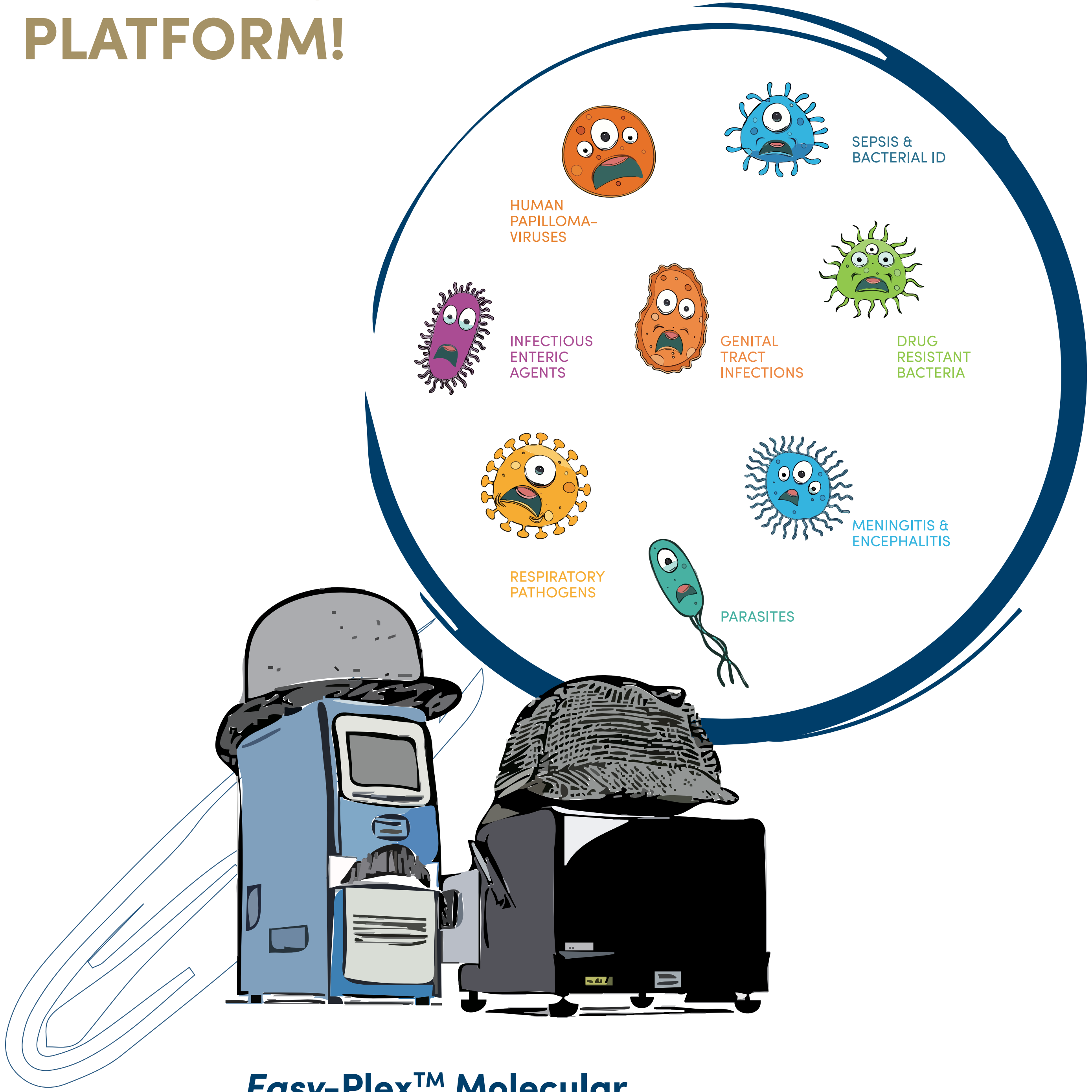
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