Abstract Booklet

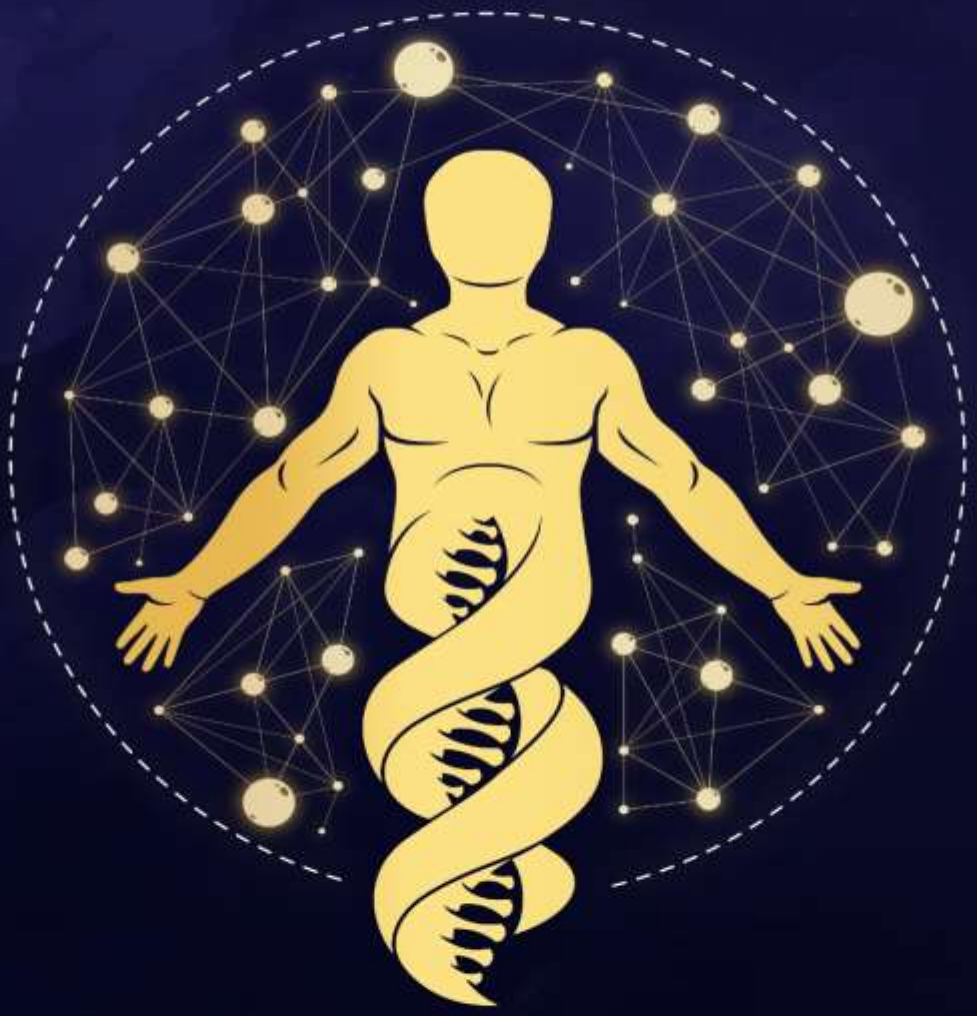
دانشگاه یزد
YAZD UNIVERSITY

2021 International Conference on Human Genetics and Genomics

1-2 December Yazd University

International Conference on Human Genetics and Genomics

With the participation of University of Algarve, Portugal
and Sechenov University, Russia



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In the Name of

GOD

the Compassionate,
the Merciful

2021 International Conference on Human Genetics and Genomics

1-2 December

Yazd University

With the participation of University of Algarve, Portugal
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Final Extension

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Topics:

- Human Molecular Genetics
- Clinical Genetics
- Bioinformatics
- Genetic Diagnosis and Counseling
- Pharmacogenomics

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International Conference on Human Genetics and Genomics

1-2 December, 2021,

Yazd University, Yazd, Iran

The Conference Chairman Message:

International Conference on Human Genetics and Genomics was held with the ambitions and efforts of the Biology Department of Yazd University in cooperation with Portugal's University of Algarve and Russia's Sechenov University.

The conference aimed to utilize country's scientific capacity to find answers of basic inquiries about genetics, become a turning point for increasing scientific research collaborations, and create a suitable platform for researchers to provide their state-of-art achievements and to create opportunities for younger researchers in order to get acquainted with current issues and basic topics of genomics.

It was our honor to host scientists and speakers from Iran, New Zealand, Brazil, Russia, Portugal, China, France, United States, Portugal, Switzerland, India and Pakistan. Besides, the side program of this conference was holding specialized workshops focusing on various genetic issues.

On behalf of the conference organizing committee, I hope this virtual conference could provide a valuable opportunity for specialists, medics, and students to exchange their opinions, achievements and innovations.

I wish you dear ones, ever-increasing success and grant my heartfelt appreciations for your participation in the International Conference on Human Genetics and Genomics.

Best Regards

Dr. Mohammad Mehdi Heidari

Conference Chairman

International Conference on Human Genetics and Genomics

Conference Oraganization

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Dr. Sina Majidian: Post-doctoral fellow oa the Faculty of Biology and Medicine, University of Lausanne, Switzerland.

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1-2 December, 2021, Yazd University, Yazd, Iran

Computational Analysis of Notch1 and its correlated miRNAs Involved in Colorectal Cancer Progression

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Abstract

Backgrounds: The advances in computational analysis facilitated the investigation for RNA analysis, and enabled us to study bimolecular interactions and cancer biomarkers more efficiently due to the ability to precisely analyze large amounts of data in a short time. In cancer pathophysiology, microRNA (a small non-coding RNA that contains 20-25 nucleotides) has received remarkable attention for its involvement in regulating the expression of a variety of genes. So far, several miRNAs have been found that express aberrantly in colorectal cancer which is one of the most prevalent occurring carcinomas worldwide. In this study, we aim to focus on discovering the crosslink between Notch1 and its related miRNAs as a key oncogene in colorectal carcinoma.

Materials and Methods: It has been reported that the overexpression of Notch1 is associated with the high proliferation of colorectal carcinoma cells; therefore, Notch1 possesses a key oncogenic role in colorectal cancer. The interaction between notch1 and its target miRNA was found by implementing the miRTargetLink database. Overall, 36 miRNA was found to be highly associated with notch1 expression. Among the predicted miRNAs, four of them were nominated for their strong correlation with notch1 in colorectal cancer. The candidate miRNAs were further examined for KEGG enrichment pathway analysis by using Diana miRpath V.2 algorithm.

Results: The analyzed data obtained from miRTargetLink databases showed that miR-181a-5p, miR-34a-5p, miR-24-3p, and miR-30a-5p are significantly correlated to Notch1. Furthermore, by using Diana miRpath algorithm, we demonstrated that these miRNAs play important roles in cell cycle, Wnt signaling, and Hippo signaling pathways.

Conclusion: Taking into account the low level of expression of miR-181a-5p, miR-34a-5p, miR-24-3p, and miR-30a-5p in colorectal cancer and their direct interaction with Notch1 oncogene, it can be observed that these miRNAs can severs as potent regulators of signaling pathways involved in colorectal cancer progression.

Keywords: computational analysis, colorectal carcinoma, microRNA, Notcth1

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1-2 December, 2021, Yazd University, Yazd, Iran

Naringenin and Resveratrol Anti-tumor Impact on the Y79 Retinoblastoma by Affecting E/N-Cadherin and Galectin-3; Possible Synergistic Effect

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Abstract

Backgrounds: One of the detrimental features of retinoblastoma is highly invasiveness of this type of cancer; the ability to metastasize into distal organs even in the early stages. This phenomenon highlights the importance of experiments targeting this characteristic to diminish the disquieting outcomes. In this study, our main aim was to assess the impact of naringenin and/or resveratrol treatment on the important genes expression in the metastasis and cancer progression pathways in the Y79 retinoblastoma cell line.

Materials and Methods: To attain the cytotoxicity dose of both reagents, an MTT assay was performed for 24 and 48 hours. The Y79 cells were then treated with a lower dose compared with the IC50. To further investigate the synergistic effect of the compounds, concurrent treatment was also done. Finally, the expression of E-cadherin, N-Cadherin, and Galectin-3 was investigated in different samples with the aid of real-time PCR.

Results: According to the MTT assay the 24 hours IC50 for resveratrol was about 100 µg/ml and 48 hours IC50 was about 50 µg/ml. Naringenin 48 hours IC50 was calculated to be 100 µg/ml. Treatment of Y79 cells with naringenin, resveratrol, or the concurrent treatment down-regulated the N-Cadherin mRNA expression level. Treatment with resveratrol or the concurrent increased the expression level of the E-Cadherin and diminished Galectin-3 expression.

Conclusion: Resveratrol seems to be more toxic for Y79 cells compared with naringenin. Two compounds didn't show a significant synergistic effect. Both compounds exert an anti-metastatic effect on these cells by inducing N-Cadherin down-regulation. Resveratrol enhanced the expression of the E-Cadherin, along with the decreasing the Galectin-3 exerts even more anti-tumor activity, and can be proposed as a beneficial reagent in cancer immunotherapy.

Keywords: Retinoblastoma, Metastasis, E-Cadherin, N-Cadherin, Galectin-3

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GJB2 gene related nonsyndromic hearing loss in Mazandaran Province, north of Iran

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Abstract

Backgrounds: Congenital hearing loss is the most common sensory deficit in the world and mutations in the GJB2 gene are the most common cause of deafness in many populations. The frequency of GJB2 mutations is estimated at 16% in Iran and varies among different provinces with a decreasing trend from north to south. The aim of this study was to investigate the frequency of GJB2 mutations in Mazandaran province, north of Iran, among non-syndromic hearing loss patients.

Materials and Methods: 262 patients from 204 families participated in this study. After genomic DNA extraction, GJB2 gene analysis was carried out using DNA sequencing of both coding and non-coding regions by the ABI 3130XL genetic analyzer.

Results: 30.15% of all subjects showed mutations in the GJB2 gene. Four mutations, including c.35delG (Gly12Valfs*), IVSI-1+1G>A, c.95G>A (Arg32His), and c.224 G>A (Arg75Gln) comprises 69.89% of all mutations in this study. 35delG and IVSI-1 were the most common mutations among patients respectively. Codon 75 mutation (c.224G>A, p: Arg75Gln) with autosomal dominant inheritance was seen in 7 cases from 3 families. 22 patients showed only one mutation in the GJB2 gene and in 126 (48.09%) individuals, parents had a consanguineous marriage.

Conclusion: The frequency of GJB2 gene-related hearing loss among patients was higher than average (16%) in this province. This study also showed the dominant inheritance of the GJB2 gene in this area. Consanguineous marriage also showed highly frequent among parents. More investigation is needed to clarify for those 22 patients with one mutation in the GJB2 gene; either two gene inheritance or another gene may be responsible for hearing loss.

Keywords: Hearing Loss, GJB2, Mazandaran, Hereditary Deafness, Nonsyndromic

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1-2 December, 2021, Yazd University, Yazd, Iran

Comparison of CD4+ and CD8+ T- lymphocyte in Helicobacter pylori-negative functional dyspepsia

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Abstract

Backgrounds: Functional dyspepsia (FD), with a global prevalence of 10-20%1, is usually characterized by persistent or recurrent abdominal discomfort or pain with no obvious cause2. The current study was designed to evaluate and compare CD4+ and CD8+ in Helicobacter pylori-negative functional dyspepsia with the control groups.

Materials and Methods: Sixty-one patients (35 patients with stomach pain and 26 with abdominal bloating), and 30 controls were reviewed based on the quantity of CD4+ and CD8+ T-cells isolated from gastric mucosa biopsy samples. The comparison between variables was analyzed with a chi-square or Fisher's exact test and logistic regression analyses.

Results: A significant difference was observed between two-group patients and the control group based on CD4+ and CD8+ presence, respectively (P=0.003 and P=0.008). Furthermore, there was a significant difference between stomach pain patients and the control group with regard to CD4 count (P=0.01) and between abdominal bloating patients and the control group with regard to CD8 count (P=0.002). There was a decrease in both CD4+ and CD8+ T-cells in gastric mucosa in patients with FD with a significant reduction in the stomach pain-patients and abdominal bloating-patients in the number of CD4+ and CD8+ T-cells, respectively.

Conclusion: The symptoms of FD have a positive correlation with the presence of CD4+ and CD8+ T cells in the gastric mucosa due to various factors. These T cells might play an important role in inflammation, which might help to find a more specific therapy for FD.

Keywords: Functional dyspepsia, T-lymphocytes, Helicobacter pylori, CD4, CD8.

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Comprehensive bioinformatics analysis of mir-616 in triple negative breast cancer

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Abstract

Backgrounds: MicroRNAs (miRNAs) are endogenous, small non-coding RNAs with function in the regulation of gene expression. The expression of miRNAs is dysregulated in numerous human cancers through various mechanisms. Mir-616 is newly confirmed to be a cancer-related miRNA. miR-616 was proved as up-regulated miRNA in triple-negative breast cancer (TNBC). It was known that TNBC patients with up-regulated miR-616 had a poor prognosis. The aim of this study is to carefully examine the molecular mechanism of mir-616 in TNBC pathogenesis.

Materials and Methods: Briefly, the mRNA dataset (GSE38959) was retrieved from GEO to identify the differentially expressed genes (DEGs). The target genes of hsa-miR-616 were predicted using miRWALK and TargetScan. Overlapping genes between DEGs and has-miR-616 targets were subjected to protein-protein interaction network (PPIN) construction via STRINGdb R package. Down-regulated genes are merely filtered out due to reciprocal regulation. Finally, GO and KEGG enrichment analyses were used.

Results: A total of 116 overlapping genes related to TNBC and miR-616 were found. Only 31 genes, out of the total 116 genes, were selected which have reciprocal regulation with mir-616 expression. Genes were enriched for pathways in cancer including estrogen signaling pathway, neurotrophin signaling pathway, JAK-STAT signaling pathway, and PI3K-Akt signaling pathway. Additionally, GO enrichment analysis indicated steroid hormone and protein kinase B signaling pathway, transcription regulation, and phosphatidylinositol 3-kinase complex.

Conclusion: In conclusion, we investigated the miR-616 molecular mechanism in TNBC and provided a comprehensive view of the underlying mechanisms. These can be further studied in detail in order to find new targeted therapies for TNBC.

Keywords: Triple negative breast cancer, MicroRNAs, Functional annotation, Signaling pathways, Differentially expressed gene

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1-2 December, 2021, Yazd University, Yazd, Iran

Evaluation of VEGFA mRNA as non-invasive diagnostic biomarker in endometriosis

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Abstract

Backgrounds: In endometriosis, a prevalent woman chronic disorder, the endometrial tissue is present outside the uterine cavity. It disrupts the quality of women's life due to complications including pelvic pain and infertility. The delayed diagnosis by the invasive disease definitive diagnosis, laparoscopic surgery, necessitates introducing non-invasive diagnostic biomarkers. Angiogenesis is one of the essential processes involved in endometriosis pathogenesis. Thus, in this study first, the VEGFA gene expression as angiogenesis's key factor is evaluated in aberrant endometrial tissue by bioinformatics analysis. Then the mRNA of VEGFA is measured in plasma of endometriotic women compared with normal women.

Materials and Methods: The VEGFA gene expression in ectopic tissue of endometriosis and normal endometrial tissue was compared using the GEO database and GEO2R analysis. Then, the gene mRNA was analyzed in 24 plasma samples of endometriotic women and compared with the equivalent number of control women by the qRT-PCR.

Results: In the GEO database, analyzing two datasets (GSE25628 and GSE120103) using GEO2R and P-value less than 0.05 and logFC more than 0 showed a significantly increased VEGFA gene expression in ectopic endometriosis tissue compared to normal endometrial tissue (with 26 samples of ectopic endometriosis vs. 24 normal endometria). However, qRT-PCR results revealed no significant increase in VEGFA mRNA expression in the case group plasma versus the control.

Conclusion: The mismatch of VEGFA gene expression profile in endometrial tissue and plasma of endometriotic women suggests no potential of this gene as a non-invasive diagnostic biomarker for endometriosis despite its importance in the pathogenesis of endometriosis.

Keywords: VEGFA, Non-invasive diagnosis, Endometriosis, GEO, qRT-PCR

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Bioinformatics-based analysis of microRNAs as crucial contributors in gastric cancer

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Abstract

Backgrounds: Gastric cancer, known to be the leading cause of cancer mortality, is particularly common across Asia. MicroRNAs (miRNAs) are small non-coding RNAs, play a critical role in posttranscriptional gene regulation, related to cell survival, proliferation, differentiation, migration, metastasis, and invasion. Recently, the presence of human epidermal growth factor receptor 2 (HER2; also known as ERBB2) expression in advanced gastric cancer has played an important role in treatment. In addition, it is known that ERBB2 gene mutation overexpression, leading to HER2, occurs early in carcinogenesis. Our study aimed to estimate the contribution of selected dysregulated miRNAs to the pathogenesis of gastric cancer.
Materials and Methods: In this theoretical study, based on bioinformatics analysis of miRNAs, by using the KEGG database we found that ERBB2 is an oncogenic related to the signaling pathways involved in gastric cancer pathogenesis. The miRTargetLink (https://ccb-web.cs.uni-saarland.de/mirtargetlink/) database was used to search the miRNAs that target the ERBB2 gene. Then, we confirmed the suggested miRNAs by the online predictive tools such as DIANA-miRPath (http://diana.imis.athena-innovation.gr/DianaTools/), Targetscan (http://www.targetscan.org/vert_72/) and OncomiR (http://www.oncomir.org/)
Results: According to the results of this study, the ERBB2 gene is the target of hsa-miR-21-5p, hsa-miR-125b-5p, and hsa-miR-125a-5p. Also, they can modulate the pathogenesis of gastric cancer by regulating ErbB and p53 signaling pathways.
Conclusion: The results of this study showed that miRNAs targeting the ERBB2 gene are involved in key molecular pathways and biological processes of gastric cancer pathogenesis, and they can be novel therapeutic options in future experimental researches on the field of gastric cancer.

Keywords: Gastric cancer, miRNAs, Bioinformatics, ERBB2

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Lesser known factors in having diabetes; focus on: aralkylamine N-acetyltransferase (AANAT)

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Abstract

Backgrounds: Today, the effect of HLA-DQA1, HLA-DQB1, and HLA-DRB1 genes in the development of diabetes has been confirmed. In this study, we intend to examine the role of aralkylamine N-acetyltransferase (AANAT) gene in having diabetes which is generally effective in regulating circadian rhythms and melatonin levels.

Materials and Methods: Two rats named I and II were tested. rat I was kept in a dark environment away from light. rat II were kept in a well-lit environment away from darkness. Both rats were kept in these environments for 3 months. The rats were similar in age and are healthy as well as the same diet. The number of insulin receptors, blood melatonin levels, and blood sugar levels was measured in two rats on a regular basis.

Results: After three months, the level of blood melatonin in rat I increased from 7.5 mg to 11.3 mg, in rat II, the level of blood melatonin decreased from 6.8 mg at the beginning of the experiment to 2.1 mg at the end.

measurements of insulin receptors in rats I and II show that by increasing melatonin levels, which means increasing the expression of AANAT, the number of insulin receptors dropped and blood sugar levels increased in rat I, in contrast, by decreasing expression of AANAT in rat I promote the number of insulin receptors increase.

Conclusion: Due to changes in the level of Insulin with an increase or decrease in the expression of the AANAT gene in rats, it seems that the AANAT gene is related to diabetes.

Keywords: AANAT, diabetes, Insulin, Melatonin, rat

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The important role of copy-number variations in hereditary spastic paraplegia

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Abstract

Backgrounds: Hereditary spastic paraplegia (HSP) is a genetically heterogeneous neurodegenerative disorder, characterized by progressive spasticity, and weakness. Different types of mutations in more than 73 genes have been identified in HSP, especially by the whole-exome sequencing (WES) method. However, WES has failed to find the causative variants in ~50% of HSP cases. Regarding that, typical WES analysis cannot detect copy-number variations (CNVs). CNVs have a highlighted role in HSP, as ~20% of the most common type of HSP, SPG4, is due to CNVs. Also, CNVs account for ~19% of SPG11 and ~14% of SPG7, the most common types of autosomal recessive HSP. Nowadays, a number of tools are proposed for CNV-detection based on WES data. Therefore, we tried to analyze seven HSP-affected Iranian families whose disease-causing genetic variants did not recognize by routine WES analysis.
Materials and Methods: We used Germline CNV Caller to identify probably pathogenic CNVs using WES data. Multiplex ligation-dependent probe amplification (MLPA) was used to confirm the CNV/CNVs.
Results: A large deletion of exon 17 of the SPAST gene was detected in a proband (1/7: ~14%) and confirmed by MLPA.
Conclusion: This finding confirms the importance of CNVs as a cause of HSP, while typical WES analysis will miss them. Due to the significant percentage of CNVs, especially in some HSP genes, like SPAST, SPG11, and SPG7, CNV analysis should be considered among this category of neurological disorders. This analysis can be performed using tools like Germline CNV Caller which helps to detect CNVs based on WES data.

Keywords: Hereditary spastic paraplegia (HSP); Copy-number variations (CNVs); whole-exome sequencing (WES); MLPA; Germline CNV Caller

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Design of a T-cell epitope vaccine against BKRF4 protein Epstein-Barr virus in Burkitt's lymphoma using immunoinformatics approaches

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Abstract

Backgrounds: Epstein - Barr virus (EBV) is a lymphotropic herpes virus and the causing factor of infectious mononucleosis (IM). It was originally discovered in cells isolated from African Burkitt's lymphoma. Later on, its widespread prevalence in the world was recognized. In this study, by utilizing immunoinformatics and reverse vaccinology approaches, we design a candidate multi-epitope vaccine against the EBV virus that is likely to be safe and immunogenic against the EBV infection.

Materials and Methods: First, the BKRF4 protein sequence was downloaded from the UniProtKB or viPR databases in FASTA format, and then in the Vaxijen v2.0 database, the protein was examined for antigenicity. NetCTL1.2 server was used to find peptides that could be detected by T-cells, and then an IEDB server was used to examine the binding of epitopes to different MHC alleles and to evaluate immunogenicity. (Threshold for this model: IC50<200)

Results: In this study, 9 T-cell epitopes were predicted. The best epitopes with the highest scores in MHC-I and MHC-II are equal to : (HLA-A*01:01(peptide:VSDTDESDY,IC50=74.40)(peptide: PSDSDESDY,IC50=76.83)) and (HLA-DRB1*01:01(peptide:MAMFLKSRGVRSCRD,IC50=17.0)(peptide:AMFLKSRGVR CRDR,IC50=17.0)) and the best immunogenicity of peptide 9 amino acids is :(VSDTDESDY: 0.035)

Conclusion: Based on the immunoinformatics results obtained, it seems that different epitopes from Epstein-Barr Virus structural proteins have a high ability to stimulate humoral and cellular immune responses, so the epitope vaccine designed with these epitopes, can help to accelerate the production of effective vaccines against EBV.

Keywords: Immunoinformatics, T cell epitopes, Vaccine design, Epstein-Barr virus

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In-Silico Analysis of single nucleotide polymorphisms (SNPs) in PTEN gene associated with T-cell acute lymphoblastic leukemia

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Abstract

Backgrounds: T-cell acute lymphoblastic leukemia (T-ALL) causes the development of T cells in the thymus. T-ALL affects almost 12% to 15% of pediatric ALL cases. The tumor suppressor gene PTEN (phosphatase and tensin homolog), which is localized 10q23, plays a key role in a wide variety of cancers. PTEN is considered as a negative regulator of the PI3K-AKT signaling pathway that often is inactivated due to various mutations. Our purpose is to determine the pathogenicity of rs121909226 and rs121909230 in cancer malignancy, particularly T-ALL.

Materials and Methods: In this study, two SNPs from the PTEN gene (rs121909226, rs121909230) have been identified using Entrez Gene on National Center for Biological Information (NCBI) website. The rs121909226 leads to L70P change and in the rs121909230, L in position 112 changes to P. These SNPs have been analyzed by bioinformatics servers predicting harmful SNPs, including SIFT, I-Mutant 2.0, and Polyphen.

Results: SIFT server indicated that the rs121909226 affects the protein function with a score of 0.00. It was predicted to be probably damaging with a score of 1.0 by the Polyphen-2. Plus, the I-Mutant server showed a large decrease (about -1.44) in protein stability. The rs121909230 affected the protein function with a score of 0.00 by SIFT, it would probably be damaging with a score of 1.00 by the Polyphen-2. Additionally, the I-Mutant server showed a large decrease (about -1.82) in protein stability.

Conclusion: This study suggested that L70P and L112P variants of PTEN would probably be pathogenic and might have a deleterious effect on the protein function.

Keywords: Acute lymphoblastic leukemia, PTEN, SIFT, Polyphen, I-Mutant

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Vanadyl Sulfate has an Apoptotic Effect on MCF-7 Breast Cancer Cell Line

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Abstract

Backgrounds: Breast cancer is the major cause of death from cancer among women. Given the drug resistance created in the treatment of this disease, it is very important to identify new therapies and new anti-cancer drugs. Some studies indicate the cytotoxic effects of vanadyl oxide sulfate (VOSO4). Therefore, this study aims to evaluate the anti-cancer effect of $VOSO_4$ in the treatment of breast cancer.

Materials and Methods: MCF-7 cell line was treated with different concentrations of VOSO4 for 24 and 48 hours. The measurement of cell death was performed by MTT assay. The cell apoptosis rate was measured using Annexin V / Propidium Iodide Assay through flow cytometry. The level of expression of *p53*, *P21*, *Caspase8*, *Sod1*, *Sod2*, and *Bcl2* mRNAs were evaluated, and Western blotting was performed for *Sod1* to confirm the results.

Results: The results showed that the half-maximal inhibitory concentration (IC50) for VOSO4 was 25 and 20 for 24 and 48 h, respectively. Indeed, VOSO4 has dose-dependent cytotoxic effects on the MCF-7. Also, the apoptosis of the cells after 24 h of exposure to VOSO4 was more than 52%. Moreover, after 24 hours of exposure to VOSO4 with IC50 concentration, the expression of *p53*, *P21*, *Caspase8*, *Sod1*, *Sod2* mRNAs increased and the expression of *Bcl2* mRNA decreased. The Western blotting on *Sod1* confirmed these findings.

Conclusion: Our results demonstrated that VOSO4 has an apoptotic and cytotoxic effect on breast cancer cells. Therefore, it is likely that this substance can be considered as a complementary agent for the medical treatment of breast cancer patients.

Keywords: Vanadyl Sulfate, Breast Cancer, Anti-cancer, MCF-7

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A bioinformatics analysis of Runx1 and its related miRNA Involved in Colorectal Cancer metastases

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Abstract

Backgrounds: Colorectal cancer is one of the most frequent carcinoma worldwide, and it is also one of the most important causes of death in the world. MicroRNAs (miRNAs or miRs) are small single-stranded non-coding RNA molecules that play key roles as master regulators of many biological processes altered in cancers such as colorectal cancers. Additionally, they can be used to diagnose, treat and monitor cancer. Here, we aimed to examine the crosslink between some of these miRNAs and a specific gene in colorectal cancer. The association between the expression of genes and miRNAs is significant, and changes in their expression levels can onset cancer.
Materials and Methods: Runt-related transcription factor 1 (RUNX1) acts as an oncogene in tumors. Abnormal upregulation of RUNX1 has been suggested to contribute to the carcinogenesis of colorectal cancer. By using the miRTargetLink database, we found out that RUNX1 is strongly associated with certain miRNAs. Finally, using the Diana miRpath V.2 algorithm, we found out that it has a significant relationship with miR-106a-5p, miR-20a-5p, and miR-17-5p.
Results: Data analysis showed that miR-106a-5p, miR-20a-5p, and miR-17-5p were significantly associated with the Runx1 gene, which could be associated with the TGF-beta, p53, and foxO signaling pathways. Due to the effect of the TGF-β signaling pathway on cell migration, this can affect cancer metastasis.
Conclusion: These results revealed RUNX1 could regulate colorectal cancer migration via the TGF-β signaling pathway, and RUNX1 might serve as a potential target for preventing colorectal cancer metastasis.

Keywords: TGF-beta, colorectal cancer, miRNA, Runx1

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SiRNA-mediated knockdown of Nrf2 gene induces apoptosis of AGS cells

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Abstract

Backgrounds: Gastric cancer (GC) is the second leading cause of death from cancer. One of the involved genes in gastric cancer is nuclear factor erythroid 2–related factor 2(Nrf2). Upregulation of Nrf2 leads to tumorigenesis of GC cells. In this study, the effect of Nrf2 knockdown using a specific siRNA was investigated on a GC cell line.

Materials and Methods: First, AGS cells that have higher expression of Nrf2 were selected for further investigations. Subsequently, the cells were cultured in a 10% RPMI medium to reach 70% confluence. Then, the cells were transfected with Nrf2 siRNA and the expression level of the Nrf2 gene was measured by qRT-PCR in the treatment groups. Finally, the cell viability and apoptosis were evaluated by MTT and annexin V-FITC/PI staining respectively.

Results: Our findings demonstrated that the siRNA-mediated Nrf2 knockdown effectively suppressed the expression level of Nrf2 which in turn reduced cell survival and increased apoptosis of the AGS cells

Conclusion: Overall, Nrf2 overexpression might contribute to GC progression and its knockdown might be considered as a potential therapeutic approach in gastric cancer treatment.

Keywords: GC, Nrf2, knockdown, siRNA, apoptosis

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Increased level of JNK (MAPK) enzyme in anuclear cell (platelet) under osmotic stress

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Abstract

Backgrounds: Mitogen-activated protein kinase (MAPK) enzymes, known only in eukaryotes, are an important family of protein kinases. These enzymes play a key role in regulating various cellular processes from cell proliferation and survival to apoptosis, which are activated by a variety of stimuli such as mitogens, oxidative stress, heat shock, and osmotic stress.

Materials and Methods: In the present study, platelets originating from the cytoplasm of bone marrow megakaryocytes and lacking any nucleus during puberty, were subjected to osmotic stress under hypertonic (1.9% NaCl) and hypotonic (0.7% NaCl) environments. As a control, isotonic (0.9% NaCl) condition was used. All of them were incubated at 37 for 15 mins and 24 hrs. After lysis of platelet samples using ultrasound waves, the extracts of test and control cells were prepared and used to measure the level of JNK enzyme using the ELISA technique.

Results: The results showed the presence of JNK enzyme in platelets in spite of they lose their nuclei in the mature stages. Meanwhile, the osmotic stress significantly increased the level of JNK in platelets (p-value < 0.05).

Conclusion: The study shows the presence of the JNK enzyme in platelets and its increased level under osmotic stress despite the fact that they do not have nuclei and genomic DNA. They probably contain pre-mRNAs encoding the JNK enzyme. The existing cytoplasmic pre-mRNAs are processed into mRNA due to platelet osmotic stress and eventually the JNK enzyme.

Keywords: JNK, Platelet, Osmotic Stress, Gene Expression

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A Comparative Study of Fluoxetine and Glatiramer Acetate Therapy in the Mouse Model of Multiple Sclerosis

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Abstract

Backgrounds: Multiple sclerosis (MS) is an autoinflammatory disorder of the central nervous system which has no certain cure. Glatiramer acetate (GA) is of conventional treatment for multiple sclerosis. Fluoxetine is a selective serotonin reuptake inhibitor and an antidepressant drug. Several assays represented the immunomodulatory and antioxidant properties of Fluoxetine. This study aims to compare the therapeutic potential of Fluoxetine with GA as the first-line treatment of multiple sclerosis.

Materials and Methods: In this study, investigation of Fluoxetine and GA effects on the gene expression profile of some pro-and anti-inflammatory cytokines in C57BL/6 experimental autoimmune encephalomyelitis (EAE) model of the disease have been performed. In addition, the extent of demyelination in the corpus callosum of the animals and the phenotype of the disease were evaluated.

Results: In the treatment groups reduction of disease score in comparison to the control group was observed. Although both drugs ameliorate clinical symptoms of EAE, GA was more effective. Our data revealed that treatment with Fluoxetine and GA resulted in a significant reduction in the expression levels of pro-inflammatory cytokines and a significant increase in the expression level of anti-inflammatory cytokines. Moreover, the assessment of the antioxidant capacity of treatments represents a higher expression of Glutathione peroxidase (GPX-1) in the Fluoxetine treated group. Staining by Luxol Fast Blue (LFB) of corpus callosum cross-sections affirmed a significant reduction in the level of demyelination in the treatment groups.

Conclusion: The results demonstrated the immunomodulatory and antioxidant effect of Fluoxetine, which has a significant healing influence on the EAE severity. However, more studies are required to confirm this drug as a first-line treatment of MS.

Keywords: Multiple sclerosis, Fluoxetine, Glatiramer Acetate, EAE, *C57BL/6*

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Bi-allelic variants in *IPO8* cause human importin- β -related disorders

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Abstract

Backgrounds: IPO8 protein encodes Importin 8 which translocates cargo molecules into the nucleus. One of them is TGF-β signaling components, dysregulated transforming growth factors, which cause connective tissue disorders. Bi-allelic loss-of-function variants in IPO8 cause a syndromic form of thoracic aortic aneurysm (TAA) with clinical overlap with Loeys-Dietz and Shprintzen-Goldberg syndromes. Here, we reported two patients (male and female) from unrelated families with variants in IPO8 with symptoms like cardio-vascular anomalies, connective tissue findings, craniofacial dysmorphic features, developmental delay, and immune dysregulation.

Materials and Methods: We performed whole-exome sequencing and Sanger sequencing to identify pathogenic variant(s) in the families. By using CRISPR/ Cas9-mediated inactivation in zebrafish, the role of IPO8 in nuclear translocation was identified. A mild to the severe defecting pattern in the early embryonic development level of zebrafish based on the IPO8'S role in TGF-β signaling was demonstrated as well as severe cardiovascular and skeletal defects. In addition, by using the C57BL/6N IPO8 knockout mouse model cardiovascular defects in both sexes are shown.

Results: A homozygous variant, IPO8: c.728del (p.Pro243LeufsTer27) in the male proband and IPO8: c.2347_2369del (p.Leu783ValfsTer5) in female patient is identified. It is demonstrated that IPO8 deficiency leads to TGF-β signalopathy which has functions in the development, patterning, and homeostasis of the affected tissues.

Conclusion: Our work demonstrated that IPO8 has an important role in TGF-β signaling and causes connective tissue defect. we know importin 8 is a TGF-β-related effector and involve in TAA pathogenesis so far, next future opportunities would be mechanistic studies and representing candidate drug targets for TAA.

Keywords: Loeys-Dietz syndrome, Shprintzen-Goldberg syndrome, thoracic aortic aneurysm, TGF-beta, importin 8

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Analysis of mRNA-miRNA Interaction between Breast Tumor Tissues and Adjacent Normal Tissues

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Abstract

Backgrounds: Breast cancer is a malignant tumor that occurs in the epithelial tissue of the breast gland and has become the most common malignancy in women. MicroRNAs (miRNAs) have been linked to a number of cancer types like breast cancer. In this analytical review, we constructed an initial effort to address the differential expression of the mRNA-miRNA interaction map between breast cancer tissue samples and normal adjacent samples.

Materials and Methods: Our inclusion criteria for recognizing differentially expressed genes (DEGs) chose from Affymetrix- GPL570 microarray platforms from Gene Expression Omnibus (GEO). Two miRNA microarray datasets (GSE40525 and GSE45666) were downloaded from the GEO database as well. The analysis was defined using the "LIMMA", "ggplot2", and "p-heatmap" packages in R software to screen remarkably dysregulated miRNAs attended by prediction of their purpose genes. Functional enrichment analyses were conducted by DAVID online tool. Enrichr and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis was applied to estimate the possible molecular mechanisms of DEGs. Dysregulated miRNAs of hub DEGs were predicted by miRTarBase and miRDB.

Results: According to the miRNA-target interaction network, of the 30 top DEGs, 20 were down-regulated and 10 were up-regulated.

Conclusion: miRNAs can modulate functional genes expression individually. Compared with normal breast samples, a panel of miRNAs was consistently dysregulated in breast cancer. Our findings will provide the association of potential biomarkers and novel approaches for breast cancer treatment.

Keywords: Bioinformatics analysis, GEO, Microarray dataset, Breast cancer, DEGs

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Evaluation of miR-382 expression change in the prefrontal cortex of the brain following alcoholism in male Wistar rats

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Abstract

Backgrounds: Alcohol has various side effects and its abuse causes severe metabolic and physiological effects in all body systems. Given that different area of the brain, including the prefrontal cortex, play a role in causing addiction; this study aimed to investigate the genetic expression of miR-382 in the prefrontal cortex of the brain in rats.
Materials and Methods: Fifty male Wistar rats weighing 200 to 250 g were prepared. Adult mice were kept under hygienic conditions at room temperature with free access to water and food for 12 hours in a light /dark period. Alcohol was administered to animals orally for 21 days at a dose of 5 mg/kg. The mouse's head was removed and then the skull was split and the prefrontal cortex was removed. The expression of miR-382 relative to the reference gene was examined using real-time PCR in this region. Statistical analysis was performed using SPSS software.
Results: The results showed that following the consumption of alcohol for 21 days, the expression level of miR-382 in the prefrontal cortex significantly decreased ($P < 0.05$).
Conclusion: The study of miRNAs as mediators of molecular mechanisms that also affect the expression of other genes can increase our understanding of the mechanism of complications of problems such as alcoholism.

Keywords: miR-382, prefrontal cortex, Alcoholism, Male Wistar rat.

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Nrf2 knockdown increases apoptosis of hepatocellular carcinoma cells

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Abstract

Backgrounds: Hepatocellular carcinoma (HCC) is the most common primary liver cancer and is a serious medical problem, as its incidence is continuing to grow. Nuclear factor erythroid 2-related factor (Nrf2) is an important transcription factor associated with HCC carcinogenesis, and increased NRF2 mRNA levels contribute to the poor patient outcome for HCC. Here, the effect of Nrf2 knockdown by siRNA was examined in the HCC cell line.
Materials and Methods: First, because of the high expression level of Nrf2, the hepG2 cell line was chosen for further research. Subsequently, the cells were cultured in a 10% RPMI medium to reach 70% confluence. They were then transfected with Nrf2-specific siRNA and the expression level of Nrf2 was evaluated by qRT-PCR. After that, changes in cell viability and apoptosis were analyzed by MTT assay and annexin V-FITC/PI staining respectively.
Results: Nrf2-specific siRNA significantly suppressed the Nrf2 expression, decreased the cell viability, and promoted the hepG2 cells apoptosis.
Conclusion: Overall, the results of this study showed that Nrf2 knockdown might be considered as a potential approach for Hepatocellular carcinoma management.

Keywords: HCC, NRF2, siRNA, knockdown, apoptosis

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The genetic basis of lactase persistence and lactose digestion in Iran and Afghanistan

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Abstract

Backgrounds: Milk, a major source of calcium, is required for bone and tooth health. The main carbohydrate in milk is lactose which, in mammals, is digested by an enzyme called lactase. Lactase is highly expressed in all human infants but its expression persists in only 32% of adults; a phenotype called lactase persistence. In some lactase nonpersistent individuals, milk consumption is associated with gastrointestinal symptoms and causes lactose intolerance. Milk avoidance places lactose intolerant individuals at a higher risk of bone fracture and osteoporosis. In addition to the physiological tests, genetic tests have also been very useful for lactase nonpersistent detection in some ethnic groups.

Materials and Methods: In this study, we have explored the genetic basis of lactase persistency in two ethnic groups in Iran and Afghanistan. We determined the phenotype of lactase persistency and the genotype of five single nucleotide polymorphisms responsible for lactase persistence.

Results: Our results show that lactase persistency phenotype is higher in Hezareh (10%) compared to a Mazani ethnicity from Shahmirzad (2.3%). Our study reveals a new genetic variant at the regulatory region of the lactase gene but failed to find a direct genotype-phenotype correlation. This suggests that other genetic variants and/or epigenetic effects are responsible for lactase persistency in these two ethnicities.

Conclusion: The identification of lactase expression status in lactose-intolerant individuals and distinguishing lactase persistent and nonpersistent individuals in a group of subjects with lactose intolerance is an important first step in devising nutritional recommendations to optimize health and manage diseases; goals of personalized nutrition.

Keywords: human genetic diversity, single nucleotide polymorphism, Lactase persistence, lactose intolerance, personalized nutrition

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Silencing CDC20 gene by siRNA-loaded nanoniosome in cancer cell therapy

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Abstract

Backgrounds: Small interfering RNA (siRNA) by targeting and degrading oncogenes or angiogenic genes may be able to inhibit tumor cell growth. Cell division cycle 20 homolog (CDC20) protein as a proto-oncogene binds to the anaphase-promoting complex/cyclosome (APC/C) and result in the promotion of chromosomal separation and mitosis process. This protein is highly expressed in several human carcinomas. Encapsulation of CDC20siRNA in nanocarriers prevents its rapid degradation by serum nucleases and enhances its stability and safety. The purpose of this study was the knockdown of CDC20 expression by siRNA-loaded nanoniosome as a novel treatment method.

Materials and Methods: The human gastric cancer cell line, AGS was maintained in DMEM supplemented with 10% fetal bovine serum (FBS) and 100 U/ml penicillin, 100 µg/ml streptomycin at 37˚C and 5% CO2. CDC20siRNA was also purchased from Dharmacon Research. At first, 1×104 cells/ml was plated on 6-well plates.

After reaching 70% confluence, the cells were incubated with 100 nM free CDC20siRNAs and 100 nM nanonoisomal CDC20siRNAs for 72 h. Untreated cells were considered as control. Then, RNA extraction, cDNA synthesis, and real-time PCR analysis were done and results were expressed with 2-ΔΔCt.

Results: we found that CDC20siRNA remarkably suppressed the expression of CDC20 at the mRNA level in AGS cells after 72 h compared to control. Free CDC20siRNA almost 10% and CDC20siRNA-loaded nanonoisome up to 40% demonstrated the inhibition of CDC20 expression at the transcriptional level.

Conclusion: It seems that the nanoniosomal CDC20siRNA has a hopeful application for the treatment of gastric cancer.

Keywords: siRNA; Gastric cancer; Niosome; CDC20

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A bioinformatics analysis of microRNAs related with breast carcinoma specific gene as a biomarker

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Abstract

Backgrounds: Breast cancer is the most common cancer among women worldwide and one of the leading causes of cancer deaths. MicroRNAs (miRNAs, miRs), are one of the most potent cancer biomarkers that can be useful in diagnosis and prognosis. Some genes in the breast cancer pathway are oncogene and there are some miRNAs that can make interact with them and decrease the expression of these genes, so these miRNAs can act as a tumor suppressor. At least, they can be useful in diagnosis, prognosis, and treatment.
Materials and Methods: We used the NCBI database to select a specific gene called "CCND1". This gene has high expression in breast cancer and it is one of the important genes among other genes in the breast cancer pathway. We used the KEGG database and found that this is an oncogene. Next, we used the miRTargetLink database and found that there is 38 miRNA interaction with strong support and 156 interactions with weak support with CCND1. Then we selected some of the miRNAs with strong support (hsa-miR-193b-3p, hsa-miR-24-3p, hsa-miR-16-5p, hsa-miR-34a-5p, hsa-miR-34b-5p, hsa-miR-17-5p, hsa-miR-20a-5p) and used the Diana miRpath V.2 algorithm to draw a Heatmap and find the expression of these miRNAs.
Results: We found that these selected miRNAs that have strong interaction with CCND1 and they have high expression in the cell cycle, p53 signaling pathway, and pathways in cancer. We demonstrated that CCND1 has specific roles in these pathways in breast cancer and we found that our selected miRNAs have high expression in these pathways.
Conclusion: We established that miR-193b-3p, miR-24-3p, miR-16-5p, miR-34a-5p, miR-34b-5p, miR-17-5p, miR-20a-5p have the potential of targeting CCND1 gene and act as a tumor suppressor in breast cancer.

Keywords: Breast cancer, microRNA, NCBI, Diana miRpath V.2, miRTargetLink

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BEST4 and *CA7* as two novel molecular signatures in CRC: a systems biology study

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Abstract

Backgrounds: Colorectal cancer (CRC) is one of the most fatal cancers in the world, and its development poses a significant therapeutic challenge. The factors involved in determining the risk of CRC advancement must be identified to develop targeted therapy for CRC patients.
Materials and Methods: In the present study, employing by systems biology approach, the co-expression network of CRC was reconstructed by combining differential expression analysis and weighted gene co-expression network analysis (WGCNA). Firstly, we analyzed the GSE156451 dataset from the GEO database. Genes with considerable variation were identified by screening of differentially expressed genes (DEGs). Then, gene co-expression networks were applied to reconstruct and explore the biological function of identified genes. In the next stage, gene ontology and KEGG pathway analysis and module networks were performed using Cytoscape. Finally, to validate the results of the study, online database analyses through XenaBrowser and GEIPA were performed to estimate hub-gene expression and discover their prognostic value.
Results: As a result, a total of 173 genes were discovered to be abnormally expressed in CRC (18 up-regulated and 154 down-regulated). In addition, among the 8 modules, the brown module was significantly related to tumor progression (r=0.93, p-value=6e-53). Based on the Venn diagram created between the brown module and DEGs, four genes were identified as DEG hub-genes. Based on gene enrichment analysis, we propped BEST4 and CA7 as two novel targets in CRC. The genes in this module are involved in the mitotic cell cycle process, DNA replication, and negative regulation of mitotic nuclear division.
Conclusion: Our findings can help better understand the association between the transcriptome and clinical data in CRC, moreover they will also allow determining targeted molecular therapies for the disease.

Keywords: *BEST4, CA7,* CRC, Systems-biology, WGCNA.

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Exosomes derived from Mesenchymal Stem cells alleviate the expressions of liver Fibrogenic genes in human hepatic stellate cells

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Abstract

Backgrounds: Hepatic fibrosis is one of the main reasons for mortality in the world, and there is no definite cure for it. The lack of effective treatments for Hepatic fibrosis is a major global problem. When hepatic stellate cells (HSCs) activate, the expression of TGF-β and αSMA (Hepatic Fibrogenic genes) will increase, which leads to hepatic fibrosis. At present, there is little information on the action mechanism of exosomes derived from Whartons' jelly mesenchymal stem cells (WJ-MSCs) in the treatment of liver fibrosis. So we decided to study the effect of exosomes of WJ-MSCs in the clinic and remedy.

In this study, we investigated the effects of exosomes on genes involved in hepatic fibrosis progression in the cholesterol-activated human HSCs.

Materials and Methods: In this experimental study, the HSCs were cultured in a DMEM medium with 10% Fetal Bovine Serum, and then the cells were treated with 100µM Cholesterol to be activated. After that, the cells were treated with the 20µM exosomes. Finally, Quantitative Real-time PCR and Western blotting techniques were performed.

Results: Exosome treatment significantly reduced the expression of TGF-β and αSMA genes in the cholesterol-activated HSCs ($P< 0.05$). Exosomes Treatment decreased the activation of HSCs by inhibiting the level of Smad3C phosphorylation.

Conclusion: In summary, treatment with exosomes of WJ-MSCs reduced HSC activation in vitro. The relevant mechanism is through inhibition of the TGF-β / Smad3C signaling pathway. According to these results, exosomes derived from WJ-MSCs can be introduced as a potential therapeutic agent for the treatment of hepatic fibrosis.

Keywords: Hepatic Fibrosis, Exosomes, TGFβ, αSMA, HSCs

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The role of cytosolic Toll like receptor 2, 4 in endometrial samples from women with hydrosalpinx

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Abstract

Backgrounds: The reaction between the immune and the reproductive systems has important consequences for the health of pregnancy and reproduction. One of the most important receptors of the innate immune system is Toll-like receptors, which in addition to their role in immunogenicity; also have physiological roles during fertilization and implantation. Tubular diseases such as hydrosalpinx have been shown to have adverse effects on the endometrium during implantation. The studies showed that women with hydrosalpinx have lower rates of implantation because it has adverse effects on embryo implantation and interferes with it. In this study, we examined the expression of TLR2, 4 genes in the endometrial samples of women with hydrosalpinx.

Materials and Methods: Endometrial tissues were obtained from two groups: case and control. The case group includes women with hydrosalpinx (n=10) and the control group includes women with Malefactors (n=10). In both groups, Q-PCR analysis was used to investigate the relative expression of these TLR genes compared between case and control.

Results: We examined the expression of Toll-like receptors 2, 4 and the results showed that there was a significant difference between the two groups of hydrosalpinx and control.

Conclusion: Lower expression of TLR2 and TLR4 genes in the endometrium of women with hydrosalpinx indicates that changes in the expression of these genes may be detrimental to embryo implantation.

Keywords: Hydrosalpinx, Toll like receptors, Innate immunity.

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Evaluation of endosomal Toll-like receptors-3 and 9 gene expressions in endometrial of hydrosalpinx women

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Abstract

Backgrounds: Infertility is the failure to achieve a pregnancy after one year of regular and unprotected sexual intercourse. Hydrosalpinx is one of the female infertilities causes which belong to tubular diseases. It refers to the blockage of a fallopian tube with an unusual liquid that maybe harm the implantation process. Reproductive health is the result of an appropriate response between the immune system and the reproductive system.
The innate immune system is the first defensive line against microbial pathogens an enormous part of which involves toll-like receptors. Toll-like receptors have important impacts on infertility and implantation time. We aim to evaluate the expression of Toll-like receptors 3 and 9 in endometrial samples of hydrosalpinx patients.
Materials and Methods: Endometrial samples were obtained from the luteal phase were divided into case and control groups. The case group was women who had Hydrosalpinx disease (n=10). The control group was infertile women with male factor causes (n=10). After sampling and extraction of RNA, a syncretization of cDNAs was done. For comparison of quantitative expression of TLR 3 and 9 between two groups, QPCR was used.
Results: Reduction in the expression of antiviral TLRs in the endometrium of women with Hydrosalpinx compared with the control group was shown.
Conclusion: As the role of the innate immune system in implantation has been identified, so alteration in the expression of one of its components, including the Toll-like receptors 3 and 9, can disrupt the implantation process in these patients.

Keywords: Hydrosalpinx, Innate immune system, TLR 3, 9

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Design and amplification of an antimicrobial peptide based on scorpion mucroporin toxin

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Abstract

Backgrounds: Many natural antimicrobial peptides have been isolated from various sources, such as venomous organisms. Small antimicrobial peptides have been isolated by affecting a wide range of microorganisms. Mucroporin with 17 amino acids was identified from Lychas mucronatus scorpion. This peptide affects various viruses such as measles, influenza, SARS-CoV, and different bacteria. The aim of this study was to design an antimicrobial peptide by enhancing the anti-microbial effect of this peptide.

Materials and Methods: To design the new anti-microbial peptide, the amino acid sequence of the Mucroporin peptide and other similar antimicrobial peptides that had been isolated from scorpions or produced by mutagenesis were examined. Effective amino acids that interact with the cell membrane and are critical for peptide impact were identified and set up in the new peptide structure. Then, the nucleotide sequence of the peptide was designed based on the optimum codon usage in E. coli. Overlapping primers were designed to make the coding part and SOEing-PCR was performed to connect the fragments.

Results: In silico studies showed that the designed sequence has the ability to interact with bacterial membranes with high affinity and also is an anti-cancer peptide. SOEing-PCR results showed that the coding fragment was amplified with the size of 68 nucleotides.

Conclusion: The obtained data showed that the newly designed peptide by increasing the positive charge to five and changing the key amino acids could be a powerful agent against different microbes.

Keywords: Antimicrobial peptides, Mucroporin, scorpion toxins

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The proliferation and migration of metformin-treated vascular smooth muscle cells are suppressed via Focal Adhesion Kinase in high glucose conditions

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Abstract

Backgrounds: Cardiovascular diseases are known as one of the important causes of death in patients with diabetes mellitus. Metformin is used as an oral medication for reducing blood sugar. In this study, the effects of metformin were investigated on the FAK gene and protein expression levels, cell viability, and migration rate of VSMCs in high glucose conditions.

Materials and Methods: The FAK gene and protein expression levels were evaluated in VSMCs treated with different values of metformin (1 mM, 5 mM, and 7 mM), based on cell viability using RT-qPCR, western blotting, and MTT techniques. The cellular migration was evaluated by scratch assay.

Results: The FAK gene expression levels reduced significantly in metformin-treated VSMCs at 24h and 48h periods ($p<0.0008$ and $p<0.0001$, respectively). The FAK protein expression levels reduced significantly at 24h (5 mM and 7 mM metformin doses) and 48h (all doses) periods ($p<0.001$). In agreement with FAK protein values, cellular migration reduced significantly at 24h and 48h periods ($p<0.001$).

Conclusion: The results showed that metformin suppresses the proliferation and migration of VSMCs via FAK-related pathways and may retard the progression of vessel stenosis in diabetes.

Keywords: VSMCs, FAK, Metformin, High-glucose, Migration

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Investigation of binding interactions between three active ingredients; Curcumin, γ-Terpinene, and Safranal with BMP 15

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Abstract

Backgrounds: Bone morphogenetic protein-15 (BMP-15) of oocyte-secreted factors, has been indicated to be a critical regulator of many granulosa cell processes which is progressively expressed by oocytes of growing follicles throughout folliculogenesis. Moreover, the valid structure of this protein can play an important role in fertility and infertility in females. Using different drugs and active ingredients can be effective for the reproductive system. Currently, one of the methods to investigate protein binding is molecular docking. Therefore, in this study, molecular docking used for three active ingredients that are commonly utilized in some supplements and Iranian foods were chosen; Curcumin from Turmeric, γ-Terpinene from Cumin, and Safranal from Saffron to find out how they interact with BMP15.
Materials and Methods: After detecting the structures of the ligands and target molecule and preparing with relevant docking software, it was decided to use AutoDock Vina software to find out the affinity between molecules and also evaluate binding energies by software.
Results: The results showed that all three active ingredients can bind to BMP15 protein with significant and suitable binding energies but curcumin gains the most affinity score with -9/4 (kcal/mol), then γ-Terpinene with -7.8 (kcal/mol) and Safranal with -7/2(kcal/mol) from software.
Conclusion: The paper indicated that bioinformatic evaluations can support the effects of different active ingredients of medicinal plants with the oocyte factors such as (BMP-15) which has been proven to be critical for normal fertility in female mammals.

Keywords: BMP 15, Curcumin, Safranal, γ-Terpinen, fertility

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Trehalose reduces the number of Stress Granules in cancer-resistant cells, increasing Sorafenib and Gemcitabine sensitivity.

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Abstract

Backgrounds: Trehalose is a disaccharide composed of Monomeric glucose units combined by glycosidic linkage and linked at anomeric carbon by α bonding. It serves as a structural and transport disaccharide for cellular components and a stress-protective mechanism for membranes. Trehalose, which has antioxidant properties, has an anti-cancer effect, which is explained by targeting cell progression, angiogenesis, and metastasis pathways at the molecular level within the cell. Sorafenib and Gemcitabine are among the anti-cancer drugs used for a range of malignancies. One mechanism of resistance to these chemotherapy drugs is the preferential retention of ATF4 expression by encoding its mRNA in the structure of ribonucleoproteins formed in cancer cells under stresses that cause translation stoppage, known as stress granules (SGs). Trehalose may be a viable option for reducing the number of SGs by increasing the dephosphorylation of eIF2α, a key component of the SGs formation pathway.

Materials and Methods: The number of SGs in Sorafenib and Gemcitabine-resistant cancer cells was determined using the protein markers TIA-1 and PABP1. The sensitivity to the Sorafenib and Gemcitabine and ATF4 expression level was measured before and after using Trehalose.

Results: Trehalose reduced the number of SGs, decreased ATF4 expression, and increased sensitivity to Sorafenib and Gemcitabine in resistant cancer cells.

Conclusion: Trehalose reduces the number of SGs by increasing eIF2α dephosphorylation and can be used in combination with Sorafenib and Gemcitabine in cancer cells resistant to both to increase efficiency and increase sensitivity.

Keywords: Trehalose, Stress Granule, Sorafenib, Gemcitabine, ATF4

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Study of nettle extract and shigatoxin effects on the inflammation-wound healing process in mouse

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Abstract

Backgrounds: The use of modern treatment strategies in wound healing and control of inflammatory processes is one of the essential needs of the medical and human community. Understanding the biological effects and cellular and molecular basis of drugs of plant and microbial origin will enable the effective and purposeful use of these products.
Materials and Methods: In this study, after creating superficial wounds on the skin of mice in both control and treatment groups, a comparative study of the simultaneous effect of nettle extract and Shiga toxin isolated from Shigella dysenteriae on the wounds in the treatment group compared with the control group was performed. TGFB gene expression was examined as an indicator of inflammation and wound healing rate was studied after comparing the wound healing process and quantifying it using Image J software.
Results: The results showed a significant decrease in TGFB gene expression in the treatment group ($p \leq 0.05$, FC=0.3) compared to the control group and the curve of changes in wound healing rate and reduction of injury area showed an acceptable slope.
Conclusion: It seems that nettle extract along with Shiga toxin can be effective in wound healing rate without causing a significant inflammatory response, by modulating the inflammatory response and increasing blood flow in the wound area.

Keywords: Wound healing, Nettle extract, Shigatoxin, Gene expression

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Identification of Survival-Associated Long Non-Coding RNAs Hubs in Papillary Thyroid Carcinoma through Bioinformatics Analysis

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Abstract

Backgrounds: Thyroid cancer is the most abundant endocrine malignancy which accounts for 1.7% of all cancer cases. It has been reported that diagnosis of thyroid cancer especially Papillary Thyroid Cancer (PTC) using a common method is problematic. So, it is essential to develop molecular biomarkers for accurate diagnosis through a clear understanding of pathogenesis. Therefore, we aimed to investigate the role of survival-related Long Non-Coding RNAs (LncRNAs) in the Competing endogenous RNA (CeRNA) network related to the pathogenesis of PTC.

Materials and Methods: RNA-seq data of the GDC database were collected; Differentially-Expressed (DE) mRNAs, lncRNAs, and miRNAs were screened between PTC patients and normal samples. The results of Kyoto Encyclopedia of Genes and Genomes (KEGG), Gene Ontology (GO), and Disease Ontology (DO) analysis demonstrated enrichment of cancer pathways including extracellular matrix, collagen-containing extracellular matrix, extracellular matrix structural constituent, protein digestion, and absorption and endocrine gland cancer. By using the Kaplan – Meier survival analysis; survival-related DEmRNAs and survival-related DElncRNAs were constructed and then a survival-related ceRNA network was established. Using MCC analysis, Hub-lncRNAs that may play a role in PTC were identified.

Results: Finally, three lncRNAs, including AL162511.1, AC090673.1, and AL365259.1 through bioinformatics analysis, were retrieved.

Conclusion: In conclusion, the established ceRNA network may lead to clear up the regulatory mechanism by which lncRNAs function as ceRNAs and support the pathogenesis of PTC. Consequentially, the targeted lncRNAs, miRNAs, and mRNAs contributed to the ceRNA network can be further investigated as potential therapeutic targets and prognostic biomarkers for PTC.

Keywords: LncRNA, Thyroid Cancer, Papillary Thyroid Carcinoma, CeRNA Network, Bioinformatic Analysis

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Prevalence assessment of *LuxS*-dependent quorum sensing system genes in *Enterobacteriaceae*

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Abstract

Backgrounds: Undoubtedly, understanding the pathogenic mechanisms and survival of pathogenic bacteria in the human digestive system can help design appropriate treatment and prevention strategies. Quorum sensing can lead to changes in the microbial flora in pathogenic bacteria and the predominance of a range of bacteria in the gut, which one of the consequences may be antibiotic resistance.

Materials and Methods: In the present study, 100 different samples of Enterobacteriaceae were collected from patients with diarrhea and intestinal infections and cultivated in Mueller-Hinton Agar (MHA) and Blood Agar (BA). The presence of the LuxS gene was screened by the colony-PCR method. The positive bacteria obtained in the next step were examined for the presence of biofilm using CRA culture. Also, the amount of diversity of colonies obtained from microbial culture was evaluated by the RFLP method and acrylamide gel for any variance in diversity.

Results: The results showed a 37% prevalence of the LuxS gene in the isolated bacteria. RFLP method by Haelll and Hinhl enzymatic mapping showed a more homogeneous pattern for the fragments belonging to LuxS + bacteria genome.

Conclusion: The present study showed the presence of athe LuxS gene can reduce the diversity and dominance of similar bacteria that can accumulate and detect the synonym signals, and therefore should be considered in antibiotic administration programs.

Keywords: *Enterobacteriaceae*, Quorum Sensing, RFLP, Colony PCR**.**

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Evaluation of a functional polymorphism in has-miRNA-196a2 (rs11614913 C/T) with breast cancer risk in west Iranian women

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Abstract

Backgrounds: miRNAs are non-coding RNAs that play a role in the gene regulation of oncogenes and tumor suppressors. Single nucleotide polymorphisms (SNPs) in miRNA genes are associated with the risk of cancer. Some of these SNPs are more common including rs11614913 in the miR-196a2. We aimed to investigate the association between these polymorphisms and the risk of breast cancer in a west Iranian population.

Materials and Methods: In this a case-control study enrolled 100 patients with sporadic breast cancer and 100 health controls incidence matched by age and geographical region. We genotyped the functional polymorphism rs11614913 (C>T) in mir-196a2 by PCR–RFLP and evaluated its relationship with the risk of breast cancer. A 123 bp fragment was amplified and then RLFP assay was performed with MvaI restriction enzymes. The PCR products and digested fragments were analyzed on 8% polyacrylamide gel electrophoresis. Allele and genotype frequencies of SNPs were determined and calculated P-value and risk of disease.

Results: Chi-square analysis show a correlation between rs11614913 (C>T) polymorphism with breast cancer (p = 0.015, OR= 1.84; 95% CI: 1.15-2.94). The frequency of T alleles for variation was 35.5% in cancer patients and 22.7% controls (P=0.01). We found that the CT genotype is associated with the risk of breast cancer (P = 0.04). In addition, the TT genotype increases the risk of breast cancer, while the comparison of the CC with the CT and TT indicated no significant association with the risk for breast cancer. No associations were found between polymorphism and BMI and age.

Conclusion: This study indicates that rs11614913 (C>T) in mir-196a2 polymorphism seems to affect breast cancer risk and is likely involved in breast cancer susceptibility in addition to environmental factors, making its potentially useful genetic biomarkers for disorder screening.

Keywords: breast cancer, mir-196a2, polymorphism, RFLP

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Thalassemia screening in relative couple: Importance of Prenatal Diagnosis Tests and Genetic Counseling

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Abstract

Backgrounds: Thalassemia screening in couples plays a role in preventing the thalassemia major in infants. Also, the investigation of thalassemia mutations and genotypes in counseling Genetics is necessary. This study aimed to evaluate the effectiveness of genetic counseling and prenatal diagnostic tests in thalassemia-carrier couples.

Materials and Methods: This cross-sectional study was performed on 241 couples who were suspected of thalassemia from April 2018 to March 2020 in Lorestan province. Statistical analysis of data was performed using SPSS software 16.0 (SPSS Inc, Chicago, IL. Also, multiplex cap PCR, ARMS-PCR, Sequencing, and MLPA-PCR have been used for the identification of thalassemia mutations.

Results: IVSII-1 (G> A), CD36-37 (-T), IVSI-110 (G> A), --Med, and α3.7 were the most common mutations in the beta and alpha genes, respectively. IVSII-1 (G> A) β0/β (26.1%), CD36-37 (-T) β0/β (21.1%), and IVSI-110 (G> A) β0/β (10.3%) genotypes were the most common in subject of study. Among alpha thalassemia carriers, the α3.7α / α α genotype had the highest frequency among women (3.7%) and men (5.3%). Alpha and beta-thalassemia were 18 and 9 times higher in related men than non-related ones, respectively. This difference was statistically significant (P <0.001). In addition, 12.8% of fetuses were thalassemia major, 31.9% beta-thalassemia minor and, 10.3% normal.

Conclusion: Thalassemia screening in related couples plays an important role in reducing thalassemia major infants.

Keywords: Mutation, Thalassemia, Genotype, Diagnosis

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In-silico study of rs3025040 and hsa-mir-199a-5p single nucleotide polymorphisms related to VEGFA gene in patients with gastric cancer

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Abstract

Backgrounds: In Iran, one of the most common malignancies is gastric cancer so the study of biomarkers of this disease is of great importance. The angiogenic factor VEGF has been investigated the most. It's linked to neoplastic disease and lymph node metastases. Levels beyond a certain threshold were linked to a poor prognosis and reduced survival rates.
Materials and Methods: A gene named is one of the genes linked with this cancer. MicroRNAs linked to this gene were discovered using the miRNA SNP database. A single nucleotide polymorphism called Rs3025040 was discovered. The DAVID database of this microRNA picked the corresponding signal signals for further analysis.
Results: For OC, 850 genes have been discovered. VEGFA genes were shown to have a high level of expression, while has-mir-199a-5p had up-expression examination of OC signaling pathways, as well as the influence of this Mir on gene targets.
Conclusion: These findings imply that VEGF1 could be a potential gene therapy target for gastric cancer. Blocking VEGF expression in GC cells induces apoptosis, which may provide a novel treatment approach.

Keywords: Stomach cancer, Bioinformatics, VEGFA gene, MicroRNA (has mir 199a 5p), Single nucleotide polymorphism (rs3025040)

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Comparison of TRBF peptide structure, in mammals using bioinformatics

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Abstract

Backgrounds: Cancer cells continue to reproduce, and for this to happen, their telomerase must be very active. This is not the case with healthy cells. To reduce telomerase activity, we need to know how to target the activity of this enzyme. Telomerase is an essential enzyme for sequential cell proliferation in metastatic cells. TRBF proteins are based on binding sites, on the telomeric regions, as well as the presence of these proteins increases and decreases telomerase activity.
Materials and Methods: The aim, was to collect and compare TRBF gene family sequences to find conserved motifs and to investigate the affinities of this gene, it was different between mammalian species. Using RT-PCR, the coding sequence of a TRBF peptide was isolated and identified. For similarity studies with the help of Mega bioinformatics Software, the obtained sequence was compared with the same TRBF sequence in other mammalian species.
Results: In this work, for the first time, studies have been carried out on 3 levels of protein, mRNA and, DNA. As the sequence of telomeric region sequences of organisms is constantly increasing and decreasing, information of these regulatory proteins and synthesis of the above telomeric region in different mammalian species has been considered. TRBF affinities between different Mammalian species were reported in the N-terminal and C-terminal segments.
Conclusion: Specific conserved amino acid fragments and the second reverse transcriptase were introduced as the functionally conserved motif of all species at the protein level. Finally, direct inhibition of telomerase and immunotherapy of telomerase can be a method of inhibiting cancers

Keywords: mammalian species, TRBF, Telomere binding, Telomerase

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Investigation of genes and pathways involved in breast cancer subtypes through gene expression meta-analysis

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Abstract

Backgrounds: Breast cancer (BC) is a malignant disease with a high prevalence worldwide. Molecular-based studies have revealed heterogeneity in BC while also improving classification and treatment. However, efforts are underway to distinguish between distinct subtypes of breast cancer. In this study, the results of several microarray studies were combined to identify genes and pathways specific to each BC subtype.

Materials and Methods: Meta-analysis of multiple gene expression profile datasets was screened to find differentially expressed genes (DEGs) across subtypes of BC and normal breast tissue samples. Protein-protein interaction network and gene set enrichment analysis were used to identify critical genes and pathways associated with BC subtypes.

Results: We identified 110 DEGs (13 DEGs in all and 97 DEGs in each subtype) across subtypes of BC. All subtypes had a small set of shared DEGs enriched in the Chemokine receptor bind chemokine pathway. Luminal A specific were enriched in the translational elongation process in mitochondria, and the enhanced process in luminal B subtypes was interferon-alpha/beta signaling. Cell cycle and mitotic DEGs were enriched in the basal-like group. TMC5 was the only DEG in the normal-like subtype.

Conclusion: Integrating researches such as a meta-analysis of gene expression might be more effective in uncovering subtype-specific DEGs and pathways than a single-study analysis. It would be more beneficial to increase the number of studies that use matched BC subtypes along with GEO profiling approaches to reach a better result regarding DEGs and reduce probable biases.

Keywords: breast cancer, microarray, BC subtype, gene expression, meta-analysis

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Prevalence of Chromosomal abnormalities in cytogenetic findings of patients studied in Golestan province.

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Abstract

Backgrounds: Chromosomal abnormalities, numerical and structural, act as the main reasons in many health conditions resulting in developmental problems. However, these are molecular and molecular-Cytogenetics platforms that become increasingly popular and practical for CA detection; sophistically, karyotyping, the conventional test for CA, still acts as the most common test for CA in many saturations. Cytogenetics findings observed in patients referred for CA study have been reported in this study.

Materials and Methods: Blood samples from 302 patients were tested by conventional G-banding Karyotype tests. Separately, two different expert lab technicians analyzed and interpreted all the spreads, and finally, all the abnormal results were recorded.

Results: Down syndrome, the most frequent finding, was observed in 14% abnormal cases; Turner syndrome was 12%, while Klinefelter syndrome was seen in 6% cases. Isochromosome X and DSD were seen 4%, and Inversion was in 14% of cases.

Conclusion: Numerical aneuploidy abnormalities are the most common CA between the patients attended to Kavosh Medical Genetics Laboratory of Golestan province from April 2016 to November 2018.

Keywords: Chromosomal abnormalities, Karyotype , Turner syndrome, Klinefelter

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Integrative meta-analysis identifies the involvement of neurotrophin signaling pathway in AML chemo-resistance

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Abstract:

Backgrounds: Chemotherapy resistance is a major problem in AML medicine that impacts on overall survival. Multiple subgroups of AMLs which are under treatment of various regimens seem to have similar regulatory gene(s) or pathway(s) related to their chemo-resistance phenotype. Despite of wide variety of studies, the pathways and deregulated gene signatures involved in AML chemo-resistance are not fully understood.

Materials and Methods: In this study, a meta-analysis of five AML libraries compiled from GEO and ArrayExpress repositories reporting on the transcriptome of chemo-resistance and chemo-sensitive AML patients was performed. Furthermore, functional enrichment analysis was performed to assess molecular mechanisms related to AML chemotherapeutic resistance.

Results: A total of 34 genes, including 17 up-regulated and 17 down-regulated genes, were found to be significantly differentially expressed between chemo-resistance and chemo-sensitive groups. Moreover, neurotrophin signaling pathway was identified as the most highly enriched pathway associated with AML drug resistance with the five deregulated mediators including the upregulation of SORT1 and AKT3 genes, and the downregulation of c-Jun, MATK, and RPS6KA2 genes.

Conclusion: The results indicate the importance of neurotrophin signaling pathway as the basis of drug resistance development in AML.

Keywords: Meta-analysis, Chemo-resistance, AML, c-Jun, Transcriptome

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Investigation of the pathogenicity of one of the missense single nucleotide polymorphism in *IKZF1* gene

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Abstract

Backgrounds: *IKZF1* (IKAROS Family Zinc Finger Protein 1) is a gene that encodes the Ikaros transcription factor. The most expression of this gene is in the lymph node, spleen, appendix, and bone marrow. Ikaros is a multifunctional transcription factor that has many effects in different dimensions of the cell cycle, lymphopoiesis, hematopoietic stem cells (HSCs) and plays as an essential regulator of lymphoid development and differentiation. In some references, Ikaros consider as an antileukemic transcription factor so we can say that effective mutation and abnormality in the Ikaros gene (*IKZF1*) probably can lead to different types of leukemia (e.g. B-cell-progenitor acute lymphoblastic leukemia).In this study, we check one single nucleotide polymorphism (SNP) that is identified as missense change in the National center for biotechnology information (NCBI) on the SNP database.

Materials and Methods: We search in NCBI/SNP database and found 36325 SNP in different parts of *IKZF1*. After that, we filter the result and we find 455 SNP that was missense. Between these 455 SNP, we discuss only one of them (rs757907717 C >T) and check its effect on the final protein product.

Results: We search in NCBI/SNP database and found 36325 SNP in different parts of *IKZF1*. After that, we filter the result and we find 455 SNP that was missense. Between these 455 SNP, we discuss only one of them (rs757907717 C >T) and check its effect on the final protein product.

Conclusion: According to the results obtained, we can propose with high probability, that rs757907717 is a probably damaging and pathogenic SNP.

Keywords: *IKZF1*, Ikaros, DNA-binding protein, SNP, Computational biology

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Effect of nuclear factor erythroid 2-related factor silencing on the MiaPac2 pancreatic cancer cells

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Abstract

Backgrounds: Pancreatic cancer (PC) is a deadly malignancy that is more common in men and elderly people (40 to 85 years old) and has an aggressive course. Its frequency has been gradually increasing in recent years. It accounts for 2% of all cancers and 5% of cancer deaths. Deregulation of Nuclear factor erythroid 2-related factor (NRF2) is proposed to play a key pathogenic role in pancreatic cancer. In this research, the effect of Nrf2 knockdown was investigated using specific siRNA in a pancreatic cancer cell line.
Materials and Methods: First, several pancreatic cell lines were screened for high expression of Nrf2, and MiaPac2 was selected for further investigations. The cells were grown in a 10 % RPMI medium to reach 70 % confluence transfected with Nrf2 siRNA. Total RNA was extracted, converted to cDNA and the expression level of Nrf2 was measured by qRT PC MTT assay, and annexin V-FITC/PI staining tests were examined used for cell viability and apoptosis analysis, respectively. MTT assay and annexin V-FITC/PI staining tests were used for cell viability and apoptosis analysis, respectively.
Results: According to our findings, Nrf2 siRNA transfection had significant effects on tumor cells. Nrf2 expression level in MiaPac2 cells was suppressed by siRNA silencing, resulting in decreased cell viability and increased apoptosis.
Conclusion: Nrf2 silencing might be considered as a potential approach for pancreatic cancer treatment.

Keywords: PC, NRF2, siRNA, knockdown, apoptosis

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Key genes in neural stem cells differentiation of mouse embryonic stem cells: a comprehensive bioinformatics analysis

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Abstract

Backgrounds: Generating neural stem cells (NSCs) from mouse embryonic stem cells (mESCs) are essential aims for regenerative medicine; although, the differentiation mechanisms and processes are not largely studied.

Materials and Methods: We used comprehensive bioinformatics analyses to identify the co-function and regulated genes related to the early differentiation of ES-like cells to neural (ELN). Undifferentiated mESCs from 14-day differentiated C57BL/6 cells were isolated and collected. Cells from this group were subjected to RNA-seq and microarray analysis by which differentially expressed genes (DEGs) was used.

Results: ClusterProfiler Package performed gene enrichment analysis in Rstudio; a protein-protein interaction (PPI) network was constructed by search tool to retrieve interacting genes such as STRING, Interaction and NCBI databases visualized in Cytoscape. We identified Hub genes with the MCODE algorithm in Cytoscape. In this bioinformatics study, we utilized 10,569 DEGs and 8 time-series profiles enriched in functional and biological processes of self-renewal, cell cycle, differentiation, and neurogenesis. The MCODE algorithm analysis identified seven integrated modules that could play an essential role in the ELN process, including mitosis/cell cycle, ubiquitination, splicing, and differentiation.

Conclusion: The study identified potential genes, integrated processes, and functional modules associated with the neurogenesis differentiation of mESCs.

Keywords: Neural stem cells, Differentiation, RNA-seq, Microarray, Neurogenesis

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Integrative Analysis of MicroRNA and Gene Interactions Associated with BRAF Gene Mutation in Melanoma

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Abstract

Backgrounds: Melanoma is the deadliest skin malignancy, and its incidence rates have tripled in the last 30 years. Due to the prevalence of V600E mutation in the BRAF gene in melanoma cases, integrative analysis of expression profiles of both mRNA and miRNA in the same sample associated with BRAF mutation could improve diagnosis and prognosis. In this study, we use Weighted Gene Co-expression Network Analysis (WGCNA) as a systems biology method to understand correlations among genes and group genes into modules that typically have coordinated biological functions and regulatory mechanisms and investigate the hub genes related to miRNA–gene interactions in melanoma prognosis.

Materials and Methods: We downloaded clinical, mRNA, and miRNA microarray data from TCGA and BRAF mutation status data from cBioportal using R software. We divided the tumor samples into two molecular trait groups: mutated and non-mutated BRAF. Integrative analysis of melanoma transcriptomic data was conducted using WGCNA.

Results: To reach the scale-free topology, we clustered samples with a threshold power of 5. 11 module eigengenes were identified. Modules of highly correlated genes and miRNAs in mutated and non-mutated BRAF groups were detected separately using a heatmap. The purple module genes had a 0.17 correlation with the p-value = 3e-04 in the non-mutated BRAF group, and the black module genes had a 0.25 correlation with the p-value = 3e-05 in the mutated BRAF group.

Conclusion: We showed that BRAF mutation had an enormous impact on gene expression at the mRNA and miRNA levels.

Keywords: Melanoma, BRAF, WGCNA, Integrative analysis, Gene expression

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Impact of Methadone and Morphine on Mental Activity and *Gfap* Expression in Male Norway Rat

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Abstract

Backgrounds: Methadone and morphine are frequently used as pain relievers. Although they can be used to substitute opioids such as heroin, they can be addictive. Abuse of these substances might lead to memory loss and anxiety.

Materials and Methods: 36 male rats weighing between 200 gr were divided into 6 groups. Each group contained 6 rats. The first group received no medicine. The second group received normal saline and consider as a positive control. The third group received methadone in high dosage, the fourth group received a low dosage of methadone. The fifth group received morphine in high dosage and the last group received morphine in low dosage for 30 days subcutaneously. After treatment, shuttle box and Plus Maze tests were used to evaluate brain activity and anxiety. Rats were sacrificed after being anesthetized with xylocaine and ketamine injection. The *Gfap* gene expression was evaluated after the hippocampus was harvested. Total RNA was extracted, cDNA was synthesized, and the expression level was determined using the RT-qPCR method.

Results: Behaviour evaluation revealed a sizable reduction in brain activity and elevated anxiety in all groups in comparison with control groups. The groups who were treated with methadone and morphine in high dosage showed a severe condition. Gene evaluation discovered identical results and it is demonstrated *Gfap* expression reduced in methadone and morphine consumer groups.

Conclusion: Taking methadone and morphine even at low doses can disrupt basic mental mechanics. One of the outcomes of methadone and morphine is a reduction in brain activity and increased tension even though reduction of *Gfap* expression. *Gfap* is a class-III intermediate filament and acts throughout the development of the central nervous system and distinguishes astrocytes from other glial cells. This study discovered that methadone and morphine consumption can disrupt Gfap expression and cause mental disorders.

Keywords: Methadone, Morphine, *Gfap*

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Association of ART3 rs6836703 polymorphism with non-obstructive Azospermia in Iranian men

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Abstract

Backgrounds: if a couple does not have children within one year after unprotected sexual activity, they suffer from infertility, which affects both men and women. Various factors affect male infertility, about 15 to 30% of which are genetic abnormalities. It is also predicted that most unknown cases of infertility are based on a genetic defect. Studies on the ART3 gene have shown that it is associated with Non-obstructive azoospermia (NOA). Therefore, in this study, we investigated the association of ART3 rs6836703 polymorphism with NOA in the Iranian infertile male population.

Materials and Methods: In this study, 100 genomic DNA samples of NOA individuals and 100 samples of control (fertile) individuals were received from Royan Research Institute, and then using Tetra ARMS-PCR technique, rs68367033 polymorphisms were examined in both groups.

Results: The results showed that the frequency of mutant A allele in the patient group was higher than the control group, but in both groups, the frequency of the normal G allele was higher than the mutant allele and no significant relationship was observed between the patient and healthy groups (P -0.067 and OR-0.672). Also, the findings of genotype showed that AA genotype is 16% in patients and 7% in the control group and normal GG genotype is 45% in patients and 53% in the control group, which indicates the higher frequency of mutated genotype in patients and the frequency of normal genotypes is higher in healthy individuals.

Conclusion: The study of rs6836703 polymorphic relationship in Iranian male population did not show a significant relationship with NOA.

Keywords: Infertility, Non-obstructive Azospermia, ART3 gene, polymorphism rs rs6836703

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Study of black-cumin on the expression of the genes related to the lipid metabolism in mice

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Abstract

Backgrounds: The use of traditional medicine in the prevention and treatment of metabolic and digestive disorders is one of the growing attractions of human societies. Numerous studies have confirmed the beneficial effects of black cumin extract in controlling the level of blood sugar and lipids.

Materials and Methods: In the present study, as a laboratory model, two groups of mice were subjected to standard diets (control group) and food rich in black cumin powder. After a one-month feeding period, weight parameters, as well as changes in adipose tissue cell size after Oil Red-O staining, were examined and quantified. The expression of Leptin and Adiponectin genes in adipose tissue was also examined by Real-Time RT-PCR.

Results: The results showed a significant decrease in the weight and relative size of adipose tissue cells ($P < 0.05$) between the control and treatment groups. The study of gene expression did not show a significant decrease in Leptin level (Sig. = 0.07), although a slight decrease in the level of this hormone can have a high effect on the desire for nutrition. Adiponectin gene expression showed a significant increase (Sig. = 0.03) that could be related to the inductive effects of black cumin extract on increasing β-oxidation of fatty acids.

Conclusion: Our results show that black cumin can be used as a suitable supplement to modulate and adjust the rate of fat metabolism in the body.

Keywords: Black Cumin, Fat Metabolism, Gene Expression, Leptin, Adiponectin

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The improvement of Anti-CD20 Antibody Affinity with site-specific mutagenesis in CDR3 (Tyr101 to Arg)

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Abstract

Backgrounds: CD20 is a membrane glycosylated phosphoprotein that first appears in the pro-B phase and increases in abundance as the cells mature. Based on the developmental stage of the leukemia cells, CD20 is a suitable target for chemotherapy. Several anti-CD20 monoclonal Antibodies are already available such as rituximab and obinutuzumab and are used for the treatment of B-cell leukemias and lymphomas in clinical trials. One of the ways to increase the efficiency of antibodies is the site-specific mutagenesis method.

Materials and Methods: In this study is used in silico site-directed mutagenesis coupled with docking simulations of models for anti-cd20 antibodies to investigate how specific amino acid substitutions impact ligand-protein interaction. We mutated the T (tyrosine) 101 to R (arginine) in the CDR3 region, the most involved region in binding to CD20, using PyMol software and docked it to the CD20 using the HADDOCK program. PyMol was also used to evaluate the amino acids involved in the interaction.

Results: The best complex predicted by HADDOCK was selected based on the Z-score and the energy levels of native and mutant antibodies. The amount of van der Waals energy decreased and the amount of electrostatic energy and the number of amino acids involved in the interaction increased in mutant compared to the native.

Conclusion: Collectively, the binding of the antibody to CD20 was improved by Y101R mutation. So, by increasing the efficiency of antibodies, they can be used as a candidate with high sensitivity in the treatment of cancer.

Keywords: CD20, CDR3, cancer, monoclonal antibody.

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The study of expression of CCAT2-Lnc noncoding gene in HT-29 and HCT-116 colorectal cancer cell line with Gemini Curcumin

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Abstract

Backgrounds: Although recent advances in therapy, colorectal cancer remain a leading cause of death in affected people. Curcumin is the main bioactive compound of turmeric that has been pointed as an impressive agent versus cancer in blocking, slowing down, or reversing the carcinogenic process. However, its paltry stableness and bioavailability limit therapeutic application. We formerly showed that the transfer of curcumin by using Gemini Surfactants nanoparticles called Gemini curcumin (Gemini-Cur) could improve its solubility, toxic trace on gastric, breast, and ovarian cancer cells.

Materials and Methods: In this study, we aimed to look into the anticancer action of Gemini-Cur on CCAT2-Lnc noncoding gene expression in colorectal cancer cells. The toxicity of Gemini-Cur on HT-29 and HCT116 was studied via MTT. Also, real-time PCR and western blotting were performed to evaluate the expression of the noncoding Lnc-CCAT2 and the underlying c-MYC genes.

Results: Our data showed that Gemini-Cur enters cells quite rapidly compared to free curcumin crystals, beyond this puts down HT-29 and HCT-116 cells proliferation in a time- and dose-dependent manner ($p < 0.001$). The IC50 values, as well as metastasis assays, showed that Gemini-Cur decreased the expression level of the lnc-CCAT2 and c-MYC genes and decreased mRNA and protein level of the c-MYC gene ($p < 0.0001$).

Conclusion: in the main, our findings showed that not only Gemini-Cur represses the proliferation of cancer cells but also inducts of metastasis and could be considered as novel nano-formulated phytochemical for cancer targeting.

Keywords: CCAT2, Gemini-curcumin, colorectal cancer

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Inhibition of miR-4270 in HepG2 cell line to suppress *in-vitro* metastasis and invasion

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Abstract

Backgrounds: microRNAs are involved in important biological processes such as apoptosis, proliferation, differentiation, angiogenesis, and metastasis. Disruption of these processes is critical to the onset, progression, and treatment of cancer. Many studies showed that miRNAs acted as a complication of tumorigenesis, and these small RNAs were responsible for a variety of cancers, such as liver cancer. We investigated the effect of miR-4270 inhibitor on metastasis and invasion in the HepG2 cell line.

Materials and Methods: At first, HepG2 cells were cultured in RPMI 1640 Medium with 10% FBS and antibiotics at 37°C and co2 5%. Then, HepG2 cells were treated with various concentrations of the specific hsa-miR-4270 inhibitor to achieve the appropriate concentrations of the specific hsa-miR-4270 inhibitor (40 nM) to inhibit metastasis. Finally, invasions and metastatic potential of treated cells were investigated relative to control cells using the wound healing assay.

Results: The wound healing assay results indicated that treatment of the HepG2 cells with miR-4270 inhibitor at 40 nM lead to the decline of in-vitro invasion and metastatic compared to untreated HepG2 cells as control.

Conclusion: our result indicated that miR-4270 inhibitor decreased in-vitro invasion in HCC cell line or HepG2

Keywords: liver cancer, metastasis, invasion, has-miR4270, HepG2 cell line.

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Expression profile evaluation of Interferon gamma and leptin genes in infertile women compared with fertile individuals

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Abstract

Backgrounds: Infertility is a reproductive system disease defined by the failure to achieve a pregnancy after 12 months of regular unprotected sexual intercourse. One cause of female infertility is LEP and Interferon-gamma malfunction. The leptin's main synthesis location and function is fat tissue and to control the body fat reserve, respectively. In addition, it is a natural controller of appetite and transmits the brain signals indicating that the body is ready for reproduction. Another gene involved in infertility is the interferon-gamma, located on chromosome 12. Interferon-gamma is a double-stranded protein produced by Th1, CD + 8t natural killer cells. In this study, we investigated the expression of these two genes in infertile and fertile women.

Materials and Methods: RNA was extracted from blood samples of fertile and infertile women, and then cDNA was synthesized. These genes expression was evaluated in infertile and fertile women using primers designed with the Real-Time PCR analysis.

Results: Interferon-gamma and leptin genes have lower expression patterns in infertile women compared with fertile individuals.

Conclusion: This study results showed a significant relationship between leptin and interferon-gamma genes expression and infertility.

Keywords: Interferon-gamma, Leptin, Obesity, Infertility.

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In silico analysis of identification miRNA-mRNA regulatory network in acute myeloid leukemia (AML) patients

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Abstract

Backgrounds: miRNAs are a class of non-coding RNA that is involved in various biological processes and diseases including cancers. Therefore, many studies illustrating the role of miRNAs in acute myeloid leukemia (AML) focused on identifying AML-specific miRNA expression patterns. AML is an invasive disease characterized by the increased proliferation and malignancy of immature myeloid cells. Therefore this study aims to investigate putative target genes and interaction networks where they are involved in AML. Also, Because of the numerous possible interactions between a single miRNA and target genes, bioinformatics analysis is very valuable to identifying putative pathways.
Materials and Methods: The original data set GSE142699 was selected from the GEO dataset (NCBI), and then the differentially expressed miRNAs in cytogenetically normal acute myeloid leukemia patients were identified using the GEO2R. Their target genes were predicted from four (Tagetscan, miRWalk, miRDB, miRmap) miRNA target prediction databases. Then, functional analysis was accomplished for the target genes using by the construction of a miRNAs-target gene network.
Results: In current study, described five miRs (miR-382-5p, hsa-miR-151a-3p, hsa-miR-495-3p, hsa-miR-409-3p, and miR-135) with down-regulation and three miRs (hsa-miR-196b-5p, hsa-miR-34a-5p, and hsa-miR-181a-3p) with up-regulation in patients with AML. The miRNAs were exposed to the most used predictions software and >200 overlap target genes predicted. Then, enrichment analysis was performed revealing the KEGG pathway, comprising the cell cycle, Transcriptional dysregulation in cancer, and cellular senescence. Network construction was generated and links between the selected miRNAs and the predicted targets.
Conclusion: In this study, we merged miRNA expression analysis with a bioinformatics-based workflow. Some genes (CDK6, HOXA9, RUNX1, and ITGB3), pathways, and interactions, putatively involved in AML development, were identified.

Keywords: miRNA, acute myeloid leukemia, network, bioinformatics

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Expression of Long non-coding RNAs (LncRNA), PWRN1 in colorectal cancer

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Abstract

Backgrounds: Colorectal cancer (CRC) is the third most common cancer in the world. Recent studies show that long non-coding RNAs (LncRNAs) play an important role in tumor formation, proliferation, migration, and apoptosis. This study aimed to investigate the expression of PWRN1 (Prader-Willi Region Non-Protein Coding RNA 1) in colorectal cancer. This lncRNA was selected based on bioinformatics data and there has been no research report on its expression in tissue samples of CRC at present. Bioinformatics studies have shown that this LncRNA may be involved in gastric, renal, and colorectal cancers, which are involved by the PTEN/Akt/MDM2/53p pathway.

Materials and Methods: The colorectal tumors along with the corresponding adjacent normal tissues were collected from thirty patients attending Milad Hospital, Isfahan, Iran. All the samples were collected following the guidelines issued by the Ethics Committee of Isfahan University of Medical Sciences (approval number: 6307603). After total RNA extraction from samples and cDNA synthesis, Real-time PCR was used to measure the PWRN1 expression.

Results: The qPCR results showed the expression level of PWRN1 was down-regulated by roughly 8.5 times in thirty paired colorectal cancer specimens (p-value = 0.0004).

Conclusion: The statistical analyses demonstrated that PWRN1 could serve as the diagnostic biomarkers to distinguish the tumor samples. Upon further validation in the bigger and more sophisticated studies, this lncRNA could have implications in clinics to improve the early diagnosis of colorectal cancer.

Keywords: Long non-coding RNA, Colorectal cancer, PWRN1, Real-time PCR

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The Role of ccr5 Receptor in Expression of *neat-1* in Breast Cancer Patients with Positive HIV

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Abstract

Backgrounds: Breast cancer is one of the leading causes of cancer-related death in women worldwide, and its prevalence is rising over time. By now, a few studies have reported on the action of NEAT-1 in breast cancer. Most studies focus on its role as a hypoxia-induced lncRNA that leads to accelerated cellular proliferation and tumorigenesis. NEAT-1 was found to be one of the several lncRNAs whose expression is altered by HIV-1 infection. This gene generates a long non-coding RNA (lncRNA) from the multiple endocrine neoplasia loci. This lncRNA is kept in the nucleus and serves as a structural component of the paraspeckle sub-organelles. It has the potential to act as a transcriptional regulator for a wide range of genres, including some involved in cancer progression.

Materials and Methods: In this study, the roles of the CCL5/Chemokine Receptor 5 (CCR5) axis and NEAT-1 were discussed in promoting breast cancer and progression in HIV-positive patients to validate the related previous findings. For this purpose, the CCR5 gene function was studied through LncRNA Disease and DAVID. Genecards database described a gene involved in HIV.

Results: The bioinformatics analysis revealed that CCR5 plays a role in HIV infection, which may contribute to the development of breast cancer by causing lncRNA NEAT-1 overexpression.

Conclusion: All things considered, it seems reasonable to assume that CCR5 is associated with HIV infection and breast cancer. As a result, suppressing lncRNA NEAT-1 in breast cancer cell lines may result in lower proliferation and metastasis.

Keywords: CCR5, LncRNA-NEAT1, Breast cancer, HIV-1

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The Study of changes in affinity of Anti-CD20 antibody with mutations Tyr101 and Tyr107 to Arg in CDR3 using docking

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Abstract

Backgrounds: CD20 as the first general B-cell marker is expressed on the surface of all late pre-B lymphocytes. Antibodies which now serve as the first line of therapy for certain cancer for diagnosis and treatment of cancer, have proven their value. Rituximab which is a chimeric mAb Anti-CD20 triggers cell death by binding to CD20 protein. Recently, using molecular simulation and modeling, designed a novel recombinant chimeric antibody and anticipated binding this antibody to epitope by molecular docking.

Materials and Methods: In this study, a potent AntiCD20 antibody that had seen selected using the PDB site, were used for designing mutation in CDR3 and docking. Since the CDR3 domain plays an important role in binding antibodies to the epitope, Tyr 101 and 107 were mutated to Arg in the CDR3 domain. HADDOCK software structural prediction of the antibody-CD20 complex was used for designing and validation of CDR3of antibodies with higher affinity for binding to CD20 receptor.

Results: The data obtained from HADDOCK, including Z-Score and bond energy, were analyzed which were -1.4 and -28.5 in the native state and -1.9 and -40.9 in the moment state, respectively.

Conclusion: Calictibly by analyzing and comparing the data obtained from HADDOCK, between normal and mutant modes, it was found that by creating this mutation in CDR3 of antibody, increased binding affinity to antigen and their properties improved predictably for their binding ability to CD20.

Keywords: Anti-CD20 Antibody, CDR3, Site-directed Mutation.

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Single nucleotide polymorphisms in BRCA2 partial sequences associated with breast cancer in human

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Abstract

Backgrounds: Single nucleotide polymorphisms (SNPs) are a type of polymorphism involving the difference of a single base pair. Although single nucleotide polymorphisms usually occur in coding regions of genes and cause changes in the produced proteins and the resulting product would have effects on health, they can be considered as genetic markers for the identification of cancer genes. Breast cancer is a good example of those malignancies which may occur due to single nucleotide polymorphisms in women all around the world.
Materials and Methods: Ten BRCA2 gene sequences of human species were taken from the NCBI database. The alignment of these sequences was done by Multalin software and the results were analyzed to see whether there are any single nucleotide polymorphisms and reveal the exact regions that those polymorphisms have occurred.
Results: The ten BRCA2 gene sequences with the highest level of similarity (more than 99% identity) in human spices were identified. They were about 8449 bp in length with 13 single nucleotide polymorphisms.
Conclusion: Nucleotide BLAST search showed that despite frequent resemblances between those sequences, some discrepancies could be seen among them as well. The nucleotides which were different can be considered as single nucleotide polymorphisms and can be used about breast cancer in humans.

Keywords: Single nucleotide polymorphisms, Breast cancer, human, Alignment, BRCA2 gene

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TXNDC8 mRNA expression Evaluation in semen of infertile men

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Abstract

Backgrounds: Azoospermia is one of the most severe types of infertility and one of the most important eras of research is the possibility of sperm retrieval. Thyorodoxin gene family especially TXNDC8 has been recently highlighted in male infertility. The corresponding protein not only acts as a specific sperm oxidoreductase agent but is also involved in the formation of disulfide bonds during sperm nuclei maturation. In the present study, the mRNA expression level of the TXNDC8 gene would be assessed in semen to evaluate its potency as a marker of sperm retrieval.
Materials and Methods: Twenty non-obstructive azoospermic men (NOA, as a patient group) and an equal number of obstructive azoospermic (OA, control group) men would enter the study. RNA extraction would be performed and cDNA would be synthesized with the help of random hexamers. mRNA expression would be performed by qRT-PCR and the Livak statistical method would be used to compare the gene expression between comparing groups.
Results: Our primary data analysis on microarray Gene Ontology Omnibus (GSE45885) showed downregulation of the TXNDC8 gene in NOA men compared to OA control individuals. The observed downregulation was completely significant (LogFC=-1.034706, p=0.012886<0.05). It is proposed that similar results would be observed in our lab experimentation.
Conclusion: Because TXNDC8 mRNA expression is related to sperm parameters and its chromatin structure, it could be a suitable molecular marker for predicting sperm retrieval in NOA patients.

Keywords: TXNDC8, Semen, Azoospermia, thyroxine

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Evaluation of *SOS1* gene mutation in breast cancer and the effect of miR-146a-5p on this gene

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Abstract

Backgrounds: Breast cancer is one of the most common cancers in the world and some people die from this disease every year. So far, various ways have been found for this disease to prevent the spread of the disease and treatment. In this study, the SOS1 gene in breast cancer and the effect of miR-146a-5p on this gene were investigated.
Materials and Methods: In this study, using the data in the NCBI, based on various criteria, the GSE-55715 database was selected. Using R analysis, studies showed that the relationship between gene expression between primary cancer cells, cell lines, and normal cells. Using the mirtarbase, microRNAs that affect mutated breast cancer genes were found.
Results: The DAVID database was used to plot this signal pathway. The SOS1 gene is involved in the PI3K-AKT signaling pathway in the cell cycle, glycogenesis, and cell proliferation. MiR-146a-5p was identified and analyzed based on studies on different breast cancer genes and taking into consideration the expression and influence of the SOS1 gene in this disease, as well as the effect of MiR-146a-5p on the SOS1 gene in breast cancer.
Conclusion: According to the results, SOS1 is one of the genes that may play a role in breast cancer. Furthermore, miR-146a-5p can be very useful in the treatment and prevention of breast cancer by modulating the expression of this gene.

Keywords: Breast Cancer, Bioinformatics, miR-146a-5p, SOS1

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Exome sequencing in the diagnosis of breast cancer

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Abstract

Backgrounds: Breast cancer is one of the most common malignant tumors in the world, which is multi-stage, and with mutation profiles of the cancer genome, new and effective targets can be identified for diagnosis and treatment. Because their identification helps in tumor progression to effective treatments and prognosis of the disease, they are studied using in-depth DNA sequencing. In this study, the Whole Exome sequencing method was used to diagnose breast cancer.
Materials and Methods: After receiving the FASTQ file from the NCBI site, the read quality and the removal of the adapters were checked by 123fastq software. SNV gene identification methods were performed by tools such as SAM Tools, GATK HaplotypeCaller, Bcftools, FreeBayes. Then the filtering step is obtained, which follows the call step of different types in VCF format. The next step was to implement annotation tools such as MutationTaster, CADD, FATHMM, and GERP ++. Therefore, filtering was done with Exact, InterVar, ClinVar, HGV, COSMIC, 1000 Genomes, nomad, DAVID databases.
Results: SNV / Indel vulnerability prediction that this step can have a significant impact on the conclusion. It was performed with the introduced tools and then the ensemble and Varsom sites were used to confirm the pathogenic mutation.
Conclusion: Next-generation sequencing technologies (NGS) have many advantages over Sanger sequencing or use in drug discovery for the treatment and prognosis of various cancers with reduced cost and increased efficiency, and the rapid advancement of targeted therapies highlights the need for more complex cancers and allows physicians to identify specific stimulus events and disease-causing mutations in individual tumors. It enables physicians to better predict treatment responses and significantly improve patient care. This study focuses on the application of the Whole Exome sequencing in breast cancer.

Keywords: Breast Cancer, Germline Mutation, Diagnosis, Whole-exome sequencing, database

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The effect of remdesivir on differentiation of human mesenchymal stem cells into osteoblast

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Abstract

Backgrounds: Remdesivir is a phosphoramidate prodrug of the C-adenosine analog GS-441524 that is metabolized within cells into the alanine metabolite (GS-704277) and further processed into the mono-phosphate derivative and ultimately into the active nucleoside triphosphate (NTP) derivative. Nucleoside analogs require active cell uptake by nucleoside vectors and intracellular activation by cellular and viral kinases to become their active NTP metabolites. RemedSivir prodrug (GS-5734) has a relatively short systemic half-life (0.9 hours) and is rapidly converted intracellularly to several intermediate metabolites (GS-704277) and GS-4471524. It is widely used to treat Coronavirus disease, but the evidence suggests that the drug has serious side effects.

Materials and Methods: In the present investigation, we decided to study the effect of this drug on the differentiation of human mesenchymal stem cells into osteoblasts. Another goal of the project was to investigate some blood factors in mice that were injected with Remdesivir. Bone marrow-derived mesenchymal stem cells were exposed to the drug at doses used to treat COVID-19 for 28 days.

Results: This study showed that Remdesivir increased the intensity of staining of cells with Alizarin red dye and increased the expression of the alkaline phosphatase gene in bone culture media.

Conclusion: It can be concluded that Remdesivir increases the differentiation of stem cells in the body into osteoblast while also affecting some blood and serum factors.

Keywords: Remdesivir, Stem cells, Osteoblast, Coronavirus disease, Blood cells

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PIK3R1 targeting by miR-5571-5p induced tumor progression and invasion in breast cancer

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Abstract

Backgrounds: Breast cancer is considered the most widespread malignancy in women worldwide. Despite a lot of effort for better management of patients, there are still problems for their clinical application due to the complexity of the disease, and thus, new biomarkers for accurate diagnosis would be of the suitable way. MiRNAs are highly conserved small non-coding regulatory RNAs involved in regulating gene expression during different cellular pathways. MiR-5571 was evaluated in a few cancers but there is no evidence of study in breast cancer. PIK3R1 gene is a tumor suppressor, inhibited proliferation, invasion, and metastatic properties of breast cancer cells. PIK3R1 was significantly down-regulated in MDA-MB-231 compared with MCF-7 cells line, thus possibly contributing to breast cancer metastasis. Therefore, this study aimed to determine the relationship between miR-5571-5p expression and correlation with PIK3R1 gene in breast tumor samples.

Materials and Methods: We investigate the expression profile of miR-5571-5p and PIK3R1 gene, as one of the putative targets of miR-5571-5p, in 50 paired breast tumors tissue and their adjacent normal concerning the clinicopathological features of patients using real-time PCR.

The correlation of both miR-5571 and PIK3R1gene expression with the overall survival of breast cancer patients was also examined by recruiting the Kaplan-Meier Plotter data portal.

Results: According to our data, significant up-regulation of miR-5571-5p and down-regulation of PIK3R1 were observed in clinical breast cancer samples compared with normal tissues ($p < 0.001$). The higher expression of miR-5571 was associated with higher grades and poor prognosis (log-rank p = 1.7*10-5), also a significant difference in overall survival was observed between patients with lower expression of PIK3R1 (log rank p = 6.1*10-12).

Conclusion: These results suggest that miR-5571 expression profiling might be clinically applicable as a prognostic biomarker in breast cancer. In addition, up-regulation of miR-5571-5p and down-regulation of PIK3R1 is associated with decreased breast cancer patient survival and poor prognosis.

Keywords: PIK3R1, breast cancer, miR-5571, overall survive

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Bioinformatics analysis of GDF 11 with three common active ingredients from Turmeric, Cumin, and Saffron

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Abstract

Backgrounds: GDFs proteins are important during embryonic development, particularly in the skeletal, nervous, and muscular systems. GDF11 as one of them has been shown to suppress neurogenesis through a pathway similar to myostatin by stopping the progenitor cell cycle during G-phase and regulatory mechanisms for muscular and neural development. Utilizing different drugs and herbal supplements can be effective for the embryo's growth and reproductive system. So, this study aimed to understand how Curcumin, γ-Terpinene, and Safranal as active ingredients interact with GDF11.

Materials and Methods: In the present study, the structures of the ligands and target molecule are prepared and get ready-made with relevant docking software as one of the methods to investigate protein binding, it was performed using AutoDock Vina software to find out the affinity between molecules and also evaluate binding energies in the complex.

Results: The data obtained from software, respectively, reported active ingredients expected to bind protein. As result, curcumin receives the most affinity score with -7.3(kcal/mol), then γ-Terpinene and Safranal with the same first number -4.7(kcal/mol) gain weak binding energies to bind GDF 11 protein as active ingredients.

Conclusion: This study offers insight that bioinformatics evaluations can predict the positive correlation of various active ingredients of medicinal plants (especially antioxidants) such as curcumin with the growth differentiation factor 11 which has been proven to be significantly vital for inhibiting muscle regeneration and decreased satellite cell expansion in an embryonic phase.

Keywords: Fertility, Bioinformatics, GDF 11, Saffron, Cumin

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Inhibitory effect of twist1 antisense oligo-nucleotides on invasion rate of androgen dependent prostatic cancer cells

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Abstract

Backgrounds: The movement of malignant cells to other tissues during metastasis is the most important cause of non-effective response to treatment in patients suffering prostate cancer. Preventing metastasis can be done by targeting effective factors as twist1, a helix-loop-helix protein stimulating EMT. In this research, we studied the inhibitory effect of two designed antisense oligonucleotides on early metastatic LNCaP cell lines.

Materials and Methods: Androgen-dependent metastatic LNCaP cell line was used as a model. Evaluating of cell invasion was done by CytoSelect™ 12-Well Cell Invasion Assay Kit (Cell Biolabs). For achieving this, 0.75*106 LNCaP cells in FBS free RPMI medium (300 µl) were used. In this case, an RPMI culturing medium containing 10 % FBS with a final volume of 500 µl was used as a chemoattractant mediator. Readily designed 2 antisense oligonucleotides were distinctly used as invasion inhibitors. The concentration of 500 nmol was selected for antisense oligonucleotides according to results was obtained from the MTT assay. Incubation was done for 48 hours in a cell culture incubator at 37o C and 5% CO2 atmosphere. Invasive cells were stained lastly and results were observed by measurement of OD560 in a microplate reader (BioTek).

Results: an anti-invasive effect of 37 and 31.4 % were observed respectively for antisense oligonucleotide 1(5' GTCCTGCATCATCTCTCGAG 3') and antisense oligonucleotide 2 (5' CACGTCCTGCATCATCTCTC 3') in the LNCaP cell line.

Conclusion: ex vivo results obtained from this study, were revealed that down-regulation of twist1 gene can act as metastasis rate limiter in the non-progressed metastatic prostate cancer cell line. Therefore, it can be used as a proper candidate for combinatorial therapy in patients with androgen-dependent prostate cancer.

Keywords: androgen-dependent prostate cancer, twist1, LNCaP, metastasis, invasion

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Homozygous Deletion of exon 7 in *SMN1* gene without phenotypic features of spinal muscular atrophy

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Abstract

Backgrounds: Spinal muscular atrophy (SMA) is an autosomal recessive disorder, resulting in symmetrical progressive weakness of skeletal and respiratory muscles and atrophy. The corresponding gene for the disease is the survival motor neuron 1 (SMN1) and SMN2 genes. Homozygous deletion of SMN1 exons is the most common underlying cause of the disease, and SMN2 copy numbers modify the disease phenotype. However, homozygous deletion of exon 7 of SMN1 in a completely asymptomatic individual is an extremely rare finding. The present report discusses a case of homozygote deletion of exon 7 of SMN1 in a healthy female.
Materials and Methods: A healthy couple with a family history of infected family members with SMA was referred for genetic counseling. Genomic DNA was extracted from the peripheral blood of the couple and the copy number of exon 7 of the SMN1 gene was assessed using real-time polymerase chain reaction (PCR) and PCR-Restriction fragment length polymorphism (RFLP).
Results: Assessment of SMN1-related ct in the female compared with control samples showed that the female had a homozygous deletion in the SMN1 gene. PCR-RFLP and gel electrophoresis results also confirmed the homozygous deletion of exon 7 in the female SMN1 gene.
Conclusion: According to the results of this study and also other findings in previous studies, the lack of symptoms in the female with biallelic deletion of SMN1 may be related to the presence of SMN2 copies or other modifier genes.

Keywords: spinal muscular atrophy, SMA, SMN1, homozygous deletion, biallelic deletion

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Determination of Pathogenic Mutations in *NT5C2* Gene using Bioinformatics Tools

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Abstract

Backgrounds: About 15% to 20% of children suffering acute lymphoblastic leukemia (ALL), experience a relapse, which is an important reason for death in children. Purine nucleotide analogs are frequently prescribed in the maintenance therapy of ALL. 5´ nucleotidase II (NT5C2) catalyzes the 5´ dephosphorylation of purine analogs. Gain-of-function mutations in the *NT5C2* gene result in resistance to the treatment with purine analogs and subsequently relapse in ALL patients. These mutations are common in relapsed ALL cases.

Materials and Methods: In the present study, we assessed the pathogenicity of single nucleotide polymorphisms (SNPs) of the *NT5C2* gene using bioinformatics tools. So, 352 missense variants were retrieved from the NCBI dbSNP database and at the first step analyzed by SIFT, PROVEAN, PMut, and PANTHER. Then, SNPs that were predicted to be deleterious by at least three of the mentioned servers were further analyzed using PolyPhen2, SNPs & Go, and PhD-SNP servers.

Results: Intronic and synonymous SNPs were 72 and 5, respectively. 121 SNPs were predicted to be functionally damaging by SIFT, PROVEAN, PMut, and PANTHER, while the rest were neutral. Then, these 121 SNPs were further evaluated by PolyPhen2, SNPs & Go, and PhD-SNP servers. Finally, 36 SNPs were predicted to be disease-related using all seven tools.

Conclusion: Recognition of biomarkers is especially significant in the prediction of relapse in the treatment of ALL patients. Here, we determined 36 high-risk and deleterious SNPs of the *NT5C2* gene that can be used to predict resistance to chemotherapy and relapse in ALL patients.

Keywords: Relapsed ALL, SIFT, PROVEAN, PolyPhen2, PANTHER

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The Study of the Pathogenicity of SNPs in MT-ND3 gene using bioinformatics sites

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Abstract

Backgrounds: MT-ND3 which encoded the NADH dehydrogenase 3 (ND3), is a Mitochondrial gene. NADH dehydrogenase is the largest of the complex of the electron transport chain and is located in the mitochondrial inner membrane, also known as complex I. The MT-ND3 gene which is one of the 7 mitochondrial genes, is coding for the 115 amino acid protein. This protein forms the core of the transmembrane region and is most hydrophobic of the subunit of complex I. The purpose of this study is the identification the pathogenicity of SNPs in the MT-ND3 gene.
Materials and Methods: Among the identified 783 missense SNPs in this gene, 6 pathogenic variants are retrieved from NCBI, also for identification of pathogenicity of these variants, used from different bioinformatics sites. Then using bioinformatics sites, the stability of structure of mutant proteins was analyzed. After the identification of high-risk mutations, the changes in the hydrophobicity of mutant proteins were considered.
Results: Pathogenic SNPs were screened using bioinformatics sites and was identified pathogenicity of SNPs in MT-ND3. Six pathogenic variants including S34T, S34P, S45P, A47T, D66N, Q26K, and I60T were identified.
Conclusion: According to the previous studies, the association of A47T and Q26K amino acid substitutions with Leigh syndrome (LS) was confirmed.

Keywords: Mitochondria, MT-ND3, mutation, SNP, Pathogenicity

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The Highest Odd Ratio of SNP rs7718919 in Multiple Sclerosis among 10 Variant of IL7R Gene

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Abstract

Backgrounds: The IL7R gene codes interleukin 7 (IL-7) receptor alpha chains. This protein is a subunit of IL-7 and the Thymic Stromal Lymphopoietin (TSLP) receptors. These receptors are inserted in the plasmalemma of lymphocytes. Since the IL7R gene is involved in the regulation of the immune system, changes in it might affect the autoimmune response and inflammation contribute to Multiple Sclerosis (MS). In this study, the variations of the IL-7R gene increasing the risk of MS development were searched.

Materials and Methods: The polymorphisms of the IL7R gene affecting the development of MS were investigated on the MS Gene website (http://www.msgene.org). Literature of review study was done through PubMed, Google Scholar, and NCBI databases. Statistical comparison on the odd ratio of 10 variants of IL7R was done through SPSS software about their efficacy on MS up to Oct 2021.

Results: Among all studied Single Nucleotide Polymorphisms (SNPs) (rs6881706, rs987107, rs11567686, rs11567685, rs7718919, rs6897932, rs1494558, rs11567705, rs11567701, rs6871748), rs7718919 had the highest ODD RATIO on IL7r gene. Therefore, this variant may have the highest risk SNP on the IL7R gene for developing Multiple Sclerosis.

Conclusion: The exact role of SNP rs7718919 is vague in the development of Multiple Sclerosis. It is possible that both genetic and environmental factors would be involved. Further studies are required to declare the exact effects of rs7718919 in MS.

Keywords: IL-7R gene, Single Nucleotide Polymorphism, Multiple Sclerosis

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Pathogenicity analysis of G297C in *GATA4* gene in non-syndromic Tetralogy of fallot (TOF)

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Abstract

Backgrounds: Tetralogy of Fallot (TOF), composed of four (tetralogy) congenital abnormalities, is the most common type of congenital heart disease (CHD) and could be controlled by specific transcription factor genes. TOF accounts for 7% to 10% of congenital defects, affecting males and females equally and occurring in 3 to 5 of every 10000 live births. So genetic variation studies in the GATA4 gene, a transcription factor for heart development is considered important in TOF cases. Mutation in this gene has been associated with cardiac septal defects.
Materials and Methods: In this study. We found a G297C mutation of the GATA4 gene in NCBI. This mutation converts glycine, a hydrophobic amino acid into cysteine, a hydrophilic amino acid. We assessed the effect of this mutation on polymorphism and phenotyping (PolyPhen) and protein functional (SIFT).
Results: Our results showed that this substitution at position 297 from G to C is predicted to affect protein function with a score of 0.00 (deleterious) (SIFT). The PolyPhen score predicts the possible impact of an amino acid substitution on the structure and function, this mutant is predicted to be probably damaging with a score of 1.00. The wild-type residue is glycine, the most flexible of all residues. This flexibility might be necessary for the protein's function. Mutation of this glycine can abolish this function.
Conclusion: The Results of this study predicted that its mutation could be damaging and it was considered potentially pathologic. However, further researches are necessary to clarify this.

Keywords: Tetralogy of Fallot, congenital heart disease, mutation, SIFT, PolyPhen

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Computational approaches to design Anti-CD52 Nano body: A new insight for B-CLL and MS therapeutic strategies

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Abstract

Backgrounds: The research in Nano bodies as therapeutics for cancer and autoimmune disease has gained attention because of their appreciable advantages compared to conventional antibodies. Delivery of monoclonal antibodies to tumor cells in vivo is limited due to their large size, while Nano bodies show excellent tissue penetration, are safe and of low immunogenicity in humans, and can simply be engineered and produced in a prokaryotic host. Epitopes that are often unreachable to conventional antibodies can be recognized by Nano bodies. Alemtuzumab is an approved mAb that is being indicated to treat B-cell chronic lymphocytic leukemia (B-CLL) as well as the relapsing forms of multiple sclerosis (MS). In this study, we propose an approach for designing and generating an anti-CD52 Nano body.

Materials and Methods: Complementarity-determining regions (CDRs) were grafted from conventional antibody layouts onto Nano body frameworks to generate antigen binders and obtain the Nano body protein sequence, using the bioinformatics tools. The reverse translation was done for obtained Nano body protein sequence, with the application of codon optimizing. We performed site-directed mutagenesis to enhance the antigen-antibody interaction affinity. The procedure was certified using in silico cloning of obtained Nano body gene sequence into the prokaryotic host.

Results: These findings propose that designing Nano bodies for targeted therapy of B-CLL and MS patients can have significant antitumor utility via enhanced affinity for the CD52-binding domain and recognizing conserved epitopes. These epitopes are mainly inaccessible to human mAbs.

Conclusion: Although new targeted therapy approaches for cancer will continue to emerge, designing Nano bodies serve as a reassuring novel tool to help the patients.

Keywords: Complementarity-determining region (CDR) grafting, B-CLL, VHH, Therapeutic antibodies, Computational biology

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The effects of nano-Curcumin adjuvant therapy in hospitalized COVID-19 patients

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Abstract

Backgrounds: The outbreak of coronavirus disease 2019 (COVID-19) in the area of Wuhan, China, has evolved rapidly into a public health crisis1 and has spread exponentially to other parts of the world. Curcumin, a natural product present in turmeric, is nominated as a potential treatment for COVID-19 due to its ability to blocking the entrance of the virus to the cell, confining the virus, and regulating different cellular signaling pathways.

Materials and Methods: In this study, a randomized placebo-controlled study was done to investigate the effectiveness and safety of nano curcumin oral soft gels as a complementary therapy on clinical outcomes in COVID-19 patients with moderate-severe disease. All forty-two COVID-19 patients were received routine treatment as Hydroxychloroquine (HCQ) plus Sofosbuvir and divided into two groups of nano-curcumin (Curcuden) and placebo. The nano-curcumin group received 140 mg of nano-curcumin soft gel, for 14 days.

Results: General information, clinical characteristics, blood laboratory tests, and chest computed tomography (CT) images were taken from all patients at time points of 0, 7, and 14 days. CRP and ESR levels significantly decreased from baseline in the nano-curcumin group at day 7. Furthermore, in the Curcuden group D-dimer, CRP, serum ferritin, and ESR levels decreased more significantly than that in the control group after 14 days. Blood levels of inflammatory cytokines including IL-6, IL-8, and IL-10 also decreased more significantly in the nano-curcumin group after 14 days compared to the placebo group. The total CT score was significantly higher in the placebo group than in Curcuden treated group after 14 days. Similarly, the CT score of patients in placebo group was significantly higher compared to in the Curcuden group on day 14.

Conclusion: Our data showed that administration of nano-curcumin as a complementary treatment for moderate-severe COVID-19 patients can speed up the time of chest clearance and recovering. Accordingly, it is suggested that nano-curcumin soft gel due to its high solubility and absorbance can consider as an effective and promising treatment against COVID-19.

Keywords: COVID-19, nano-Curcumin, complementary therapy, Curcuden

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In-silico evaluation of single nucleotide polymorphisms in *PSEN1* gene in patients with Alzheimer's disease

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Abstract

Backgrounds: Alzheimer disease (AD) is a progressive neurodegenerative disease associated with cognitive decline and is the most common form of dementia characterized by neuropathologic findings of intracellular neurofibrillary tangles (NFT) and extracellular amyloid plaques that accumulate in vulnerable brain regions in the elderly. Approximately 45% of people over the age of 85 are estimated to have AD. Mutations in the PSEN1 gene are the most common cause of familial Alzheimer's disease (FAD).

Materials and Methods: We identified ten non-synonymous single nucleotide polymorphisms (nsSNPs) in the *PSEN1* gene: ((rs63749805) (Phe117Arg), (rs63749835) (Leu235Pro), (rs63749880) (Gly209Arg), (rs63749962) (Tyr115Asp), (rs63750155) (Ser178Pro), (rs63750231) (Glu280Ala), (rs63750599) (Leu85Pro), (rs63751141) (Cys92Ser), (rs63751223) (Ala426Pro), (rs661) (Cys410Tyr)) using dbSNP and then analyzed their effect on the structure of Presenilin 1 protein using PyMOL and Expasy, pathogenicity and protein function through PolyPhen-2, SIFT and GVGD and stability by I-Mutant.

Results: Our data from structural analysis showed that nsSNPs change the interaction patterns, polar groups, length of hydrogen bonds and hydrophobicity of the Presenilin 1 protein. The results of Poly Phen-2 predict scores equal 1, in the SIFT, scores are less than 0.05, in the GVGD, they are classified in the class C65 and in the I-Mutant, all ten aforenamed SNPs are pathogens that their stabilities decrease and have the most interfere with function of Presenilin 1 protein.

Conclusion: According to in-silico assays, all of ten mentioned SNPs can be harmful although it should be noted that in-silico methods have their own advantages and limitations and their results are predictions which require confirmation.

Keywords: AD, PSEN1, nsSNP, Structure prediction, Pathogenicity

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Alignment and phylogenetic tree analysis of some corona and influenza type-A viruses based on nucleocapsid protein sequences

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Abstract

Backgrounds: The nucleocapsid (N) proteins of viruses, as with most enveloped viruses, have received less attention than the surface glycoproteins and generally have been perceived to be of lesser concern. Interest in this class of proteins, however, has been stimulated in recent years especially in this pandemic age. The nucleocapsid phosphoprotein of the severe acute respiratory syndrome coronavirus (SARS-CoV N protein) packages the viral genome into a helical ribonucleocapsid (RNP) and plays a fundamental role during viral self-assembly.
Materials and Methods: In this article by using multalin software and their phylogenetic tree by neighbor-joining method protein sequence of 10 subfamily of corona viruses and four subfamily of influenza A viruses from National Center for Biotechnology Information GenBank were analyzed.
Results: Alignment showed low similarity in consensus. The phylogenic tree displayed that influenza and corona virus have a common ancestor and delta corona virus subfamily has more difference compare to other types of corona virus.
Conclusion: We discussed their relativity and how they change during the mutations that they had. This high number of mutations and variations in sequences can provide resistance to vaccine and drugs.

Keywords: Corona virus, Influenza virus, Nucleocapsid, Pandemic, Alignment

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In Silico Analysis of Anti-Microbial Peptides on HER2 Protein in Breast Cancer

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Abstract

Backgrounds: HER2 (Human epidermal growth factor receptor 2) is a member of the human epidermal growth factor receptor (HER/EGFR-/ERBB) family. Amplification or over-expression of this oncogene has been known to have a key role in the development and progression of certain destructive kinds of breast cancer. Hence, there is a necessity to search and design novel drugs, which potentially serve as novel leads for breast cancer by inhibiting the upregulated HER2 signal pathway. Anti-microbial peptides (AMPs) are a group of small peptides that widely exist in nature. AMPs are small cationic or amphipathic molecules produced by eukaryotic and prokaryotic organisms which against types of cancers.

Materials and Methods: RCSB PDB database, PhytAMP, StraPep, HADDOCK 2.2, AlgPred, hemopred, toxinpred, TargetAntiAngio, and ACPred, UCSF Chimera software version 1.15, SWISS-MODEL modeling tools, BIOVIA Discovery Studio Visualizer 3.0 were used to obtain information about peptides.

Results: Based on our analysis, the Bacteriocin lactococcin-G subunit beta from Lactococcus lactis subsp. lactis peptide had the best affinity to HER2 compared to 300 peptides and the binding energy of this interaction was equal to -190.5 +/- 4.4 kcal/mol. The sequence of wild-2JPK had side effects. Consequently, by mutation, side effects were eliminated.

Conclusion: Based on research, drugs being investigated for breast cancer have side effects. For instance, Abemaciclib has side effects such as nausea, vomiting, stomach pain, constipation, sores on the lips, and others. Therefore, AMPs can be used for treatment due to low price and consumption as pills or dairy products.

Keywords: AMPs, Drug design, Breast cancer, Mutant, HER2

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Bioinformatics evaluation of targetom hsa-miR-146a-3p signaling pathways and related to The *IFNAR2* in COVID-19 patients

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Abstract

Backgrounds: In individuals, the receptor heterodimer (*IFNR1-IFNR2*) trigged the immune system in response to cytokines or pathogens. Type I IFNs mediate their activity by binding to dimeric receptor composed *IFNAR1/2*, activating JAKs kinases and phosphorylating STAT 1/2, which in turn, lead to transcription of IFN-signature genes (ISG). The type I interferons were known as the first cytokines discovered and named for their powerful ability to inhibit viral replication. Insufficient virus-induced type I IFN production is characteristic of severe disease caused by SARS-CoV-2. Also, previous studies in COVID19 patients with a dysfunctional immune response showed that there is a massive chemokine and cytokine release, referred to as the 'cytokine storm'. So based on studies *IFNAR2* can assist to identify severe illness due to SARS-COV-2 and help to develop an effective drug against the infection.
Materials and Methods: To find the bioinformatics relationship between these two components (Gene, miRNA) NCBI sites, miRBase, miRWALK2.0, and DAVID were used.
Results: Studies done on the hsa-miR-146a-3p determined that this microRNA binds to the 3 UTR of the *IFNAR2* gene transcription with great power and acts on its inhibitory action.
Conclusion: Studies done on the hsa-miR-146a-3p determined that this microRNA binds to the 3 UTR of the *IFNAR2* gene transcription with great power and acts on its inhibitory action the expected expression of *IFNAR2* and the negative regulatory function of the microRNAs would be expected. The expression of hsa-miR-146a-3p is expected to decrease and consequently increase the expression of the target gene and activation in the "JAK-STAT Signaling pathways".

Keywords: Bioinformatics, COVID-19, hsa-miR-146a-3p, *IFNAR2* gene, miRNA, SARS-COV-2

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The impact of FAS gene expressions in endometriosis

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Abstract

Backgrounds: Endometriosis is an estrogen-dependent inflammatory disease associated with pelvic pain and infertility. It is one of the most common diseases in women, affecting 1 in 10 women's childbearing age. Early diagnosis of the disease can prevent its progression and seek treatment, which requires awareness and increased research on the disease. The FAS gene encodes the death receptor (FAS) at the cell surface. By binding the FAS receptor to FASL, the apoptotic pathway is activated. Apoptosis is one of the factors in controlling cell growth that plays an essential role in endometriosis.

Materials and Methods: In this study, 25 samples of endometriotic tissue and 25 healthy tissue samples were collected, and cDNA synthesis was performed after RNA extraction. Dedicated primers were designed. Then, using GAPDH as internal control, the amount of FAS expression was evaluated by a real-time-PCR method.

Results: Our results showed that the FAS gene expression in endometriotic samples was higher than in healthy samples. The expression level of the FAS gene in control samples is 1.029 and in endometriotic samples is 1.627. The P-value is equal to <0.0001, which indicates that the FAS gene expression is significant between the two groups.

Conclusion: So, changes in FAS gene expression in endometriosis can be raised as an important finding.

Keywords: Endometriosis, FAS, FASL, Apoptosis, GAPDH

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In-silico analysis of *SHOX* Gene for Following Pathogenicity Single-Nucleotide Polymorphisms (SNPs) in Patients with Short Stature Deficiencies

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Abstract

Backgrounds: The *SHOX* gene (short-stature homeobox) is in pseudo-autosomal region 1(PAR1), located on Xp22.33 and Yp11.32 chromosomes, encodes a transcription factor that regulates the differentiation and apoptosis of chondrocytes in the epiphyseal growth plates. *SHOX* mutations are related to different dysplasia, including, Leri- Weill dyschondrosteosis (LWD), Langer mesomelic dysplasia (LMD), and idiopathic short stature. Also, the loss of the X chromosome causes a sex-chromosome aneuploidy deficiency called Turner syndrome with signs of short stature in women.
Materials and Methods: This gene has 8 exons, and the seventh exon is a hotspot one with 69 missense variants. These SNPs (single nucleotide polymorphisms) were analyzed for pathogenicity in SIFT (sorting intolerant from tolerant), Polyphen-2, I-Mutant, PANTHER, PROVEAN.
Results: All 69 SNPs are analyzed in SIFT server at first, and only 11 ones are "AFFECTED", thereby these selected variants are considered in four other servers. In polyphen-2 five SNPs of 11 variants are more severe (score:1.000, sensivity:0.00, and specificity:1.00) with prediction "probably damaging", resulting in I-Mutant with 5 more pathogenic variants in negative DDG (about 0.80-1.16), in PROVEAN also five SNPs with a high degree of "Deleterious" (score: from -4.178 to -5.454), finally for PANTHER, which all of 11 considered variants shown a degree of conservation750 million years with the prediction of "probably damaging".
Conclusion: Actually, between all of these considered pathogens SNPs with rs1221356869 and rs1319210411 could be the most pathogens related to the disease that may be as a point in the treatment of disorders with these variants in the future.

Key words: SHOX gene, SNP, Mutation, Variant, Pathogenicity

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In-vitro antioxidant therapy and improvement of sperm parameters and quality in asthenoteratozoospermia patients

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Abstract

Backgrounds: Spermatozoa are very vulnerable to oxidative stress caused by an imbalance between ROS and antioxidants in the male reproductive system. Despite clinical studies reporting positive effects of oral antioxidants on sperm physiology and fertility, only a few studies have been performed to evaluate their effects on sperm in vitro. In sperm cells, Co-enzyme Q10 is the most important intracellular antioxidant, so that motility and other energy-dependent processes depend on the amount of access to this antioxidant. The main purpose of this study was to evaluate the effect of adding CoQ10 to a sperm preparation medium on the functional parameters.

Materials and Methods: Semen samples, obtained from 30 oligoasthenospermia patients were enrolled in this study.

Spermatozoa were washed with Ham's F-10 media containing 10% human serum albumin and the antioxidant, and then the motility, Viability and DNA fragmentation of the spermatozoa were assessed.

Results: The addition of this antioxidant to the sperm preparation medium significantly improved the motility and viability of the spermatozoa compared with the control group. Moreover, Co-Q10 also decreased the DNA fragmentation rate of the spermatozoa. Main results declared that in specimen, total sperm motility is maintained by in vitro treatment with CoQ10 whereas a significant decrease of these parameters occurs in parallel samples incubated in medium alone.

Conclusion: Supplementing sperm preparation medium with Co-Q10 improved the overall functional parameters of the spermatozoa.

Keywords: Sperm parameters, Antioxidant therapy, DNA fragmentation, Asthenoteratozoospermia

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Genes contributing to the adverse effects of lithium therapy in bipolar disorder

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Abstract

Backgrounds: Bipolar disorder is a mental illness involving periods of depression and abnormally-elevated mood that can last several weeks. Pediatric bipolar disorder affects children like in adults. Lithium ion is the first-line treatment acting as a mood-stabilizing agent in the disorder. Neuroimaging studies indicate that lithium accumulates in the hippocampus and that chronic lithium medication causes the hippocampal volume to become larger than normal.
Materials and Methods: RNA-seq data related to human hippocampal progenitor cells treated with low (0.75 mM) and high (2.25 mM) doses of lithium was obtained from GEO repository (GSE184930). Cell parameters implicated in neurogenesis were used as the dependent factor. Data analysis was performed using DESeq2, and functional genetic enrichment implemented by Cytoscape tools.
Results: Quality control of the sequencing and gene count data was carried out by checking the group boxplots, and indicated cross-comparable groups. Differential gene expression analyses as done for low-lithium and high-lithium treatments compared to control, revealed two genes essential in lithium-induced progenitor cell growth. ZMPSTE24 encodes the CAAX prenyl protease 1 homolog, and DHX35 encodes the RNA helicase DHX35. Functional enrichments showed that these genes are involved in regulating the volume of the molecular layer of the dentate gyrus.
Conclusion: Results of this study suggest that the effects of lithium on human hippocampal volume may be mediated by provoking the adult hippocampal neurogenesis in the bipolar disorder brain.

Keywords: Bipolar disorder, Lithium therapy, Network pharmacology, Systems biology, Differential expression

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In-silico analysis of SNPs in mitochondrial MT-ND4 gene

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Abstract

Backgrounds: MT-ND4 is a mitochondrial gene encoding a subunit of the mitochondrial complex I. LHON is a maternally inherited disease and Mitochondrial DNA replacement mutation in this disease was identified. To identify the structural and functional effects of mutations, various powerful bioinformatics tools are available. The aim of this study is the identification of high-risk non-synonymous single nucleotide variants in the MT-ND4 gene via bioinformatics tools.
Materials and Methods: SNPs for the MT-ND4 gene were collected from a web-based data source such as NCBI/dbSNP database. Among the identified polymorphisms in this gene, 821 missense variants are retrieved. Then, the pathogenicity of missense variants are considered using different bioinformatics tools. The stability of these mutant proteins, conservation of amino acids structural changes are analyzed by bioinformatics tools. After the identification of high-risk mutations, the changes in the hydrophobicity of high-risk amino acid substitutions are considered.
Results: We found 821 missense mutations in MT-ND4 that 32 of 821 mutations were pathogenic. Deleterious single nucleotide polymorphisms (SNPs) were screened using the bioinformatics tools such as SIFT, Polyphen, PHD-SNP, PROVEAN and SNP&GO. The results obtained from the set of bioinformatics tools identify high-risk mutations in the MT-ND4 gene.
Conclusion: Collectively, six mutations including R340S/G, R340H, T109A, I165T and V313I for further studies were identified. A Better understanding of related diseases caused by mutations in the MT-ND4 gene was achieved using In-silico prediction. All of these mutations constitute possible candidates for further genetic studies.

Keywords: Mitochondria, MT-ND4, Gene, SNP, In-silico analysis

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Inferring cell lineage differential gene expression analysis using single-cell RNA-seq

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Abstract

Backgrounds: Single-cell RNA sequencing (scRNA-seq) analysis can investigate gene expression at single-cell resolution and track the trajectories of distinct cell lineages. Intra-tumor heterogeneity (ITH) includes cellular differences in tumors and is associated with clinical outcomes such as drug resistance. Expression profiling of cells individually allows monitoring ITH and may unravel the dynamics of specific sub-population of tumoral cells. To identify differentially expressed genes in different lineages of Acute Lymphoblastic Leukemia (ALL), we utilized a scRNA approach to scrutinize the ETV6-RUNX role in promoting tumorigenesis.
Materials and Methods: We used the Seurat R package to analyze 3094 Pre-B t (12;21) [ETV6-RUNX1] ALL cells sequenced by 10x Genomics' scRNA-seq technology. Raw data retrieved from SRA public database (SRR9264343) and was processed to obtain count matrices using Cellranger count tools. UMAP algorithm and Slingshot was applied for dimensionality reduction and identifying branch-specific changes in gene expression respectively.
Results: We found 9 clusters and 2 lineages in our data. 12 genes were differentially expressed between 2 lineages, including TERF2, ID3, XRCC6, ATF4, and DDX17. We focused on ID3 and its biological networks. Our data not only showed a significant aberrant pattern of cellular heterogeneity between normal and tumoral cells but also ETV6-RUNX is intriguingly showed a distinguished cellular signature.
Conclusion: Based on our findings ID3 may be considered as a critical marker in ETV6-RUNX harboring cells. Its crucial biological roles in cell cycle, regulation of DNA replication and regulation of cell differentiation, may pave the way for generating of a new subtype of cells and should be considered as one of the key genes related to evolvability of lymphoblastic progenitors in ALL.

Keywords: scRNA-seq, Acute Lymphoblastic Leukemia (ALL), ID3, ETV6-RUNX1, Intra-tumor heterogeneity

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Long noncoding RNA TP53TG1 alteration impact on breast cancer progression

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Abstract

Backgrounds: Breast cancer is still one of leading causes of death in women worldwide. The molecular mechanisms underlying the disease have been extensively studied focusing on protein-coding genes. However, recent studies demonstrate that the majority of the genome is transcribed to non-coding RNAs (ncRNAs) which do not encode any protein.
Materials and Methods: In this study, we examined ncRNAs in breast cancer patients and cell lines using bioinformatics analysis and in vitro experiments. We focused on investigating the effect of long non-coding RNAs (LncRNAs) in breast cancer subtypes mainly triple negative breast cancer (TNBC) which is the most challenging category. We performed loss- and gain-of-function experiments and evaluated the LncRNAs roles in regulating cancer cell characteristics.
Results: Our result shows that ncRNAs such as MALAT1, PDCD4-AS1 and TP53TG1 play regulatory roles in breast cancer progression. In particular, our data shows TP53TG1 is a cytoplasmic, relatively abundant and poly-adenyaletd transcript which plays a tumor suppressive role in breast cancer. Upon loss-of-function experiments, we observed increased metastatic properties in breast cancer cell lines. We studied the TP53TG1 level and its effect on survival in breast cancer patients in The Cancer Genome Atlas (TCGA) patient database. TP53TG1 lower level correlated with poor survival in breast cancer patients. We further studied the TP53TG1 roles in regulation of cis- and trans-genes including CROT and UBE2V1.
Conclusion: Breast cancer is categorized in different subtypes such as Luminal A/B, HER2 + and triple negative (TNBC). Among all subtypes, TNBC patients show the worst prognosis. Here, we studied LncRNA players in breast cancer and proposed some molecular markers with potential applications in TNBC patients.

Keywords: LncRNA, Breast cancer, TP53TG1, Tumor suppressor, TCGA

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Computational analysis of single nucleotide polymorphisms (SNPs) in human *MPO* gene

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Abstract

Backgrounds:
Myeloperoxidase (MPO) as a haem peroxidase-cyclooxygenase enzyme with vital antimicrobial and antiviral role expressed circulating neutrophils, monocytes and some tissue macrophages. MPO is encoded by the *MPO* gene on chromosome 17q23. MPO-derived oxidants lead to inflammatory diseases, cancers, neurodegenerative diseases, cardiovascular diseases, kidney diseases, and immune-mediated diseases. The aim of this study is the computational analysis of single nucleotide polymorphisms (SNPs) in human *MPO* gene. Protein function and structure can be altered by SNPs.

Materials and Methods: Four *in silico* SNP prediction algorithms including PolyPhen, nsSNPAnalyzer, SNPs&GO and PROVEAN were used to identify functional SNPs in the coding regions of *MPO* gene and predict the effect of these variants on MPO function. Polymorphisms data were retrieved from NCBI database of SNPs (dbSNP) for *MPO* gene.

Results: In total, 235 SNP for human *MPO* gene were showed by the dbSNP-NCBI database which contained 26 missense SNPs. The missense SNPs were used for our further investigations. 14 missense SNPs (53%) are predicted to be probably damaging to MPO function, 8 SNPs (30%) are possibly damaging and 4 missense SNPs (15%) are benign by PolyPhen-2 (Polymorphism phenotyping) algorithms predicting the potential impact of amino acid substitutions on protein function and structure. Other three in silico tools predicted the same phenotypic effects of SNPs with their specific scores.

Conclusion: These computational SNPs analysis can be beneficial for better understanding of the genetic causes of MPO mediated diseases like inflammatory diseases and cancers for diagnosis and drug design.

Keywords: Myeloperoxidase, Single nucleotide polymorphisms, Inflammatory diseases, in silico

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The influences of chicken embryo extract on the fate of epidermal neural crest stem cells

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Abstract

Backgrounds: Epidermal neural crest stem cells (EPI-NCSCs) in the bulge of hair follicles are a promising source for cell-replacement therapies in neurodegenerative disease, so that is important to know how to increase their efficiency and effectiveness. The factor that can affect the proliferation, morphology and gene expression of these cells is their culture medium. The aim of this study is to observe the effect of different culture media on the proliferation, morphology and gene expression in these cells.

Materials and Methods: In this study, the highly pure population of EPI-NCSCs was obtained from the bulge of mouse hair follicle. Cells were implanted in four different culture media. After eleven days, first passage was done and when the flasks were full, the second passage was done. On the 21st day, the cells were transferred to 6-well and 12-well plates to extract RNA and assess cellular morphology, respectively.

Results: The results showed that the presence of chicken embryo extract increased the migration of stem cells from the bulge of hair follicle and increased cell proliferation. Also, this extract significantly affected the morphology of the treated cells. In addition, evaluation of Nestin, Sox10, GFAP and β-Tubulin genes in this study showed that this extract can also alter gene expression.

Conclusion: The obtained data showed the effect of 11-day-old chick embryo extract in the culture medium on the migration, proliferation and morphology of epidermal neural crest stem cells.

Keywords: Chicken embryo extract, Culture medium, Epidermal neural crest stem cells, Stem cells

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Bioinformatics analysis of potential interactions between hsa-miR-143-5p and E6 and E7 mRNAs from HPV-16

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Abstract

Backgrounds: Human Papillomavirus type 16 (HPV-16) is the most common cause of cervical cancer which induces carcinogenesis through the permanent expression of E6 and E7 oncogenes. The expression level of some miRNAs changes in response to the permanent expression of these oncogenes. Deregulated miRNAs in cervical cancer tissue can be used for the detection and treatment of cervical cancer. Identification of the interactions between miRNAs and E6 and E7 mRNAs may help us to find the most suitable miRNAs. hsa-miR-143-5p which is down-regulated in cervical cancer targets ELK1 and inhibits the progression of cervical cancer. However, the interactions between E6 and E7 mRNAs and hsa-miR-143-5p are unclear. The aim of the present study is the prediction of these interactions.

Materials and Methods: The sequences of E6 and E7 genes from HPV-16 and hsa-miR-143-5p were obtained from GenBank (NC_001526.4) and miRBase databases, respectively. The gene sequences were converted to mRNA sequences using a transcription tool. Then, the interactions between E6 and E7 mRNAs and hsa-miR-143-5p were predicted using RNA22 v2 and RNAhybrid v2.2.

Results: Based on the obtained results of RNA22 v2, the complementary relationship between E6 mRNA and hsa-miR-143-5p was significant (P = 4.95e-2). However, E7 mRNA has no interaction with hsa-miR-143-5p. RNAhybrid v2.2 showed that hsa-miR-143-5p had a complementary relationship with E6 mRNA (MFE = -26.7kcal/mol) and E7 mRNA (MFE = -24.3kcal/mol). It seems the E6 mRNA sponges hsa-miR-143-5p and reduces its expression level in the tumoral cells.

Conclusion: hsa-miR-143-5p has strong interactions with E6 mRNA and can be a good target for the detection and treatment of cervical cancer.

Keywords: Cervical cancer, E6 and E7 oncoproteins, hsa-miR-143-5p, HPV-16

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In silico analysis predicting effects of deleterious SNPs of human *ETV6* gene on its functions

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Abstract

Backgrounds: An ETS transcription factor is encoded by ETV6. An N-terminal pointed (PNT) domain that is involved in protein-protein interactions with itself and other proteins, as well as a C-terminal DNA-binding domain, make up the product of this gene. It appears to be essential for hematopoiesis and the preservation of the growing vascular network, according to mouse knockout experiments. This gene has been connected to chromosomal rearrangements associated with leukemia and congenital fibrosarcoma. A familial thrombocytopenia and leukemia propensity condition is caused by germ line mutations in ETV6. Thrombocytopenia is usually mild and almost entirely penetrant. Leukemia is reported in ~30% of carriers and is most often B-cell acute lymphoblastic leukemia. In this study, 5 single nucleotide polymorphism (SNP) are checked which are identified as missense change in the National center for biotechnology information (NCBI) on the SNP database.

Materials and Methods: In NCBI/SNP database 5,389 SNPs were found for *ETV6*. Missense variant and pathogenic filters were applied and the result shows 5 SNP (rs724159947 P>L, rs786205155 L>P, rs724159946 R>L, rs724159945 R>S, rs786205226 R>G). Their effect on the final protein product was checked.

Results: The results of this research with bioinformatical tools (SIFT, PolyPhen-2, PROVEAN, SNP&GO, Phdsnp) shows that Reference SNP for instance (rs) 786205155 causes change L (Leu) to P (Pro) in 349rd amino acid residue in *ETV6* transcript, can produce an abnormal protein that can have an inappropriate effect on patients with this polymorphism.

Conclusion: Based on the results were obtained these SNPs most probably deleterious and only rs724159947 in the PROVEAN and SNP & GO databases were declared neutral.

Keywords: ETV6, SNP, Bioinformatics

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Inhibition of LSD1 by gsk-lsd1 small molecule inhibitor stimulates fetal hemoglobin in CD34+ cells

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Abstract

Backgrounds: B-thalassemia and sickle cell disease together include the most common inherited diseases. switch from fetal γ globin to β globin genes expression occurs at birth, several adult-stage γ globin repressors, such as bcl11a, gata1 and sox6 have been identified that interact with repress the γ globin genes. The strong recent results showed one of the modifying repressor is LSD1.

Materials and Methods: We examined the effects of the GSK-LSD1 inhibitor concentrations on CD34+ cells are isolated from cord blood. Cell number and viability were determined by trypan blue and flow-cytometric analysis. We treated the cells with 0, 0.5, 1.5, and 5 μm of the gsk-lsd1 inhibitor on days 4 to 14 of the differentiation culture, and then we performed an analysis of the expression of LSD1 and γ globin genes comparable levels throughout differentiation with Real-Time PCR.

Results: After treatment GSK-LSD1 inhibitor at 0.5, 1.5, and 5 μm did not alter cell proliferation or viability, but 5μm gsk-lsd1 reduced cell proliferation and delayed differentiation without affecting cell viability. In 1.5-μm concentration of the gsk-lsd1 inhibitor, the mean of γ-globin mRNA expression was induced up to 33-fold, we observed a decrease in the LSD1 mRNA expression in a 5-μm concentration of the gsk-lsd1 inhibitor.

Conclusion: Our results indicated that LSD1 played an important role in γ-globin silencing in adult erythroid cells. Further, the GSK-LSD1 inhibitor increase concentration of HBF induction within the therapeutic plasma concentration. LSD1 is a molecular- targeted, promising therapeutic epigenetic drugs target for γ-globin induction, can be realized for patients with SCD.

Keywords: Fetal hemoglobin, Hemoglobinopathies, lsd1, gsk-lsd1, Epigenetic drugs

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Introducing prognosis biomarkers of acute myeloid leukemia by weighted gene co-expression network analysis

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Abstract

Backgrounds: Acute myeloid leukemia (AML) is a cancer of blood and bone marrow which is a major subtype of leukemia that characterized by abnormal proliferation of immature myeloid cells. Although the prognosis approaches of AML have gradually improved but there is demand to find more confident AML biomarkers for prognosis and diagnosis. Some of the most important differentially expressed genes which have immunological functions are reported as biomarkers in this paper.

Materials and Methods: We carried out differential expression analysis in 37 samples (19 patients and 18 controls) with two sets of public RNA sequencing data (PRJNA576867, PRJNA576718 bioprojects). After preprocessing of raw data, we used DESeq2 package in R to recognize differentially expressed genes. Finally, weighted gene co-expression network analysis (WGCNA) performed to detect hub genes.

Results: Our RNA sequencing results showed 547 genes up regulated and 464 down regulated genes. Downstream analysis revealed that six major genes includes *MYCNOS*, *APPL2*, *TREML4*, *S100A8*, *S100A9* and *VSIR* (*VISTA*) which were significantly dysregulated (padj < 0.05) are effective in immune response of AML patients.

Conclusion: In this study, we introduced six genes that are effective in immunological response of AML patients. Our data demonstrated that *MYCNOS* was upregulated and five other genes were downregulated. Downregulation of *APPL2*, *TREML4*, *S100A8*, *S100A9* and *VSIR* (*VISTA*) are effective to enhance proliferation of AML cells. Further studies are required for better understanding of the molecular mechanisms to utilize these markers applicable for prognosis and diagnosis of AML.

Keywords: Acute myeloid leukemia, RNA sequencing, Differential expression, Biomarkers

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Comparative study of expression of non-coding circular RNAs circBIRC6 and circCORO1C in cord blood CD34+ stem cells and its differentiated cells

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Abstract

Backgrounds: Umbilical cord blood hematopoietic stem cells (UCB HSCs) transplantation has attracted the attention of many researchers due to the low probability of GVHD and HLA mismatching; however, the use of this resource for adults has been limited due to the inadequate number of CD34+ HSC from any individual donor. On the other hand, nowadays, circular RNAs (circRNAs) have been shown to be involved in stem cell properties. In this study, several candidate circRNAs, including circCORO1C and circBIRC6 were selected from circBase and their functional role in CD34+ HSCs was investigated.

Materials and Methods: UCB CD34+ HSCs were separated using the MACS system, and its purity was confirmed by flow cytometry. The StemMACS HSC-CFU medium was used to differentiate the cells until the appointed days (7th and 14th days) and the total RNA was extracted from them. Then, the expression level of these circRNAs was measured using qRT-PCR. The quantitative analysis of GATA-1 gene and PU1 gene as well as quantitative analysis of NANOG and SOX2 genes were used to conduct molecular evaluation of differentiated cells.

Results: The results showed that the expression levels of circBIRC6 and circCORO1C as well as the expression levels of NANOG and SOX2 were significantly downregulated during differentiation. Furthermore, the expression levels of GATA-1 and PU-1 were upregulated on the 7th day compared with the control group and were downregulated on the 14th compared with the 7th day.

Conclusion: The present study showed that circBIRC6 and circCORO1C were involved in the process of self-renewal of CD34+ HSCs, and their expression is downregulated by differentiating these cells. Moreover, in future applied studies, the effect of manipulation on these genes can be investigated in order to achieve maximum proliferation without differentiation of umbilical cord blood stem cells.

Keywords: Hematopoietic stem cells, circRNA, circBIRC6, circCORO1C

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In vivo identification of novel target genes in colorectal adenocarcinoma by the cDNA-AFLP technique

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Abstract

Backgrounds: Homeobox-containing genes are composed of a group of regulatory genes encoding transcription factors involved in the control of developmental processes. The homeodomain proteins could activate or repress the expression of downstream target genes. These proteins have been reported to regulate various embryonic developmental processes such as axis formation, limb development, and organogenesis. A number of gene alterations in homeobox genes have been established to be involved in diseases such as neuroblastoma, leukemia, and cancer. This study was conducted to in vivo identify the potential target gene(s) of *TGIF2LX* in colorectal adenocarcinoma.

Materials and Methods: A human colorectal adenocarcinoma cell line, SW48, was transfected with the recombinant pEGFPN1-TGIF2LX. The cells were injected subcutaneously into the flank of the three groups of 6-week-old female athymic C56BL/6 nude mice (n = 6 per group). The transcript profiles in the developed tumors were investigated using the cDNA amplified fragment length polymorphism (cDNA-AFLP) technique.

Results: The real-time RT-PCR and DNA sequencing data for the identified genes indicated that the N-terminal domain-interacting receptor 1 (Nir1) gene was suppressed whereas Nir2 and fragile histidine triad (FHIT) genes were upregulated followed by the overexpression of *TGIF2LX* gene.

Conclusion: Downregulation of Nir1 and upregulation of Nir2 and FHIT genes due to the overexpression of *TGIF2LX* suggests that the gene plays an important role as a suppressor in colorectal adenocarcinoma.

Keywords: Target genes, Colorectal adenocarcinoma, Homeobox, cDNA-AFLP

Iranian Journal of Pediatric Hematology Oncology

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Selection of a CD19 specific scfv by phage display with future prospect in CAR-T cell therapy of leukemia cancer

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Abstract

Backgrounds: Targeting tumor cells through artificially modified T-cells showed promising results in preclinical and clinical studies during last decades. CD19 is the most used target for chimeric antigen receptor T-cell against B cell leukemia. Chimeric antigen receptor through witch targeting occurs, is composed of a targeting moiety often a single chain antibody, a costimulatory domain and a CD3ζ domain of a T-cell receptor. scfv antibodies have been used extensively for targeting surface markers of cancer cells. Their small size, easier production and their high affinity make them an ideal substitute for monoclonal antibodies.

Materials and Methods: In this study, we selected a CD19 scFv from a human scFv library using phage display. Briefly, we amplified the library culture, and then we added the commercial helper phage to the culture then incubated the culture three days for bacteriophage production. We then purified phages using PEG 8000 by ultracentrifugation and their titer was calculated before selection. In each round, titrated phage was subjected to CD19 coated beads in solution. After washing of unbound phages, bound ones were recovered and their affinities were analyzed using ELISA against CD19 and then transformed for another round of phage production and selection. After three rounds of selections, clones with the highest affinity were selected, sequenced and then cloned into pET28a.

Results: Three scFvs were selected in this step, expressed in BL21 and analyzed in SDS-PAGE. They are then extracted using IMAC and affinity of them was measured by ELISA. A thin protein band of ~27 kDa was observed in SDS-PAGE and visualized in western blot using HRP-conjugated anti-his tag antibody.

Conclusion: Our results showed that clone 26 is able to recognize CD19 better than two other clones.

Keywords: CD19, scFv, CART cell, Phage display

Iranian Journal of Pediatric Hematology Oncology

International Conference on Human Genetics and Genomic

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Investigating differential expression of mTOR1/UCA1 in tumor samples of colorectal cancer compared with tumor marginal samples

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Abstract

Backgrounds: Colorectal cancer (CRC) is the second and third most common cancer in men and women respectively, and the fourth cause of cancer death of individuals. Mutations in specific genes can lead to colorectal cancer. UCA1 is one of the oncogenic genes that have been shown to stimulate cell proliferation. mTOR1 is another gene that leads to the growth of cancer cells through anabolic processes and autophagy inhibition. In this study, we evaluate the expression of these two genes in different phases of CRC that helps the early detection of colorectal cancer which can increase the survival rate.

Materials and Methods: First, we collected 25 colorectal cancer tumor tissues and 25 adjacent normal tissues as a control group. Then, RNA was extracted from tissue samples and cDNA synthesized. The UCA1 and mTOR1 expression was evaluated in CRC tissues compared to adjacent normal tissues by Real Time PCR after synthesizing specific gene primers.

Results: Our results showed that the UCA1 and mTOR1 expression in the tumor tissues was significantly higher than in the adjacent normal tissues ($P < 0.05$). There was also a significant difference in Lynph inv and Vescu inv with mTOR1 expression ($p < 0.05$).

Conclusion: Our results showed that UCA1/mTOR1 may be important genes involved in colorectal cancer. *mTOR1* was also identified as one of the possible genes in metastasis of colorectal cancer. Thus, UCA1 and mTOR1 can probably be considered as biomarkers in CRC therapy and diagnosis.

Keywords: Colorectal cancer, *mTOR* gene, *UCA1* gene, Biomarker

Iranian Journal of Pediatric Hematology Oncology

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Identifying the miRNA and mRNA-associated networks to reveal potential prognostic biomarkers for Breast cancer

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Abstract

Backgrounds: Despite significant breakthroughs in breast cancer diagnosis and therapy, the prognosis remains unfavorable. MicroRNAs (miRNAs) appear to play a key role in the genesis and progression of human malignancies, according to mounting data. However, most miRNAs' regulation mechanisms and clinical relevance in breast cancer are yet unknown.
Materials and Methods: The gene expression profiles for miRNA and mRNA were collected from the Gene Expression Omnibus (GEO), in this study we systematically analyzed the expression profiles of mRNA (GSE54002 dataset) and miRNA (GSE42525 dataset). Using Cytoscape, a miRNA-mRNA regulatory network was built and visualized. The STRING database was used to build the protein-protein interaction (PPI) network, and the cytoHubba plugin was used to extract hub genes. The functions and signaling pathways associated with these differentially expressed mRNAs were discovered using Gene Ontology and the Kyoto Encyclopedia of Gene and Genomes.
Results: We found 225 differentially expressed miRNAs (DEmiRNAs), and 665 DEmRNAs in total. The enrichment results from analyzing DEmRNAs was shown to be associated with Interactions between immune cells and microRNAs in tumor microenvironment, B Cell Receptor Signaling Pathway and Cancer immunotherapy by CTLA4 blockade. Also construction of PPI network of the DEmRNAs showed 564 nodes and 3899 edges in total from which one most significant module was identified. We also selected the key deregulated miRNAs and mRNAs based on statistical significance.
Conclusion: Our results show the significant roles of miRNA-mRNA regulatory networks in breast cancer and identified a new prognosis predictor and some potential prognostic biomarkers as well as involved genes and miRNAs in patients with breast cancer.

Keywords: Breast cancer, GEO, DEmiRNAs, DEmRNAs, microRNA

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Evaluation of the Effect of Ni on Expression Changes of NKILA in leukemia

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Abstract

Backgrounds: Acute lymphocytic leukemia (ALL) is a type of cancer of the blood. In the United States, the majority of ALL cases occur in children, with an incidence of 3 per 4/100,000 in patients aged 5 to 14. The purpose of this research was to determine how Ni-thiosemicarbazone complexes altered the expression of the NKILA in an acute lymphoblastic leukemia cell line.
Materials and Methods: Two concentrations of Ni Thiosemicarbazone complexes were prepared: 104µM at 24h and 51µM at 48h. The JurkatE6.1 cell line was purchased from Pasteur Institute and treated with prepared doses of the Thiosemicarbazones complexes Ni at 24 and 48h after cell passage. The expression changes of NKILA and GAPDH were studied using Real-Time PCR after RNA extraction and cDNA synthesis. Finally, Rest 2002 Software was used to analyze the data.
Results: The results showed that the expression of NKILA in comparison with the GAPDH decreased after 24h of Ni treatment at 104µM. According to the findings, changes in NKILA gene expression increased after 48h at 51µM that increase was statistically significant These changes included 104µM (0.896) at 24h and 51µM (1.214) at 48h, respectively (P <0.001).
Conclusion: According to the present study results, alternation in NKILA expression after treatment with Ni, at 51µM was effective in increase of LncRNA NKILA expression. Evidence showed that the Ni requires a longer time and lower concentration for better efficacy because the drug was ineffective in increasing gene expression at higher concentrations in 24h.

Keywords: Thiosemicarbazones, Ni, NKILA, GAPDH, Leukemia

Iranian Journal of Pediatric Hematology Oncology

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Molecular and prenatal diagnosis in retinoblastoma affected family: findings from Next-Generation Sequencing

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Abstract

Backgrounds: Retinoblastoma (RB) is a malignant tumor that usually develops in early childhood, usually before age five years. This form of cancer develops in the retina, which is the specialized light-sensitive tissue at the back of the eye that detects light and color. This disease develops from cells that have cancer-predisposing compound heterozygous or homozygous variants in the retinoblastoma gene (*RB1*). Heritable RB is an autosomal dominant disease with high penetrance. Individuals with heritable RB are also at increased risk of developing non-ocular tumors.

Materials and Methods: Whole exome sequencing (WES) was performed for detection of disease-causing mutation at peripheral blood in RB affected family's proband. Prenatal diagnosis (PND) was also performed for the family's next pregnancy.

Results: The molecular analysis of the affected family showed the c.1960G>C (p.Val654Leu) likely pathogenic mutation in exon 19 of the *RB1* (NM_000321.3) gene in the affected boy with bilateral retinoblastoma. PND test revealed no mutation in the fetus.

Conclusion: Retinoblastoma as a highly malignant intraocular tumor requiring an early diagnosis and immediate treatment. Mutations in the *RB1* gene are responsible for most cases and genetic screening of retinoblastoma patients and relatives is important for precise classification, efficient treatment or management and genetic counseling purposes. In addition, RB1 gene mutation studies may help decipher the molecular mechanisms leading to tumors with different degrees of penetrance or expressivity. Today use of next-generation sequencing (NGS) methods as efficient and comprehensive approaches was demonstrated for the identification of a wide spectrum of pathogenic variants in RB patients.

Keywords: Retinoblastoma, Next generation sequencing, Whole exome sequencing, Molecular diagnosis, Prenatal diagnosis

Iranian Journal of Pediatric Hematology Oncology

International Conference on Human Genetics and Genomic

International Conference on Human Genetics and Genomics

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Assessment of lead heavy metal on the genome of *E. coli*

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Abstract

Backgrounds: According to studies, heavy metals and cations have antibacterial properties, so when it enters the human food chain, it can damage the natural flora of the humans, especially the natural flora of the intestine, and any reduction in microorganisms in the intestine can lead to disease. There are some studies that point out indirect mechanisms of genotoxicity such as damage of DNA.

Materials and Methods: At the first MIC (minimum Inhibitory concentration) and MBC (Minimum Bactericial Concentration) test was done to obtain that prevents bacterial growth. Growth rate of bacteria at different concentrations of lead was evaluated using spectrophotometer at 600 nm. In order to investigate the effects of lead heavy metal on the genome, the chain reaction techniques of Enterobacterial Repetitive Intergenic Consensus (ERIC-PCR) was employed. The results obtained from electrophoresis of PCR products on agarose gel were analyzed.

Results: The minimum inhibitory concentration for *Escherichia coli* was less than 10 mg/mL and the Minimum Bactericidal Concentration (MBC) was twice the MIC concentration. The results of the study revealed that lead heavy metal not only affects the growth of bacteria but also affect the sequencing of genomic DNA and leads to the changes of them in different points. The result of the gel analysis was that the primer did not bind to some areas of the heavy metal DNA fragments.

Conclusion: Results of current study showed that lead has the ability to damage and mutations in the genome.

Keywords: Heavy Metal, Escherichia coli, ERIC-PCR, MIC, Lead

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International Conference on Human Genetics and Genomic

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In vitro and *Drosophila* models of rare monogenic disorders

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Abstract

Backgrounds: Primary cilia (PC) are immotile sensory cellular organelles that transduce diverse extracellular cues to direct development and homeostasis. Ciliary dysfunction has been determined as a cause of inherited ciliopathies with skeletal, renal, nervous system and other abnormalities. We investigated the molecular underpinnings of novel and known skeletal dysplasias, short-rib thoracic dysplasia 16 (SRTD16) and achondrogenesis type 1A (ACG1A) that are associated with *IFT52* and *TRIP11*, respectively.

Materials and Methods: We evaluated four affected foetuses, two each from two families, with ACG1A phenotype. Exome and genome sequencing were used to identify candidate variants in *TRIP11*. Molecular analysis of *TRIP11* mRNA, protein and PC features were done to demonstrate pathogenicity in patient-derived fibroblast cells. In a separate study we investigate the role of *IFT52* in PC dependent manner in osteogenic differentiation using lentiviral shRNA knockdown (KD) in C3H10T1/2 mesenchymal stem cells and explored the role of *IFT52 in vivo* using *Drosophila*.

Results: We demonstrated a pathogenic biallelic deep intronic variant c.5457+81T>A in *TRIP11* that causes ACG1A. We observed severe impairment of primary ciliogenesis, not reported so far in patient cells with *TRIP11*-related disorder. Further we show that silencing *Ift52* leads to impaired primary ciliogenesis and abrogated osteogenic differentiation *in vitro*. In *Drosophila IFT52* KD led to significant deficits in chordotonal structure and function, such as adult climbing, larval mobility and hearing.

Conclusion: Our studies have evaluated the molecular pathology of ACG1A and SRTD16. It uncovered the essential role of primary cilia in these disorders underscoring its fundamental function in skeletal development.

Keywords: Achondrogenesis 1A, Short-rib thoracic dysplasia 16, IFT52, TRIP11, Primary cilia

Iranian Journal of Pediatric Hematology Oncology

International Conference on Human Genetics and Genomic

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H. pylori and its *cagA* gene Prevalence in gastric cancer or peptic ulcer patients at in Qom

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Abstract

Backgrounds: Iran has a high incidence rate for gastric cancer among the Middle East countries. In addition to gastric cancer, peptic ulcer is also life-threatening; thus, investigating the prevalence of Helicobacter pylori infection and other risk factors are essential. The present study was aimed to assess the frequency of *H. pylori* and the cagA-positive strains in patients with gastric cancer or peptic ulcer at a teaching hospital in Qom, one of the most populated cities of Iran.
Materials and Methods: The presence of *H. pylori* was investigated in gastric cancer and peptic ulcer biopsy specimens using the standard culture method. PCR analysis was performed to detect the presence of the *cagA* gene.
Results: The frequency of H. pylori isolates among 86 investigated biopsies was 20 (23.2%). Likewise, the rate of *H. pylori* was the highest when samples were examined from patients with gastric cancer (25.8%), while it was 21.8% when obtained from peptic ulcer patients. The frequency of the *cagA* gene in *H. pylori* isolates was 9 (56.2%), as confirmed by PCR.
Conclusion: Our results indicated that *H. Pylori* infection and its virulent strains are frequent and widely spread in Qom city. The *cagA* gene was present in almost half of *H. pylori* isolates from peptic ulcer or gastric cancer patients. Therefore, it is necessary to screen it in all cases with H. pylori infection for early detection of gastric cancer.

Keywords: *Helicobacter pylori*, cagA, Gastric cancer, Peptic ulcer, Qom

Iranian Journal of Pediatric Hematology Oncology

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Reconstruction of Hippo Signaling Pathway Co-Expression Network in AML

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Abstract

Backgrounds: Acute myeloid leukemia (AML) is the prevalent form of adult leukemia with poor overall survival (OS), increasing AML incidence. It has been shown that the Hippo signaling pathway (HSP) can influence patient survival outcomes in malignancies. The expression pattern of some Hippo members is also associated with predicting AML. This study carried out a co-expression analysis to reconstruct the HSP in AML.
Materials and Methods: The microarray data GSE114868 from GEO database was analyzed by limma and WGCNA package in R to reconstruct the HSP in AML. The module preservation analysis was performed to assess preserved modules, including HSP genes in the AML network. Subsequently, a protein-protein interaction (PPI) network using STRING followed by functional enrichment analysis by ClueGO Cytoscape plug-in was done. Then, the prognostic significance of co-expressed genes was explored in terms of overall survival by GEPIA2.
Results: Five preserved modules out of 17 modules were detected through network clustering. Our results indicate the Purple preserved module containing 74 members of HSP, which suggest dysregulated co-expressed AML biomarkers including *cebpa*, *nrxn2*, *cyp4f3,* and *tacstd2* interact with transcription factors such as *gli2*, *snai2*, *tead1*, *tead4*, *tp73*, and *wwtr1*. Moreover, our data show some key HSP members contribute to AML, such as *frmd1*, *yap1*, *tgfb3*, *fgf1*, and *wnt* Family Members. ClueGO revealed the purple module was mainly enriched in adherens and tight junction, JUN kinase activity, Wnt signaling, Hedgehog signaling, and kinase regulation pathways. Moreover, overall survival analysis confirmed the poor prognosis by HSP members dysregulation and new suggested regulatory factors between leukemia and normal samples.
Conclusion: We established the co-expression network signature correlated with genes potentially involved in AML development and the prognostic potential of the HSP. These findings can further reveal the importance of HSP and novel genes contributing to AML.

Keywords: Acute myeloid leukemia, Hippo signaling pathway, Weighted gene co-expression network analysis, Survival rate

Iranian Journal of Pediatric Hematology Oncology

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Evaluation of apoptosis induction in HepG2 cell line by inhibition of miR-4270

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Abstract

Backgrounds: Hepatocellular carcinoma (HCC) is the most common type of liver cancer and a very common disease worldwide. Therefore, the discovery of new treatments in HCC is essential. MicroRNAs are small non-coding RNAs that play a role in post-transcriptional gene suppression and play a key role in regulating the cell cycle, including apoptosis. Apoptosis or programmed cell death has been shown to be most effective in inhibiting cancer growth. One of the distinctive biochemical features of apoptosis is DNA degradation by caspase-activated DNase which makes DNA fragments 180-200 bp in length and are known as DNA ladders.
Materials and Methods: For this purpose, HepG2 cells were cultured in RPMI 1640 Medium with 10% FBS and antibiotics at 37°C. Then MTT assay was performed to determine the cell viability and the appropriate concentrations of the specific hsa-miR-4270 inhibitor for DNA laddering assay. Finally, DNA was extracted from hsa-miR-4270 inhibitor at concentrations 20, 40 and 80 nM and were electrophoresis onto the agarose gel to investigate DNA laddering and apoptosis.
Results: The results showed treatment of HepG2 cells with the hsa-miR-4270 inhibitor at 40 and 80 nM concentrations induced laddering pattern of DNA and apoptosis compared to 20 nM of hsa-miR-4270 inhibitor and untreated HepG2 cells.
Conclusion: Inhibition of miR-4270 (known as an oncomiR) induced apoptosis in the HepG2 cell line and inhibited the growth of HepG2 cells.

Keywords: Liver cancer, Apoptosis, has-miR4270, HepG2 cell line, HCC

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Investigate the association of 2650000 and 6544714 polymorphisms in the *ABCG8* gene with high cholesterol

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Abstract

Backgrounds: Cholesterol is a lipid-like substance with the chemical structure of C22H45OH that is produced in our body and is also found in food becomes. There are different types of cholesterol inside the cell and in the bloodstream. Excessive increase in blood cholesterol causes various diseases, including hypercholesterolemia. Research shows that mutations in certain genes are associated with high cholesterol. One of these genes is the *ABCG8* gene, which is located on chromosome 2 and transports cholesterol to the bile. The aim of this study was to investigate the association of 2650000 and 6544714 polymorphisms in the *ABCG8* gene with high cholesterol.
Materials and Methods: We collected 90 peripheral blood samples and extracted the genomic DNA of each sample. Then, we generated and analyzed the gene using Tetra Arms PCR.
Results: 2650000 polymorphism genotypes include homozygous GG, TT and heterozygous GT genotypes. The T allele has been linked to high cholesterol. in the other hand, recessive GG genotype was observed in 17.5% of patients and 47.5% of healthy individuals, which indicates a higher percentage of this genotype in healthy individuals. Homozygous CC and GG genotypes and heterozygous GC genotypes were also observed in polymorphism 6544714. The predominant GG genotype was 5% in patients and 62.5% in healthy individuals. On the other hand, the recessive CC genotype was 42.5% in patients and 7.5% in controls. The P-Value for 2650,000 polymorphisms was less than 0.05 and equal to 0.01. This shows that there is a significant difference between the alleles of healthy and sick people. The value of P-Value for polymorphism 6544714 was also zero.
Conclusion: The predominant TT genotype related to polymorphism is 2650000 and the homozygous CC genotype related to polymorphism 6544714 is factors for increasing cholesterol in people with high cholesterol.

Keywords: High cholesterol, *ABCG8* gene, Polymorphism, rs 2650000, rs 6544714

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In Silico analysis identification of long noncoding RNAs associated with genes involved in response to trastuzumab antibody treatment in gastric cancer cells using microarray data

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Abstract

Backgrounds: Gastric cancer, the fourth most common cancer worldwide and the second leading cause of cancer death was known as a heterogeneous, multifactorial, highly malignant type of cancer. Long noncoding RNA (LncRNA) is functional RNA, longer than 200 nucleotides without the potential for coding protein. Like protein-coding genes, lncRNAs are regulated by transcription factors and other regulators. Therefore, by discovering LncRNAs associated with genes involved in the therapeutic response to trastuzumab, further experiments can be performed to identify pathways that lead to drug resistance, especially trastuzumab, as possible goals of inhibiting relapse.

Materials and Methods: Using the GEO database and analyzing the expression profiles of genes of gastric cancer patients (cells N87-TR1, N87-TR2, N87-TR3, N87-TR4, NCI-N87) who received trastuzumab (Datasets GSE77346 and Illumina HumanHT platform), genes were examined. Then, five more significantly different genes were identified and LncRNAs associated with genes involved in the therapeutic response to trastuzumab were identified through the LncRNA2Target v2.0 database.

Results: Based on the analysis of GEO2R software and using LncRNA2Target v2.0 database, five LncRNAs were identified that were associated with genes involved in the therapeutic response to trastuzumab, including: (KLK6 = HOXC-AS3, TACSTD2 = NBAT1, KRT19 = NBAT1, ADGRG1 = ACOO7128.1, MSLN = HOXC-AS3).

Conclusion: Considering the identification of two common LncRNAs between 4 different genes, it can be said that NBAT1 and HOXC-AS3 are two of the main LncRNAs when treated with trastuzumab for therapeutic response in patients with GC. Therefore, with further testing, the identified LncRNAs, including ACOO7128.1 and especially HOXC-AS3, NBAT1, can be mentioned as possible targets for inhibiting GC recurrence.

Keywords: Long noncoding RNAs, Gastric cancer, Trastuzumab antibody

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Effects of cytotoxic concentrations of ibuprofen on *BAX*, *BCL2* gene expression in cervical cancer cells (HELA)

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Abstract

Backgrounds: In recent years, the number of patients suffering from cervical cancer is increasing and many studies have shown that non-steroidal drugs can be effective on apoptotic genes active in cervical cancer. Conventional methods in investigating the causes of cervical cancer are insufficient. The aim of this study was to investigate the effects of cytotoxic concentrations of ibuprofen on *BAX*, *BCL2* gene expression in HELA cervical cancer cells.
Materials and Methods: In this experimental study, ibuprofen was purchased and measured in vitro. Then, HELA cells were extracted from freezing medium and cultured in a completely sterile space. MTT tests were performed.
Results: The cytotoxic effects of ibuprofen on cervical cancer cells indicate that the cytotoxic concentration (2 mg / ml) of ibuprofen significantly increases the expression level of BAX and anti-apoptotic *BCL-2* genes.
Conclusion: The findings of this study showed that the concentration of IC50 ibuprofen induces apoptosis in cervical cancer cells.

Keywords: Cervical cancer, Ibuprofen, BCL2, BAX

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Evaluation of genetic variants of exon 7 of *SPATA6* gene in infertile men with acephalic spermatozoa syndrome

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Abstract

Backgrounds: Acephalic spermatozoa syndrome is one of the most severe forms of teratozoospermia. In this syndrome, the sperm's head is separated from the flagellum because there is a problem in head –tail junction. This condition was caused by a defect in the spermatogenesis stage in the testicle. It is an autosomal recessive type defect and probably has genetic implications in many cases. Furthermore, *SPATA 6* (Spermatogenesis Associated 6) produces a testis-specific protein that localized in the mature spermatozoa head-to-tail linkage site and plays a role in the attachment of the head-tail of the flagellum during spermatogenesis. In this study we investigated the variants of exon 7 of *SPATA6* gene in infertile men with acephalic spermatozoa syndrome.

Materials and Methods: In the present study, 4 infertile men with acephalic spermatozoa syndrome as a case group and 4 fertile men as a control group were recruited. DNA was extracted from peripheral blood and after designing primers, PCR reaction and sanger-sequencing were performed. The results of sequenced segments were analyzed by Finch TV and Blast.

Results: Sequencing results revealed no genetic variations in men with acephalic spermatozoa syndrome and controls.

Conclusion: Despite the fact that there is no relationship between the genetic variations of exon7 of *SPATA6* gene and acephalic spermatozoa syndrome (in present study), since *SPATA6* is necessary for head- tail junction, it seems for a closer look it should be suggested to examine other exons in this gene, splice sites and the promoter.

Keywords: Male infertility, *SPATA6* gene, Acephalic spermatozoa syndrome

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MMP-2 enriching protein-protein and functional interaction networks in neurogenesis and neural stem cells differentiation

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Abstract

Backgrounds: Matrix Metalloproteinase-2 (MMP-2) is a zinc-containing enzyme with an extensive feature involving components of the extracellular matrix, cell surface, various bioactive molecules, and signaling pathways. MMP2 is investigating essential roles in various signaling pathways and progress in neural stem cells.
Materials and Methods: According to the neurogenesis and neural stem cell differentiation network, this paper proposes a protein-protein interaction (PPI) extraction method. Our model does rely on bioinformatics tools.
Results: We use the PPI extraction models heavily to rely heavily on parsing results from natural language processing tools like R language. We evaluated our model based on seven PPI extraction Cdkn1a, Stat3, Ctsb, Lcn2, Ccl2, Fgf2, and mTOR in neural stem cells differentiation and Sparc, shh, Gsk3b, Sdc1, Angpt2, Angpt1 is high co-function in neurogenesis by MMP-2.
Conclusion: These studies show an essential role of MMP2 in neurogenesis and neural stem cells differentiation and confirm its importance in NPC activities crucial to brain development, growth, and recovery from injury.

Keywords: MMP-2, Signaling pathways, Protein-protein interaction, Differentiation, Neurogenesis

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Can Recombinant Cryptococcus neoformans HSP70 be a Candidate for Developing an ELISA Kit?

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Abstract

Backgrounds: Cryptococcus neoformans is an encapsulated fungal pathogen that causes life-threatening meningoencephalitis in immunocompromised patients. This yeast secretes several potent immunogenic proteins by secretory vesicular mechanisms, such as HSP70 chaperone. This study aimed to evaluate the immunogenicity of recombinant C. neoformans HSP70 for the development of a simple and sensitive method for the diagnosis of Cryptococcus infections.
Materials and Methods: The PCR-amplified HSP70 gene was cloned into a PET-28a (+) expression vector. The purified recombinant HSP70 (rHSP70) was evaluated by western blotting using an anti-His Tag-HRP antibody and then used for immunization of a rabbit. The serum of the immunized rabbit was tested against the whole lysate of C. neoformans in ELISA.
Results: The antibodies in the rabbit's serum recognized lysate of C. neoformans yeast. The highest antibody levels were achieved after the third booster injection.
Conclusion: Recognition of the HSP70 available in the whole cell lysate of C. neoformans by antibodies in serum of the rabbit immunized with rHsp70 showed that the purified recombinant protein presents the antigenic epitopes. Moreover, the results showed that rHSP70 efficiently induced a specific antibody response in the immunized rabbit with a high titer, indicating the desirable antigenicity and immunogenicity of the recombinant protein. The rHSP70 showed to be a reliable candidate for the designing and development of an ELISA kit for early detection of cryptococcosis, and to screen a large number of specimens.

Keywords: Cryptococcus neoformans, ELISA, Recombinant, immunogenicity, HSP70

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Molecular modeling of Wuhan SARS-CoV-2 RBD in complex with ferritin nanoparticle

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Abstract

Backgrounds: In regard to finding treatment strategies for managing the SARS-CoV-2 outbreak, nanoparticle vaccines are currently the most effective vaccines against this virus. Ferritin-based vaccines such as ferritin-RBD vaccines in SARS-CoV-2 cause not only a stable antibody response but also a long-term response. However, the atomistic structural mechanism of this complex is not well understood. In this study, molecular modeling to build up the model of the SARS-CoV-2 RBD-ferritin nanoparticle complex was used, for the first time, aiming to improve the effectiveness of the current commercial vaccines.

Materials and Methods: The protein structures obtained from protein data bank (PDB id: 2fg8 and 7lo4. Molecular docking was performed using a haddock 2.4 server to dock ferritin and Receptor Binding Domain proteins together and biomolecular visualization of the complex was carried out by PyMOL.

Results: The complex structure of the RBD modeled (residues: 333-338, 358-365, 385-393, 516-532) with ferritin nanoparticle (residues: 595-613). Examination of the molecular docking outputs showed that among the energetic terms of the interactions, the driving force of this attachment is electrostatics. The most probable binding pose is through a loop in the ferritin units on the opposite side of the receptor binding motif site. The reliability of this model was confirmed by a very small RMSD value among previous docking results (0.3 Å).

Conclusion: The SARS-CoV-2 RBD - ferritin nanoparticle complex modeled and calculations showed that the electrostatic is the driving force of this interaction. This is the first atomistic model of ferritin-RBD nanoparticles reported.

Keywords: Nanoparticle, Ferritin, Molecular docking, SARS-CoV-2 RBD

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The Impact of Single-Nucleotide Polymorphisms rs852977 of *NR3C1* Gene on Depression in North of Iran

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Abstract

Backgrounds: Depression (major depressive disorder) is a common and serious medical illness that negatively affects how you feel the way you think and how you act. This disease is considered to be the most common psychiatric/psychological disorder and is characterized by complex and very diverse physical, mental and behavioral symptoms in individuals (especially in the adult and elderly age groups). The biological mechanisms involved in the relationship between immune system activation and depression can be influenced by the underlying genetic vulnerability. Various studies have shown increased levels of inflammatory cytokines and their receptors in the peripheral blood and cerebrospinal fluid (CFS) of patients with major depression.
Materials and Methods: In this study, we are investigating the effect of single nucleotide polymorphisms; rs852977 of *NR3C1* genes on the depression, we are sampling and genotyping 61 patients with depression using T-ARMS PCR with the statistically interpreting of results by MedCalc software.
Results: Disruption of the glucocorticoid signaling pathway leads to depression. Three SNPs of the *NR3C1* gene (rs258750, rs6188 and rs852977) showed significant relationships with the expression of a large number of genes that could be candidates for genetic modifiers of regulatory pathways associated with chronic fatigue. In this study, after receiving the statistical results, it will be investigated what effect the single nucleotide polymorphisms will have on depression.
Conclusion: *NR3C1* gene encodes the glucocorticoid receptor. Mutations in the *NR3C1* gene are associated with general glucocorticoid resistance. Intermittent splicing of this gene results in transcript variants that encode similar or different isoforms.

Keywords: *NR3C1*, Single nucleotide polymorphism, SNP, Depression, MDD, Glucocorticoid

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Autism and *FOXP2* gene involved

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Abstract

Backgrounds: A single genetic factor on 7q31 contributes to both autism and language disorders. FOXP2 regulates the transcription of genes into messenger RNAs, or mRNAs, the precursors of proteins — directing protein expression and repression during development. It is through these partner genes and their networks that FOXP2 may have its greatest impact on speech and autism.
Materials and Methods: We used different sites. We specifically selected autism and a gene and LNC and examined each case carefully and got all the necessary information about them and we obtained the association of the gene with the disease and SNP with the disease.
Results: As disease expression increases, LNCs show different expressions. If ΔG binding become zero or positive, it is in the interest of separation and the more negative it is in the interest of connection.
Conclusion: Autism has a strong genetic basis. *FOXP2* is contributes to autism and it has different SNPs. Autism has different LNCs that cause different diseases.

Keywords: SNP, LNC, Neurodevelopmental, Polyglutamine, Expression

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Integrated analysis of gene expression profiles of T-lymphocytes in human T cell leukemia virus type 1 (HTLV-1) associated disease: A bioinformatics analysis

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Abstract

Backgrounds: Human T-lymphotropic virus type 1 (HTLV-1) is the cause of adult T-cell leukemia-lymphomas (ATL) and HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP). The goal of present study was to investigating the gene expression analysis of gene expression pattern for ATL HAM/TSP.

Materials and Methods: Microarray gene expression profiling of T lymphocytes from HTLV-1 associated disease and healthy control were obtained from Gene Expression. Bioinformatics tools (GEO accession: GSE19080) were performed to identify differentially expressed genes (DEGs). Among the generated DEGs, we constructed protein-protein interaction (PPI) of HAM/TSM and ATL in comparison to asymptomatic carriers (ACs). Subsequently, gene ontology and PPI analysis were performed. Topological properties of each PPI were measured using Network-Analyzer, a network analysis plug-in of Cytoscape, to identify the most important functional hub genes within the networks.

Results: We found that the majority of DEGs in ATL and HAM/TSP were importantly implicated in immune response categories. The nodes and edges number of normal-AC, AC-ATL and ATL-HAM/TSP PPIs were 168 and 145, 116 and 97, and 275 and 327, respectively. Based on the topological analysis of protein-protein interaction networks, APP (Amyloid Beta Precursor Protein) was detected as the critical player of HTLV-1 disease progression. The expression of APP had a significant negative correlation in ATL (down-regulated) and HAM/TSP (up-regulated) samples. PTK2, PIK3R1, COPS5, CALM1 and HLA-B associated with disease progression.

Conclusion: Dysregulation of immune response associated transcripts play a critical role in HTLV-1 disease progression. Immune response associated genes may be biomarker for prognosis in cancer development and therapeutic targets.

Keywords: HTLV-1, ATL, HTLV-1-associated myelopathy/tropical spastic paraparesis, Gene expression

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Regulatory T lymphocytes, the pivotal role in inhibiting GVHD

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Abstract

Backgrounds: In many patients with blood malignancies and bone marrow failure, allogeneic hematopoietic stem cell transplantation is the only chance for treatment. One of the major problems with stem cell transplantation is the absence or lack of a donor with full compatibility, which in turn causes GVHD. GVHD is a serious and potentially life-threatening condition in which transplanted stem cells attack the recipient's healthy cells, causing numerous problems and, in acute cases, death. Regulatory T cells play a key role in inhibiting immune and inflammatory responses, which due to their suppressive properties; these cells can be used in various malignancies.

Materials and Methods: In this study, cord blood regulatory T cells were used. The cell suspension contains human regulatory T cells and is used as an allogeneic with viability equal to or greater than 70%. Microbial and viral tests, HLA, colony assay and flow cytometry are performed on samples that meet the minimum standard requirements, and finally stored at -196 ° C in storage tanks and used as needed.

Results: In order to summarize and describe the study data, descriptive statistics were used for quantitative consequences. Safety and efficacy assessments will be performed within 180 days from the patient's admission to the end of the final follow-up.

Conclusion: This cell product increased the strength of the immune system and reduced the symptoms of GVHD in cell recipient patients.

Keywords: Stem cells, GVHD, Regulatory T cells, Blood malignancies, Inflammatory responses

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Study of injury and involvement related to lung squamous cell and adenocarcinoma caused by miRNA-486 in children with Duchenne muscular dystrophy

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Abstract

Backgrounds: Duchenne muscular dystrophy is caused by mutations in the X-linked dystrophin gene with a prevalence of 17.7 per 100,000 boy births. Neuromuscular disorders encompass a heterogeneous group of conditions that impair the function of muscles, motor neurons, peripheral nerves and neuromuscular junctions. MicroRNAs are the well-studied members of the ncRNAs family. Several reports have highlighted their crucial roles in the post-transcriptional manipulation of several signaling pathways in different pathological conditions. miR-486 has central roles in several types oncological and non-oncological conditions such as lung, liver, breast cancers, autism and..., respectively. Cancer comprises a highly heterogeneous and complex set of diseases associated with a variety of genetic and epigenetic aberrations. Nearly 50% of primary lung carcinoma patients present with distant metastasis at their first visit.

Materials and Methods: In this study, Raw data associated to miRNA-486 were extracted from databases TCGA, UALCAN, Fun-Rich and GEPIA. Then it was analyzed and evaluated with bioinformatics techniques and software such as cytoNCA, MCODE and SPSS26.

Results: Inhibition of microRNA-486 in Duchenne children causes LUSC and LUAD due to similar inhibition. According to this study, the expression level of this microRNA in LUSC and LUAD is 77.3 Read per million (Normal = 893.3) and 81.8 (Normal = 676.5), respectively. The P(-value) of patient survival in the graph is equal to 0.65 and 0.53, respectively.

Conclusion: Bioinformatics analysis shows the importance of this inhibition in children's Duchenne. Genetic testing in Duchenne indicates early risk of lung cancer, and early preventive measures are taken. It will greatly help the patient, family and medical staff increases the success rate of the struggle for survival in Duchenne children.

Keywords: Lung adenocarcinoma, Lung squamous cell carcinoma, miRNA-486, Duchenne Muscular Dystrophy, Bioinformatics

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Network-based Prediction of microRNAs targeting *RdRp* and *N* coronavirus-2 genes

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Abstract

Backgrounds: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for the 2019 Epidemic (COVID-19). Coronaviruses are relatively large enveloped, positive-sense, single-stranded RNA viruses. Experimental evidence suggests that microRNAs can mediate an intracellular defense mechanism against viral genome. Most biological processes are regulated by microRNAs, which have emerged as promising therapeutic candidates for several diseases. Due to the corona epidemic and high mortality, a new treatment strategy is essential. Here, we report the miRNAs of human genome that can target *RdRp* and *N* genes and suppresses their translation.
Materials and Methods: Sequences of *RdRp* and *N* genes were first obtained from the NCBI resources. Then, miRNAs were studied and predicted using online tools including miRBase, Targetscan, RNA22, Cytoscape, and Metascape.
Results: Regarding the scores and E-Values, it was concluded that hsa-miR-3691-3p, hsa-miR-8066 and hsa-miR-1307-3p have maximum tendency to target *RdRp*, *N* and 3'UTR of coronavirus genome, respectively.
Conclusion: Given the potential suppressive effect of these microRNAs, it may be useful to prevent virus replication by employing these molecules as therapy, whether by synthetic siRNAs or by increasing their expression in the body.
Further research on the identification of targeted microRNA against the SARS-COV-2 genome and understanding the importance of microRNA as a cellular defense mechanism against pathogenic coronavirus infections will be useful.

Keywords: *RdRp*, *N*, microRNA, SARS-COV-2, Coronavirus

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Clinical, radiological, and genomic characteristics of mitochondrial leukodystrophies in Iran

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Abstract

Backgrounds: Mitochondrial disorders are a group of genetic disorders with diverse clinical manifestations which arise mainly due to impairments of the mitochondrial respiratory chain. This study has been conducted due to the relative lack of sufficient cohort reports on a combination of clinical, genomic, and imaging data of childhood mitochondrial leukodystrophies.

Materials and Methods: A total number of 301 patients with a definite diagnosis of leukodystrophy or genetic leukoencephalopathy were enrolled in Myelin Disorders Clinic Registry (MDCR) system in the time period between 2016 and 2020. All relevant clinical information, neuroimaging, genomic data and their clinical follow-up notes were recorded. Brain imaging and molecular studies were performed; in 39 out of 301 cases (12.9%) a diagnosis of mitochondrial leukoencephalopathy was approved as the most common type of leukodystrophy or genetic leukoencephalopathy. WES was performed on 36 patients (92.30%), while the single-gene method (i.e., Sanger sequencing) was performed on 3 patients (7.7%).

Results: All 39 patients were homozygous for the causative variant/mutation. In total, 34 patients were diagnosed with previously reported mutations, while novel variants were detected in 5 cases. Herein, we also showed that the most common mutations were those that their affected genes were involved in the Complex I subunits (n = 14; 35.8%). Defects in Complex IV (e.g., SURF1 and APOPT1) and energy production were placed as the second and third groups affecting 23% and 12.8% of patients, respectively. For novel variants, *in silico* pathogenicity scores and conservational analysis was performed.

Conclusion: In three-dimensional structural models, we showed that the substitutions may change the protein stability or function. Conservational analysis showed that each novel variant changes the highly conserved region in putative genes. However, to arrive at a conclusive conclusion, doing functional analysis is suggested using animal models.

Keywords: Mitochondrial disorders, leukodystrophies, mutation

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Impact of oxidative stress SNPs on sperm DNA damage and male infertility

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Abstract

Backgrounds: We examined four single nucleotide polymorphisms in four antioxidant genes (*PON1, CAT, GPx1*, and *SOD2*) in 100 infertility cases and 100 controls from an Iranian population-based case-control study to confirm the assumption that polymorphisms in oxidative stress genes increase the risk of sperm DNA damage and idiopathic male infertility.
Materials and Methods: Restriction fragment length polymorphism and tetra-primer amplification refractory mutation system PCR were used to identify genotypes. Sperm DNA damage was assessed using the Sperm Chromatin Dispersion test (Halo Sperm), and the total antioxidant capacity of seminal fluid was determined using the FRAP assay.
Results: Our findings demonstrated that alleles Arg-PON1 (rs662) and Ala-MnSOD (rs4880) variant genotypes were considerably linked with a higher risk of male infertility.
Conclusion: Linear regression analysis revealed that those with the *PON1* Gln192Arg or *SOD2* Val16Ala variants have significantly higher levels of sperm DNA fragmentation and lower levels of the total antioxidant capacity in seminal fluid.

Keywords: Male infertility, Oxidative stress, Polymorphisms, DNA damage, Total antioxidant capacity

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In silico polyepitope vaccine design against SARS-COV-2 infection

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Abstract

Backgrounds: The COVID-19 pandemic caused by the SARS-COV-2 virus has unexpectedly affected global health and it is accelerated mortality rates since SARS-COV-2 outbreak in December 2019 in Wuhan, China. In this pandemic situation, an immunoinformatics approach could be a fast and reliable option for quicker vaccine development. This study aimed to predict the protective epitopes with *In silico* tools for vaccine development against SARS-COV-2 virus.
Materials and Methods: The liner B-cell epitopes, cytotoxic T lymphocytes (CTL) and helper T lymphocytes (HTL) epitopes from Membrane, Nucleoprotein, Spike, Envelope, non-structural protein 13 and papain-like protease of SARS-COV-2 were predicted. The epitopes were analyzed and selected for their immunogenicity, antigenicity scores, allergenicity and toxicity correspondence to their ability to trigger immune response. After molecular docking, the vaccine candidate was constructed by fusing best epitopes by linkers.
Results: The constructed vaccine sequence was found to be a good vaccine candidate with proper stability and antigenicity, non- allergenicity and non-toxicity to human body. Molecular docking showed a stable and high binding affinity of epitopes from M, N, S, E, nsp13 and PLpro proteins with human pathogenic toll-like receptors-3 (TLR3).
Conclusion: Altogether, our results indicated that the designed vaccine candidate not only proved effective in various computer-based immune response analysis but also showed good population coverage. So, the construct may be considered for clinical validation to fight against this global threat, Covid-19.

Keywords: *In silico*, Epitope prediction, SARS-Cov-2, Vaccine design

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Pathogenic analysis of R456C mutation in the *GATA6* gene in atrial septal defect (ASD)

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Abstract

Backgrounds: Atrial septal defect (ASD) is an autosomal disorder characterized by formation of a hole in the atrial septal, which may vary in size and severity. It accounts for 5-10% of all congenital heart defects (CHD). GATA6 is a member of the GATA transcription factor family, which is located on chromosome 18 and plays an important role in the development of the heart. Mutations in this gene are associated with several congenital heart defects including ASD.
Materials and Methods: In this study, we identified from the National Center for Biotechnology Information (NCBI) database the pathogenic mutation that altered a positively R group amino acid, Arginine, at position 456, to a polar uncharged R group amino acid, Cysteine. This missense mutation is located in the DNA binding region of GATA6 protein.
Results: Our results showed that R456C mutation is probably damaging with a score of 1.000 at Polymorphism Phenotyping (PolyPhen) database and a score of -7.733 at Provean database, which is predicted to be deleterious. Also at Sorting Intolerant From Tolerant (SIFT) database, substitution at position 456 from R to C is predicted to affect protein function with a score of 0.00.
Conclusion: According to the results of this study, the R456C mutation altered the function of corresponding protein and predicted that it could possibly be damaging. However, further investigations are necessary to clarify this.

Keywords: ASD, GATA6, Mutation, R456C, Database

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In silico design and evaluation of signal peptide for secretory expression of interferon a2b in *E. coli*

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Abstract

Backgrounds: Interferons are a group of signaling glycoproteins that belong to a large group of cytokines and are a group of proteins that are released from virus-infected host cells. Most of the recombinant proteins are produced in *E. coli*; it has many advantages in the production of heterologous recombinant proteins. The inability of proteins to fold rapidly to form natural structures turns them into insoluble substances called inclusion bodies or inactive proteins. One approach to solve this problem is to transfer heterologous proteins to the periplasmic space of bacterial hosts using a suitable signal peptide at the N-terminal end of the protein. Expression in the periplasmic space creates an excellent space for proper bonding and twisting. Protein impurities and protease activity in the periplasm are less than in the cytoplasm. This study is based on structural understanding and finding the appropriate signal peptide for the secretory expression of interferon a2b in *E. coli*.

Materials and Methods: For this purpose, the amino acid sequence of 61 signal peptides was obtained using bioinformatics software and then their physicochemical properties and intracellular location were predicted by in silico methods and inappropriate signal peptides were removed. The selected signal peptides for the high levels of secretory expression in the *E. coli* host were compared and measured.

Results: Based on the analysis and research, most of the signal peptides associated with interferon a2b are in the space around the periplasm. Interferon a2b was insoluble in fusion with most signal peptides.

Conclusion: Base on results, sfm C, flgL, ompC are signal peptides showed the highest score and found as most suitable signal peptides for periplasmic expression of IFN-a2b.

Keywords: Interferon a2b, Signal peptide, Secretory production, *E. coli*, *in silico*

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Bachelor's thesis in plant orientation biology coronavirus

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Abstract

Backgrounds: This study aimed to provide a general overview of corona virus, such as history, origin structure, reproduction rate, genetic analysis, signs, transmission routes prevention and treatment.
Materials and Methods: This study is done by using reliable and international scientific resources and information from new researches.
Results: In the virus disease quarantine is not enough to prevent the spread of COVID-19 and the global impact of this viral infection on the economy is one of the main concerns drugs such as remedicivir favipiravir flopinavir retionavir etc. have a wide effect on this disease. In addition to therapeutic cell methods treatment with plasma and available medicines some countries are making vaccines for the corona virus that has been able to receive the WHO approval and these vaccines are administered in different doses between doses of 2 and 3 doses, although these vaccines do not cause certain safety against the corona virus it prevents the sick from becoming hospitalized and prevents them from being hospitalized.
Conclusion: Corona virus is a challenging disease in today world that can be easily infected at public places therefore it is valuable to prepare individuals to cope with the infectious disease and to control and control the severe disease caused by corona virus in places where the disease is suspicious or certain.

Keywords: SARS_COV_2, Genetic evolution, Transmission, Prevention, Treatment

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Non-invasive screening of G370C, S249C and R248C mutations of *FGFR3* gene in urinary epithelial cells in patients with bladder cancer

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Abstract

Backgrounds: Bladder cancer is a heterogeneous disease. The mutation in human *RAS, TERT, FGFR3,* and *PIK3CA* genes have been proposed as potential molecular biomarkers in the bladder tumor, that the active mutations of *FGFR3* are characterized by non-muscle invasive bladder cancer.

Materials and Methods: In this study, heterozygosity rate, allelic frequency, and the presence of G370C, S249C, and R248C mutations in the FGFR3 gene region were examined by using the ARMS–PCR method. After genotyping G370C, S249C, and R248C mutations in 100 healthy individuals and 100 patients with bladder cancer, the data were analyzed using MedCalc statistical software and SPSS.

Results: According to analysis of results, the frequencies of CC, TC, and TT genotypes for the S249C mutation in the patient's group were 72%, 25%, and 3%, respectively, and in the control, group were 99% and 1% for CC, and TC genotypes. The TT genotype was not found in any healthy individual. The results showed a significant difference in the genotype frequency of TC between the patient and control groups ($p<0.0001$). Interestingly, individuals with TC genotype were estimated to be more susceptible to bladder cancer (p-value = 0.00002, Fisher's exact test), the odds ratio was 2.18 (controls versus bladder cancer patients) with 95% CI: 1.247-4.584. The mutations of G370C and R248C were not observed in any of the samples. S249C mutation probably plays a vital role in causing bladder cancer.

Conclusion: Altogether, the results suggested that FGFR3 mutations could be considered as a risk factor in the prevalence of bladder cancer in the Iranian population.

Keywords: Bladder cancer, *FGFR3* Gene, Mutation, Biomarker, S249C

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The expression profiles and prognostic values of Annexin family genes in breast cancer

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Abstract

Backgrounds: Breast cancer is one of the most common malignant tumors in women. Annexins are calcium-binding proteins and play an important role in different tumor cells. However, the role of the Annexin family in breast cancer remains unclear.
Materials and Methods: We obtained the data of differential expression and survival time of ANXA genes in BC from an online open-access database including UALCAN, GEPIA, Cancer Genome Atlas (TCGA) database, cBioPortal, Metascape, and STRING.
Results: The transcriptional levels of ANXA1, ANXA2, ANXA3, ANXA5, ANXA6, ANXA8 and ANXA11 were significantly reduced in breast tumor tissues, while the transcriptional levels of ANXA9 were significantly increased**.** High mRNA levels of ANXA2, -3, -5, -8 and -13 predicted a decrease in overall survival (OS). CCL7 and CCL8 were associated with decreased relapse free survival. Expression of ANXA1, -2, -3, -4, -5 and -8 was highest in TNBC. Finally, we analyzed the possible mechanisms of ANXAs in different subtypes of breast cancer through GO and KEGG analyses and the correlation between ANXAs and immune infiltration in the tumor microenvironment.
Conclusion: Taken together, our results indicate that Annexins might play important roles in BC and have the potential to be used as markers for subtype classification.

Keywords: Annexin, Breast cancer, Prognosis, Public databases

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A study of associations between DROSHA (rs10719), DICER (rs3742330), RAN (rs14035) and XPO5 (rs11077) polymorphic variants and recurrent pregnancy loss in Southeast Iranian women

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Abstract

Backgrounds: DROSHA, DICER, RAN and XPO5 are factors which involved in microRNA biogenesis and have a potential physiological role in placental development. Genetic polymorphisms in these genes may affect the reproductive-related molecular pathways, thereby predisposing pregnant women to recurrent pregnancy loss (RPL). The aim was to investigate four single nucleotide polymorphisms (SNPs) of DROSHA (rs10719), DICER (rs3742330), RAN (rs14035) and XPO5 (rs11077) genes in southeast Iranian women with RPL.

Materials and Methods: In this study, we recruited 100 proven RPL women (mean age 32.27 ± 4.43 years) and 100 control women (mean age 31.68 ± 5.23 years) with normal pregnancy history from southeast Iranian population. Genomic DNA from whole blood was extracted and the polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) technique was used for the selected polymorphisms.

Results: A significant difference was found in the C-allele and CC genotype frequency of DROSHA rs10719 polymorphism in RPL group compared to healthy subjects (p-value<0.05 before and after adjustment). Multinomial regression analysis showed that an association of rs10719 with risk of RPL in the recessive model after adjustment (p-value = 0.009). Regarding the RAN rs14035 polymorphism, the prevalence of T-allele compared to C-allele was significantly different between two groups (p-value<0.001 before and after adjustment). As well, the CT and TT genotypes of rs14035 were associated with RPL. The genetic polymorphisms of DICER rs374233 and XPO5 rs11077 reflected no association with RPL.

Conclusion: The results of this study revealed that the DROSHA rs10719 and RAN rs14035 gene polymorphisms might serve as predisposing factor for RPL in Iranian women.

Keywords: Recurrent abortion, DROSHA, DICER, RAN, XPO5

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Gene expression analysis of Parvovirus B19 in primary and continuous cell lines

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Abstract

Backgrounds: Parvovirus B19 is a widespread pathogenic virus that only causes infection in humans. The virus can complete and multiply its lytic cycle when it infects its host cells. The main host of the virus is erythroid progenitor cells in the human bone marrow. Studies have shown that the virus has the ability to enter some cells but cannot multiply in them. In this study, expression of non-structural (*NS1*) and capsid (*VP1* and *VP2*) viral genes in different cell lines were evaluated.
Materials and Methods: Gene expression analysis was performed in several primary (mesenchymal stem cells and cord blood cells) and continuous cell lines (HEK-293, MCF-7, K562). Total RNA from the cells was extracted, cDNA synthesized and reverse transcription PCR was performed using Corbett PCR machine by specific primer designed against *NS1*, *VP1* and *VP2* genes.
Results: The results demonstrate high expression of *NS1* gene in selected continuous cell lines. Also, detectable expression of *NS1* gene was observed in selected primary cells. On the other hand, *VP1* and *VP2* were not expressed in any of the studied cell lines.
Conclusion: Expression of viral genes in several cells indicates strong infective capability of B19 virus. Especially in cord blood cells, it shows that the virus can infect fetal cells either during pregnancy or immediately after birth. Also, presence of viral gene expression in mesenchymal stem cells can be a remarkable subject which should be considered in safety of stem cell products.

Keywords: Parvovirus B19، NS1،VP1، VP2, Cell lines

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The synergistic cytotoxic and apoptotic effect of resveratrol and Naringenin on Y79 retinoblastoma cell line

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Abstract

Backgrounds: Resveratrol is a phenolic natural product which is found in red grapes also in Japanese knotweed root (Polygonum cuspidatum). Naringenin is one of the flavonoid compounds found in landing grape and other citrus fruits. Both agents exert antioxidant and anti-inflammatory properties. In this study, we investigated the effect of Resveratrol and Naringenin in an in vitro model of retinoblastoma of the eye.

Materials and Methods: XTT and Trypan blue assays used to evaluate the anti-proliferative/cytotixic effect of resveratrol and naringenin in Y79 cells. By the aid of AnnexinV/PI flow cytometry the kind of cell death investigated. To access important gene expression level at mRNA level, involve in apoptosis, Real-time PCR utilized.

Results: Naringenin and resveratrol significantly decreased proliferation and stimulated cell death (mostly apoptosis) in Y79 cells at 50 and 100 (µg/ml) after 24 and 48 hours. More cytotoxic effect observed after 48 hours. Furthermore, expression level of Bax and Bcl2 mRNAs altered significantly in all samples treated with 50 (µg/ml) of naringenin, resveratrol, or simultaneously with both. P21 mRNAs expression altered in all mentioned samples except those treated with 50 (µg/ml) of resveratrol.

Conclusion: Based on the results, it can be concluded that resveratrol and naringenin can decrease cell viability in retinoblastoma cells in an in vitro dose/time-dependent manner. Albeit more studies needed to shed the light on the mechanism of action, our data reveals a potential synergistic cytotoxic effect of naringenin and resveratrol on Y79 cells in 48 hours.

Keywords: Resveratrol, Naringenin, Retinoblastoma, Synergism, Cytotoxic, Y79 cell line

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In silico Molecular docking of lead nitrate interaction with replication compounds of *E. coli*

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Abstract

Backgrounds: According to studies, Lead is a major used extensively in industry. Native lead is rare in nature. Currently lead is usually found in with nitrate or others salt lead no fundamental function in the human body. Most heavy metals can be soluble in water and this is a big threat. Lead nitrate is toxic to human and it has large impact on protein metabolism and the genetic system. *Escherichia coli* is a Gram-negative, facultative anaerobic bacterium. DNA replication is a biological phenomenon. It requires a complex of enzymes and proteins to occur. Bacterial replication enzymes have vital functions, disruption of each of which can cause serious damage to the bacterial genome.

Materials and Methods: At the first the amino acid sequences of some of replication enzymes and proteins are obtained from National Center for Biotechnology Information (NCBI) Protein Database. The lead Nitrate molecular formula is provided from PubChem and the crystal structure containing the lead heavy metal was designed by chemical engineering software then so as to carry out energy minimization, it transferred into Hyperchem software. In order to investigate the mode of the lead with enzyme active site docking study was performed by Molegro Virtual Docking software.

Results: Docking data revealed the hydrogen bond and hydrophobic interactions were involved in the lead-receptor interactions.

Conclusion: Our results revealed the possible attachment sites of lead ions and their interactions with domains that have metal bonding properties.

Keywords: Heavy metal, Simulations, Molecular dynamics, Docking, Lead

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A functional evidence for *ATF7IP* association with human intellectual disabilities

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Abstract

Backgrounds: Intellectual disability (ID) is considered a multifactorial disorder with a high prevalence that compels considerable burdens on societies. A genome-wide association study (GWAS) on Iranian ID families reported an association of a novel genetic mutation in the *ATF7IP* gene. Although this demonstration has diagnostic importance, its functional role needs to be scrutinized. *Drosophila melanogaster* is a unique and well-known model organism to perform such functional investigations as its tiny brain resembles a high level of neurogenetics and neurofunctional identities to the human brain.

Materials and Methods: The Gal4/UAS system is a highly applicable tool in *Drosophila* genetics that offers over-expression and/or silencing of a particular gene in a time- and tissue-specific manner. Therefore, the RNAi approach was employed to knock down the *wde* gene, fly ortholog to *ATF7IP*, in flies' brain. Following confirmation of *wde* down-regulation, its pathologic effects on the structure and function of neurons were assessed by brain microscopy and validated behavioural assays including olfactory conditioning, and courtship conditioning learning and memories.

Results: Based on huge functional similarities between the selected *ATF7IP* gene and its orthologs in *Drosophila melanogaster*, down-regulation of the *wde* gene led to neuronal dysfunction and induction of some sort of ID-like symptoms in flies.

Conclusion: Since the transgenic Drosophila with brain-specific down-regulation for the selected gene display abnormalities in neuronal structure and functions, and memory performance then it can be considered as evidence for the statement on the association of observed genetic alterations and familial ID in the Iranian population.

Keywords: Intellectual disability, *ATF7IP* gene, Functional assay, *Drosophila melanogaster*, *wde* gene

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Study of Silibinin effect on *PTEN* in human breast cancer cell line

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Abstract

Backgrounds: Breast cancer is the most commonly diagnosed cancer amongst women worldwide. Amongst several naturally-occurring flavonoids, silymarin drawn out from milk thistle plant (scientifically named *Silybum marianum*) has positively contributed to treatment cancer. The *PTEN* gene acts as a tumor suppressor found in almost every tissue of the body. Loss or alteration of *PTEN* gene/protein level is often observed in various human cancers. This study aims to evaluate the cytotoxicity of silibinin on *PTEN* gene in T47D cell line.

Materials and Methods: T47D (human epithelial breast cancer) cell line was purchased from National Cell Bank, Tehran, Iran. T47D was cultured in DMEM/F12 media and treated with different concentrations of silibinin (50-250 µg/mL) for 24, 48 and 72 hours. The cytotoxic effect of silibinin on T47D viability was determined using Methyl-Thiazolyl-Tetrazolium (MTT) assay by IC50 determination. To assess the alterations of *PTEN* transcriptions, the real-time PCR reactions were performed using the Power SYBR-Green PCR Master Mix according to the manufacturer's protocol. The relative gene expression levels were calculated using the $2^{-\Delta\Delta CT}$ method.

Results: The IC50 values for silibinin in T47D Cell Line at 48 hours were obtained 144.6 µg/mL. To extracted cell total RNA, T47D was seeded and incubated with IC50 concentration of SB for 48h.

Conclusion: mRNA expression levels demonstrate that SB significantly increased *PTEN* expression in T47D cell line, as compared to control groups.

Keywords: Breast cancer, T47D, Silibinin, *PTEN*, RT-PCR

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GJB2 Polymorphism rs7329857 is associated with autosomal recessive non-syndromic hearing loss in Iranian population

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Abstract

Backgrounds: Hearing loss is one of the common disorders. This study aimed to determine the relationship between single nucleotide changes of rs7329857 *GJB2* gene and rs7333214 *GJB6* gene in patients' non-syndromic sensorineural deafness with autosomal recessive inheritance.
Materials and Methods: 32 whole blood samples with EDTA from Iranian patients and 32 actual blood samples from healthy people were prepared. It examined the presence/absence of band results from the reaction. Bands reported by Tetra-Arms-PCR method.
Results: Studies performed on 32 deaf patient samples and 32 control samples for the *GJB2* gene with rs7329857 report that in the control sample, the percentage of healthy allele frequency CC was 84.4%, and the mutant allele frequency percentage TT and CT was15.6% and 0.0%, respectively. In the patient sample, the percentage of healthy allele frequency CC was 68.7%, and the ratio of mutant allele frequency TT, CT, and P-Value was 31.3%, 0.0%, and 0.0400, respectively. It was statistically significant. The healthy allele frequency of GG was 78.1%, mutant allele frequency of TT and GT was 0.0% and 21.9%, respectively, for the *GJB6* gene with rs7333214 in the control sample. The healthy allele of GG was 65.6%, the mutant allele TT and GT rate was 9.4% and 25%, respectively, in the sample of patients. P-Value: 0.1005 reported, it was not statistically significant (0.05 P-Value> is substantial).
Conclusion: This study showed that rs7329857 (C/T) polymorphism in *GJB2* gene is an effective polymorphism in increasing the risk of ARNSHL; however, rs7333214 (G/T) in *GJB6* gene does not demonstrate a significant relationship with the incidence of ARNSHL in the Iranian deaf population.

Keywords: ARNSHL, GJB2, GJB6, Polymorphism

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Bioinformatics evaluation of targetom has- miR-513a-3p signaling pathways and related function of SOD1 in patients with amyotrophic lateral sclerosis

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Abstract

Backgrounds: Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disorder that targets motor neurons, leading to paralysis and death within a few years of disease onset. While several genes have been linked to the inheritable or familial form of ALS, some familial cases (FALS) are linked to mutations of superoxide dismutase 1 (SOD1), an antioxidant enzyme whose activity is preserved in most mutant forms.
Materials and Methods: For finding more bioinformatics information we used NCBI, miRbase, miRWALK2.0, Target scan, DAVID database and KEGG pathway.
Results: Mutant SOD1 promotes apoptosis. Considering that changes in SOD1 mRNA levels have been associated with sporadic ALS (SALS), a molecular understanding of the processes involved in the regulation of *SOD1* gene expression could not only unravel novel regulatory pathways that may govern cellular phenotypes and changes in diseases but also might reveal therapeutic targets and treatments. The latest *SOD1* gene expression study demonstrated that SOD1 mRNA level is elevated in specific nervous areas typically affected by ALS disease. Moreover, increased SOD1 mRNA expression has been detected in peripheral system as lymphocytes from SALS patients compared to healthy people.
Conclusion: In the present project, if according to bioinformatics predictions, the binding site of this microRNA is precisely SOD1 and negative regulatory function of microRNAs, the expression of has- miR-513a-3p is expected to decrease and consequently increase the expression of the target gene (SOD1), miR-513a-3p may be a tumor suppressor cancer. Has-miR-513a-3p expression is predicted to decrease, resulting in less binding to SOD1 mRNA and increasing SOD1 gene expression, leading to ALS.

Keywords: Amyotrophic lateral sclerosis, miRNA, miR-513a-3p, SOD1

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In-silico analysis of Site Direct Mutagenesis of Tyr102 to Arg in CDR3 of Anti-CD20 antibody

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Abstract

Backgrounds: Antibodies are the main proteins of the immune system to identify and eliminate the target pathogens of the infected organism that play an essential role in humoral immunity. This molecule has the potential to be used in both immunological diagnostics and immunotherapy. The most significant property of antibodies is their ability to recognize targets with high affinity and high specificity, which is mainly performed by CDRs. Monoclonal antibodies due to antigen-specific binding, were improved as a Research tool and diagnostic agent. In this study, monoclonal antibodies were prepared against leukemia cells and their activity was investigated against anti-CD20.

Materials and Methods: We prepared an anti-CD20 antibody by PDB server and the physicochemical analysis was performed using the protein structure prediction and Protein-ligand docking software (HADDOCK).

Results: In this study, we introduced a point mutation on "102" residue in the CDR3 domain of the antibody that Tyr, a non-polar hydrophilic AA, was converted to Arg, a polar hydrophilic AA. Our result showed that the number of binding residues in the antibody-antigen binding site was increased. HADDOCK Z-score was -1.5 into -1.4 for mutant and native, respectively. Also, electrostatics energy calculated by HADDOCK was decreased in the mutant compared to the native.

Conclusion: Base of our results, this mutation increased the solubility and specificity, therefore, improved the binding affinity. However, further investigation is essential to clarify this binding.

Keywords: Antibody, CD20, CDR3, Site direct mutagenesis

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Ki-67 marker and neurotrophic genes expression in metformin-treated mesenchymal stem cells in 48 hours

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Abstract

Backgrounds: Metformin is the foremost common prescribed drug for type 2 diabetes. There is increasing evidence that metformin can be used in a variety of therapeutic conditions due to its biological effects. The Ki-67 antigen is expressed in all proliferating cells (normal and tumor cells), so this marker is used to determine the rate of cell population growth. Neurotrophic factors are large polypeptides that contribute to development and survival of the central and peripheral nervous systems.

Materials and Methods: In this study bone marrow cells were isolated from the femora and tibia bones, after the third passage the extracted stem cells were cultured in a 96-well plate and treated with 1, 5, 10, 15, and 50 µM of metformin for 48 h. The proliferation rate of cells and genes expression was assessed by Ki-67 marker and RT-PCR method.

Results: The results of this study indicate that the proliferation rate in the 10 µM of metformin group showed a significant increase compared to control groups. Analysis of gene expression showed that the expression of BDNF and GDNF genes in 50 µM and NT3 in 10 µM had the highest expression.

Conclusion: Metformin may be suggested as a pre-therapist to strengthen mesenchymal stem cells before transplantation for the treatment of neurodegenerative diseases and seems an appropriate inducer factor to induce neurotrophic genes and can be used to treat neurodegenerative diseases like Alzheimer's.

Keywords: Ki-67 marker, Mesenchymal stem cells, Metformin, Neurotrophic genes

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In silico study of association of has-mir-5698 with COVID-19 severity in diabetics

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Abstract

Backgrounds: Coronavirus disease (COVID-19) is an infectious disease caused by the newly discovered coronavirus. Increased severity of COVID-19 has been observed in patients with diabetes mellitus. This study aims to identify common genes in a comparison between two pathways, diabetic cardiomyopathy and coronavirus disease, and find an important regulator. MicroRNA (miRNA) is a powerful regulator of gene expression. Almost all the proteins in the pathways are controlled by specific miRNAs.
Materials and Methods: In this study, I predicted by use of miRbase, miRWalk, NCBI, David, KEGG.
Results: In the study, 22 common genes with high-expression were found that are involved in diabetes and COVID-19. The expression of these genes is regulated by various factors, such as miRNAs. By using bioinformatics methods, I found has-mir-5698 targets 11 of 22 common genes: *mapk10, mapk11, mapk12, mapk13, mapk14, mapk8, nfkb1, pik3ca, pik3r1, pik3r2, pik3r3, prkcb*.
Conclusion: These 11 genes are involved in the pathway of coronavirus disease, in cytokine inflammation and the cytokine storm that cause disease severity. They are also involved in phagocytosis. On the other hand, the same genes are involved in the pathway of diabetes, in fibrosis, and in cytokine inflammation which predisposes diabetics to asthma and pulmonary fibrosis. Thus, high expression of these genes in diabetes paves the way for COVID-19 and cytokine storm. hsa-mir-5698 expression is expected to be low in the patients. It is suggested that the expression of these genes be reduced by increasing the expression of has-mir-5698 in diabetic patients infected with the coronavirus.

Keywords: Has-mir-5698, COVID-19, Diabetes, Inflammation, Fibrosis

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A case report of a man with Klinefelter Syndrome having healthy two Neonates with normal karyotype

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Abstract

Backgrounds: Klinefelter syndrome also known as 47, XXY is one of the most prevalent chromosomal abnormalities among men. Infertility could be named as one of the most primary features of this health condition. At the same time, there are some other associated aspects like thin and tall appearance, absent, delayed or incomplete puberty, small and firm testicles, small penis, and gynecomastia.
Materials and Methods: Blood sample from patient was tested by conventional G-banding Karyotype test. Separately, two different expert lab technicians analyzed and interpreted all the spreads, and finally, the abnormal result was recorded.
Results: This study reports a mosaic Klinefelter patient whose karyotype consisted of 47, XXY/46, XY. The only complaint of this couple was two miscarriages, followed by a boy with a normal karyotype who was born who had only taller than the average at the age of two and normal girl.
Conclusion: Being mosaic KS dramatically increases the chances of having healthy offspring with normal genetic patterns compared to males who had complete KS, and these people can hope to have healthy children without performing artificial insemination methods such as IVF.

Keywords: Klinefelter syndrome, Chromosomal abnormality, Recurrent abortion

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The Affinity optimization of Anti-CD20 antibody with site-directed mutagenesis of Tyr107 to Arg107 in CDR3 region

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Abstract

Backgrounds: Antibodies are glycoproteins that bind specifically to their antigen with high affinity and cause the destruction of cancer cells and therefore have many applications in therapy. High expression of CD20 in leukemia and lymphomas and having extracellular epitopes detected with different antibodies make these proteins a suitable target for immunotherapy with monoclonal antibodies. The aim of this study was to target mutagenesis in CDR3 of Anti-CD20 antibody to produce optimal antibody in the diagnosis and treatment of leukemia.

Materials and Methods: Tyr 107 in the antibody was mutated to Arg using PyMOL software. Then, the native and the mutant antibody were docked to CD20 using HADDOCK server. Binding residues had been analyzed by PyMOL. Docking tools were used to investigate the tendency of the complex antibody-CD20 to bond better.

Results: Haddock Z-score were -77.6 and -77.8 for the native and mutant, respectively. Electrostatic energy for the complex of antibody-CD20 was -105.5 in the mutant compared to -234.2 for the native.

Conclusion: We can conclude that mutation of a nonpolar amino acid to a polar and charged One, improved the interaction of antibody to the CD20 antigen. So, it is worth to further investigate the application of this engineered antibody in the treatment and diagnosis of cancer.

Keywords: Antibody optimization, CDR3, Docking, Site-directed mutation

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Construction and affinity enhancement of a new anti-CD20 single-chain variable antibody fragment

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Abstract

Backgrounds: The B-lymphocyte antigen CD20 exists on the surface of normal and most malignant B-cells. CD20 is responsible for the regulation of calcium influx, and is able to start intracellular signaling pathways. The technology of monoclonal antibody (mAb) led to an effective targeted therapy for a variety of diseases like autoimmune diseases and cancer. Anti-CD20 mAbs could be applied in the treatment of various diseases. Rituximab combined with chemotherapy has revolutionized the treatment of $CD20^+$ B-cell non-Hodgkin lymphomas, but patients often relapse. Despite the recent advances in development of anti-CD20 mAbs, challenges remain to develop novel antibodies with improved properties.

Materials and Methods: We have already proposed DNA-based immunization for the production of pharmacologically active anti-CD20 mAbs, with consequent development of D4 mAbs against the native extracellular domain of CD20 with new desirable characteristics. The major aim of the present study is to isolate genes encoding D4 variable domains to design a single-chain variable antibody fragment (scFv), in turn, allowing the conduct of studies on intermolecular interactions between CD20 epitopes and D4. Through a computational design approach, the sequence was first immune-annotated and used to construct a model of scFv structure. An accurate model of CD20 was then built and docked to the scFv. Extensive structural analyses were performed to identify appropriate substitution positions, followed by a comprehensive free energy-based mutation screening to enhance the scFv-CD20 interaction affinity.

Results: In epitope motif and binding orientation analyses, the antibody and the derived fragment showed the character of type II antibodies. Affinity enhancement screening identified the novel triple-mutant scFv variant, H: A64F/H: E108R/L: I37R, representing a more favorable antibody-antigen binding.

Conclusion: Altogether, the data reported here support future subsequent procedures to produce large quantity of recombinant D4 anti-CD20 antibodies, which can be utilized in therapy and diagnosis of malignancies.

Keywords: Affinity enhancement, CD20, Epitope, In silico design, Single-chain variable antibody fragment

Iranian Journal of Pediatric Hematology Oncology

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International Conference on Human Genetics and Genomics

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Bioinformatics study and evaluation of neurotoxin botulinum A optimized gene expression as a vaccine candidate

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Abstract

Backgrounds: Botulism is a deadly disease caused by neurotoxin, one of the seven types of Clostridium botulinum. Carboxyl part of the heavy chain neurotoxin Clostridium botulinum type A (BoNT/A-Hc) has immunogenic properties that can be used as a recombinant candidate vaccine against botulism. The aim of this study was to investigate the bioinformatics investigation and production of the recombinant neurotoxin-binding protein of BoNT /A.
Materials and Methods: Nucleotide and protein sequences according to *botA* gene were extracted from GeneBank and Uniprot databases. To increase the probability of protein expression, gene codons and various parameters affecting expression were optimized and thermodynamic analysis of mRNA structure was performed to evaluate the stability. The antigenicity of the binding domain and its physicochemical properties were investigated. The third protein structure was predicted, the quality of the predicted structures was evaluated, linear and spatial epitopes were determined.
Results: The Codon adaptation index (CAI) belonged to the natural gene WAS 0.28, while the optimized gene had the index 0.96. The percentage of highly prevalent codons in the gene was improved to 64. Thermodynamic analysis of the mRNA structure showed that the predicted structure is stable. The third structure predicted based on the RaptorX server showed good quality. Conformational and linear epitopes were seen in the protein.
Conclusion: The results showed that the protein obtained could be a suitable immunogenic against Clostridium betulonium serotype A.

Keywords: Neurotoxin botulinum A, Bioinformatics design, botA, Vaccine candidate

Iranian Journal of Pediatric Hematology Oncology

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Pathogenicity analysis of missense mutations in *MT-ND6*, a mitochondrial gene that encoded NADH dehydrogenase 6

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Abstract

Backgrounds: Mitochondrial DNA (mtDNA), the circular genomes of microorganisms derived from the early ancestors of modern eukaryotic cells. An mtDNA molecule could be a powerful tool for detection generations through the mother; therefore it is used to search for the ancestors of many species over hundreds of generations. The mitochondrial genome encodes 37 genes, including 13 genes encoding proteins. Many of these genes encode the transmission chain. Related diseases with MT-ND6, a mitochondrial genome that encodes NADH dehydrogenase 6, include Encephalopathy, Leber, Lactic Acidosis, and Stroke-Like Episodes.

Materials and Methods: We used the NCBI database to find missense and Pathogenic SNPs and then the physicochemical analysis was performed by protein structure prediction and annotation protein software.

Results: In this study, we found 639 missense mutations in MT-ND6 that 11 of 639 mutations were pathogenic. We explain the most important ones in the following.

1) In a first mutation converts a conserved Lue (60), a hydrophobic AA into Ser, a hydrophilic AA. Our result showed that this mutation alters hydrophobicity in substituted position by EXPASY resource portal score: (-0.511), PROVEAN score: (-5.99), SIFT score: (0.00), and the PolyPhen database score: (1.00) is deleterious and probably damaging.

2) Tyr (59), hydrophilic AA into Cys, a polar hydrophilic AA. EXPASY changing score is (0.422), PROVEAN score is (-8.85), SIFT score is (0.00) and PolyPhen with score (1.00) is deleterious and probably damaging.

Conclusion: Our results were predicted that it might conceivably be harmful, so MT-ND6 mutation was considered potentially pathologic. However, more investigations are essential.

Keywords: Mt-DNA, MT-ND6, Mitochondria, Mutation, Pathogen

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Potential biomarkers and signaling pathways associated with the pathogenesis of primary salivary gland carcinoma: A bioinformatics study

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Abstract

Backgrounds: Salivary gland carcinoma (SGC) is rare cancer, which constitutes 6% of neoplasms in the head and neck area. The most responsible genes and pathways involved in the pathology of this disorder have not been fully understood. We aimed to identify differentially expressed genes (DEGs), the most critical hub genes, transcription factors, signaling pathways, and biological processes (BPs) associated with the pathogenesis of primary SGC.

Materials and Methods: The mRNA dataset GSE153283 in the Gene Expression Omnibus database was re-analyzed for determining DEGs in cancer tissue of patients with primary SGC compared to the adjacent normal tissue (adjusted P-value < 0.001; |log2 Fold Change| > 1). A protein interaction map (PIM) was built, and the main modules within the network were identified and focused on the different pathways and BP analyses. The hub genes of PIM were discovered, and their associated gene regulatory network was built to determine the master regulators involved in the pathogenesis of primary SGC. Furthermore, the results were validated using another independent dataset.

Results: A total of 137 genes were found to be differentially expressed in primary SGC. The most significant pathways and BPs that were deregulated in the primary disease condition were associated with the cell cycle and fibroblast proliferation procedures. *TP53*, *EGF*, *FN1*, *NOTCH1*, *EZH2*, *COL1A1*, *SPP1*, *CDKN2A*, *WNT5A*, *PDGFRB*, *CCNB1*, and *H2AFX* were demonstrated to be the most critical genes linked with the primary SGC. *SPIB*, *FOXM1*, and *POLR2A* significantly regulated all the hub genes.

Conclusion: This study illustrated several hub genes and their master regulators that might be appropriate targets for the therapeutic aims of primary SGC.

Keywords: Biomarkers, Gene regulatory network, Pathogenesis, Protein-protein interaction network, Salivary gland carcinoma

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Social work and infertile women

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Abstract

Backgrounds: One of the helpful jobs is medical social work. This profession can help infertile women and their families reduce issues related to infertility shock, mental health problems, family pressures and social stigma.

Materials and Methods: The General Health Questionnaire (GHQ-30), the Beck Depression Inventory (BDI), and the Hospital Anxiety and Depression Scale (HADSA) are to be administered to a number of infertile women as they visit a fertility clinic.

Results: Women suffering from infertility are significantly higher in all criteria of psychological pathology outcomes. And probably the regression results of this study predict the socio-demographic variables of infertile women due to the effects of age, not having at least one child, physical illness and in some cases poor support from the husband, level of education and income depression and anxiety.

Conclusion: Infertility is not a new problem, but associated with the increasing number of infertile people and the complexity of their problems and the need for medical intervention. Thus, infertile women face psychological problems, family and social issues, and labels during their infertility. On the other hand, often have personality traits that experience higher levels of stress and anxiety than other people. Social workers can change their lifestyle to some extent by training them. Also, social medical workers, aware of the financial and economic problems of these people, can reduce infertile women by collecting grants. In general, social health care providers with a holistic view and training to work in medical settings can act as an essential element in reducing the personal, family and social problems of infertile women. So they can spend their treatment with more peace and comfort along with family support to have children.

Keywords: Infertile women, Medical social work, Mental health problems, Family problem, Social tag

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Suppressive effect of Gemini Curcumin on the expression of LncRNA CCAT2 AGS gastric cancer cells gastric cancer

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Abstract

Backgrounds: It has been shown that curcumin has effective anti-cancer properties. However, the absorption efficacy of curcumin is too low to have notable achievement in therapy. To overcome this problem, we employed Gemini Surfactant nanoparticles to improve the stability of curcumin, and then studied the metastatic effects of this compound on the AGS gastric cancer cell line.
Materials and Methods: Human gastric carcinoma AGS cell lines were treated with Gemini curcumin, and cell viability was assessed by MTT assay. The scratch test was performed to evaluate the metastasis of cancer cells. The expression of the noncoding RNA CCAT2 gene and its downstream c-MYC was evaluated by qPCR and western blotting.
Results: Gemini curcumin affected the cell viability of AGS cells in a dose- and time-dependent manner with IC50 values of 57.92 μM and 38.85 μM at 24 h and 48 h, respectively. Our data showed that Gemini curcumin nano compound down-regulates lnc-CCAT2 and c-MYC genes. Scratch test also confirmed its anti-metastatic properties on AGS cells.
Conclusion: Taken together, our results confirmed anticancer effect of Gemini curcumin on gastric cancer. However, further studies on molecular level are needed to demonstrate this finding.

Keywords: Gemini curcumin, c-MYC, LncRNA CCAT2, Gastric cancer, Scratch test

Iranian Journal of Pediatric Hematology Oncology

International Conference on Human Genetics and Genomic

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Association study rs3810688 of *NLGN4* gene with Autism spectrum in an Iranian population

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Abstract

Backgrounds: Autism is a heterogeneous and multifactorial disease that results from the interaction between genetic vulnerability and environmental factors. Mutations of the *NLGN4* gene define a new, relatively less complex genetic syndrome identified within families with ASD. The *NLGN4* gene is located on chromosome Xp22.33, in an X-specific region near the junction of the pseudo-autosomal region. The aim of current study is to detect the genetic association of *NLGN4* gene variant rs3810688 with occurrence of ASD in Iranian population.
Materials and Methods: Samples were obtained from 60 patients diagnosed with Autism and 60 controls subjects. Genomic DNA was extracted from whole-blood samples and genotyped by tri-primer amplification refractory mutation system PCR (Tri-ARMS-PCR). Finally, the statistical analysis was performed by MedCalc software.
Results: In rs3810688 polymorphism of *NLGN4* gene There is no difference allelic frequency in this polymorphism between cases and controls, but in GG genotype significantly increased the risk of Autism in comparison with the CC genotype in the co-dominant model (OR = 4.22, 95% CI 1.25-14.05; p = 0.019).
Conclusion: In conclusions rs3810688 of *NLGN4* gene is associated with occurrence of autism in an Iranian population.

Keywords: Autism, *NLGN4*, *AUTS2*, Polymorphism

Iranian Journal of Pediatric Hematology Oncology

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Evaluation of miR-200a expression pattern in the blood of non-small cell lung cancer patients compared with normal individuals

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Abstract

Backgrounds: MicroRNAs (miRNA) are part of small noncoding RNAs family and one miRNA may regulate many genes as its targets, while one gene may be targeted by many miRNAs. In NSCLC (non-small cell lung cancer), a significant number of abnormally expressed miRNAs have been discovered. MiR-200a may have an important connection with apoptosis and *XIAP* gene in NSCLC. However, the role of miR-200a in NSCLC is unknown.
Materials and Methods: Total 30 blood samples of new case NSCLC patients and 30 blood samples of normal individuals were acquired from the Dr. Masih Daneshvari Hospital. The plasma samples were separated from whole blood and RNAs were extracted. After the cDNAs synthesis of interest (miR-200a) and reference (miR-16) miRNAs, the quantitative PCR were performed to estimate the expression level.
Results: The results have shown an impressive change in miR-200a level in the plasma of NSCLC patients compared with normal individuals.
Conclusion: There is a significant correspondence between miR-200a expression pattern and NSCLC.

Keywords: miRNA, miR-200a, NSCLC, Quantitative PCR, Expression pattern

Iranian Journal of Pediatric Hematology Oncology

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Evaluation of the plasma levels of LncRNAs as biomarker for late-onset Alzheimer's disease

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Abstract

Backgrounds: Alzheimer's disease (AD) is a neurodegenerative disorder and one of the leading causes of death in old people across the world. Recent studies demonstrated that long noncoding RNAs (LncRNAs) play important roles in AD. These circulating LncRNAs are a novel promising biomarker in AD as they possess characteristics of stable. This project was aimed at investigating the diagnostic and prognostic value of long noncoding RNAs involved in AD pathogenesis.
Materials and Methods: Total RNA was isolated from plasma samples. The expression levels of 90 LncRNAs were estimated using the PCR arrays containing 90 LncRNAs and by real-time qRT-PCR. Then, by analyzing the preliminary results of profiling, the genes BC200, NDM29, NEAT1, FAS-AS1 and GAS5-AS1 were selected for further studies in all samples. In the next step, biomarker potency of each factor was analyzed by ROC Curve analysis. we further performed transcriptome analysis to identified expression patterns of LncRNAs in AD.
Results: We found that the NEAT1 and BC200 level in the plasma samples of the AD patients were significantly up-regulated compared with the control groups (P = 0.0021, P = 0.02, respectively). ROC curve analysis showed that NEAT1 with 72% sensitivity and 84% specificity and BC200 with 54% sensitivity and 92% specificity appropriately discriminated AD patients from healthy controls. In addition, negative correlation was between plasma LncRNA NEAT1and BC200 levels with age. 13down-regulated and 33 up-regulated LncRNAs were identified, compared with normal brain samples as a result of RNAseq.
Conclusion: This study elucidates the role of LncRNAs in the pathogenesis of AD and presents new LncRNAs that may be exploited as a promising biomarker for early diagnosis of AD.

Keywords: Alzheimer's disease, Long non-coding RNA, Biomarker, Early diagnosis, RNAseq

Iranian Journal of Pediatric Hematology Oncology

International Conference on Human Genetics and Genomic

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Bioinformatics' analysis of microRNA in angiogenesis pathway of breast cancer: biomarker role of microRNA

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Abstract

Backgrounds: Breast cancer is commonly invasive neoplasms in women. Various factors play a role in the development and promotion of breast cancer; most of them involve changes in the expression of certain genes, including those encoding noncoding RNAs. Recently, many studies have elucidated the key roles of microRNAs (miRNAs) in controlling gene expression during cancer development. MiRNAs are small subclass of ncRNAs with almost 19–24 nucleotides. Multigene regulatory features of these small RNA molecules allow them to change signaling pathways, facilitate or block signal transmission to downstream effectors in various ways. MiRNAs can regulate key signaling pathways positively or negatively, therefore they can affect tumorigenesis.

Materials and Methods: We used NCBI database to nominate a gene called "MMP9", which is highly expressed in breast cancer. We demonstrated that MMP9 is involved in the development of angiogenesis in cancers. By studying in miRTargetLink database we found that 6 miRNAs have strong interaction with MMP9 gene. We selected two of them (hsa-miR-491-5p and hsa-miR-29b-3p) for more investigations. Then, we used DIANA TOOLS database and drawing Heatmap by this database we found that selected miRNAs have high expression in PI3K/AKT signaling pathway and pathway in cancers.

Results: MMP9 gene has high expression and it has specific roles in pathway in cancer. Other analysis showed that our selected miRNAs have high expression in PI3K/AKT signaling pathway and pathway in cancer. So, these miRNAs can bind to our selected gene and change its expression and function that can make some changes in cancer.

Conclusion: We established that hsa-miR-491-5p and hsa-miR-29b-3p interaction with this gene can change important pathways in cancer and they can play significant roles so, they can be used as a functional biomarker and diagnosis in breast cancer.

Keywords: Breast cancer, microRNA, NCBI, miRTargetLink

Iranian Journal of Pediatric Hematology Oncology

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Unravelling the molecular mechanism of miR-128 in oligodendrocyte differentiation

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Abstract

Backgrounds: Neurodegenerative diseases are regarded a major threat to human health. They are incurable and debilitating conditions leading to progressive degeneration of neurons and their myelin sheaths. So unravelling cellular and molecular aspects of myelin synthesis pathways are basic importance in order to open new avenues for developing a cell-based therapy for demyelinating neurodegenerative disorders such as multiple sclerosis. Among different micor RNAs with potential or proved roles in oligodendrocyte differentiation, exact molecular mechanism of miR-184 is not yet well understood.

Materials and Methods: We performed RT-PCT and western blotting to measure expression level of mir-184 in neural progenitors (NPs). Also, luciferase assay was performed to explore mir-184 effects on genes involved in neural and astrocyte differentiation such as SOX1 and BCL2L1. Moreover, we assessed oligodendrocyte differentiation after blocking mir-184.

Results: We observed that overexpression of miR-184 in NPs can induce differentiation of oligodendrocyte progenitors. Assessing the related genes involved in this pathway using the above mentioned techniques, revealed that several crucial developmental genes are likely affected by miR-184 and this miR directly represses positive regulators of neural and astrocyte differentiation, i.e., SOX1 and BCL2L1, respectively. Moreover, blocking miR-184 diminished the number of committed cells to an oligodendrocyte lineage.

Conclusion: We assessed the function of miR-184 and observed that it could induce oligodendrocyte differentiation. Herein we propose a novel factor to improve oligodendrocyte differentiation with outstanding potential effects in cell therapy of neurodegenerative diseases.

Keywords: miR-184, Oligodendrocyte differentiation pathway, Neurodegenerative disease

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Genetic variants of Cystic Fibrosis disease in Azeri Turkish population

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Abstract

Backgrounds: Cystic fibrosis is the most common lethal autosomal recessive with more than 1,500 mutations and 300 polymorphisms. The aim of this study was to investigate the genetic variants in patients with cystic fibrosis disease in the Azeri Turkish population.
Materials and Methods: In a descriptive study conducted for cystic fibrosis patients in the Azeri Turkish population in Iran from 2015 to 2020, the spectrum of cystic fibrosis transmembrane conductance regulator (*CFTR*) mutations was reviewed based on medical records. In some patient's DNA testing has been carried out with standard kits that test only a limited number of common variants and others performed DNA analyses of the whole gene until the variants were identified.
Results: Out of 262 patients, 36 known variants were identified when the ΔF508 (19.84%) was the most common mutation among patients. The variant of 1677delTA was observed in 3% of patients which was followed by variants of R334W, 2183AA->G, E92K, and G542X with frequency 5 (2.2%). The frequency of other variants was very low. Most variants were related to exons 8 and 11 and included for all 5 classes.
Conclusion: These findings indicate a low frequency of the ΔF508 mutation and a heterogeneous spectrum of the mutations in this ethnic group. Therefore, many exons need to be examined to diagnose this disease.

Keywords: Cystic fibrosis, CFTR, Variants, ΔF508, Spectrum

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Predicting biomarker microRNAs for differentiating ER/PR positive and negative breast cancers using bioinformatics

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Abstract

Backgrounds: Breast cancer (BC) is the most common malignancy in females and despite significant advancements in treatment strategies; it remains the second leading cause of cancer-related death worldwide. Classification of BC is based on hormone-receptors expression status and identifying the molecular subtypes of BC plays a crucial role in the treatment approach and monitoring the efficacy of therapy. The majority of BCs have shown overexpression of estrogen receptors (ERs) and progesterone receptors (PRs). Furthermore, evaluation of ER and PR in breast tumors is important for prognosis and management of therapy. According to recent studies, dysregulation of small none-coding RNAs such as miRNAs is involved in the initiation and progression of a variety of diseases including BC. Therefore, miRNAs can be considered as non-invasive biomarkers for diagnose of the ER/PR-positive and -negative breast tumors.
Materials and Methods: We investigated the differentially expressed miRNAs in different subtypes of breast tumors by reanalyzing the available data in TCGA, GSE26459, GSE20685 and GSE29173. In the next step, other databases including UCSC, SRA, mirBase and RNAfold were used to clarify some characteristics of our candidate miRNAs such as conservation, expression status within tumor and non-tumor tissues, and their secondary structure, respectively. Moreover, some bioinformatics online tools such as miRDB, MiRnalyze, KEGG, and TargetScanHuman 7.1 were applied to predict potential target genes for our candidate miRNAs.
Results: This study indicates that due to the specificity (AUC = 0.938) of our candidate miRNAsin differentiating ER/PR positive and negative breast tumors, they could represent a new biomarker for Luminal and none-Luminal breast cancer diagnosis.
Conclusion: We identified ten candidate miRNAs with significant differential expression within ER/PR-positive and -negative breast tumors. Some of these miRNAs play pivotal roles in regulating the expression of ER/PR hormone receptors. These miRNAs will allow us to incorporate such method for identifying patients who are most likely responding to specific therapies based on ER/PR status.

Keywords: Breast cancer, Estrogen receptors, Progesterone receptors, miRNAs, Biomarker

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Investigation of the role of LncRNA TTTY14 in colorectal cancer using Real-time PCR

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Abstract

Backgrounds: Colorectal cancer is the 2nd leading cause of death in humans because of cancer. Molecular tools have been emerging as the potential biomarkers. Long non-coding RNA (LncRNAs) have shown promising capabilities to be used in clinics. The aim of this study was to investigate the expression of TTTY14 (Testis-Specific Transcript, Y-Linked 14) in colorectal cancer. This LncRNA was selected based on bioinformatics data and because of there has been no research report on its expression in tissue samples of CRC at present.
Materials and Methods: qPCR was used to measure the expression level of TTTY14. For this purpose, the colorectal tumors along with the corresponding adjacent normal tissues were collected from thirty patients attending Milad Hospital, Isfahan, Iran. All the samples were collected in accordance with the guidelines issued by the Ethics Committee of Isfahan University of Medical Sciences (approval number: 6307603), regarding the 64th World Medical Association General Assembly of Helsinki declaration amended in October 2013. After total RNA extraction from samples and cDNA synthesis, Real-time PCR was used to measure the TTTY14 expression.
Results: The qPCR results showed the expression level of TTTY14 was down-regulated in thirty paired colorectal cancer specimens (p value = 0. 0085).
Conclusion: Our comprehensive approach suggested that TTTY14 could be an important down-regulated LncRNA in colorectal cancer. This is highly recommended to profile TTTY14 in bigger colorectal cancer cohorts to see whether the aberrant expression could have clinical relevance.

Keywords: Long non-coding RNA, Colorectal cancer, TTTY14, Real-time PCR

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Exploration of potential key genes in oral squamous cell carcinoma by gene network analysis

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Abstract

Backgrounds: Oral cancer is one of the most prevalent malignancies in the world, with a delayed clinical diagnosis, poor prognosis and costly treatment options. Oral cancer is a kind of malignant neoplasia that develops on the lip or oral cavity. It is usually classified as an oral squamous cell carcinoma (OSCC) since squamous cells are histologically responsible for 90% of malignancies in the dental field. Oral cancer is a preventable illness in which smoking and alcohol—both significant risk factors—are present in 90% of cases, both having a synergistic impact. Patients are managed using traditional histologic criteria such as TNM and tumor grading, although novel molecular and cellular markers have been explored to enhance therapy and survival.

Materials and Methods: Microarray dataset GSE30784 was downloaded from gene expression omnibus (GEO). Then, the transcriptome analysis console (TAC) was used to normalized and analyze differential expression genes (DEGs). The genes with adjusted p-value (FDR)< 0.05 and $|log_2FC| > 1.5$ were selected as DEGs between normal and OSCC samples. String, cytoscape and gephi were used to construct protein-protein interaction (PPI) and visualization, respectively.

Results: 2601 genes were obtained as DEGs (1335 upregulate, 1266 downregulate). Our analysis revealed 5 hub genes, namely, IL6 (interleukin 6), MYC (v-myc avian myelocytomatosis viral oncogene homolog), ITGB1 (integrin beta 1), PTPRC (protein tyrosine phosphatase, receptor type, C) and MMP9 (matrix metallopeptidase 9). Furthermore, the results of the KEGG pathway analysis revealed that these genes were enriched in significant pathways, including proteoglycans in cancer, focal adhesion and pathways in cancer.

Conclusion: Consequently, the critical genes and pathways associated with the pathogenesis and prognosis of OSCC were identified by bioinformatics analysis. Studying the regulatory network would lead us to create a competent approach to prediction models of the illness.

Keywords: Oral squamous cell carcinoma, Systems biology, Bioinformatics, Biomarkers

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Silibinin inhibits MCF7 breast cancer cell proliferation and migration by GREB1 targeting

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Abstract

Backgrounds: Growth Regulation by Estrogen in Breast Cancer 1 (GREB1) is an estrogen receptor (ER) target gene and its expression is correlated with estrogen levels in breast cancer. ER-positive breast cancer cell lines, express GREB1 at high levels. GREB1 helps transcription regulation of ER target genes. Silibinin is a bioactive component of Silymarin from seeds of milk thistle. This component possesses several pharmacological properties such as anti-inflammatory, antioxidant, anti-cancer, and estrogenic effects. Therefore, the aim of the present study was the assessment of Silibinin on proliferation, migration, and GREB1 expression.

Materials and Methods: MCF7 breast cancer cells cultured in RPMI1640 comprising FBS (10%), 100 U/ml penicillin/ streptomycin at 37°C in a humidified atmosphere containing 5% CO2. Cells were treated with different concentrations of Silibinin and then cell cytotoxicity was investigated by the MTT assay. Scratch test used to evaluate the rate of cell migration. To determine the expression of the *GREB1* gene, qPCR in Silibinin treatment was analyzed.

Results: MTT analysis showed that in MCF7 cells treated by Silibinin, cell proliferation is significantly inhibited. Furthermore, the % of an open wound in migration analysis in both control and treated cells indicates that Silibinin prevented cell migration. Gene expression analysis revealed downregulation of the *GREB1* gene in MCF7 cancer cells.

Conclusion: Silibinin treatment has an inhibitory effect on MCF7 breast cancer cell proliferation and migration, also downregulates the *GREB1* gene. Therefore, the GREB1 targeting by Silibinin in the MCF7 cell line can be proposed as a therapeutic pathway in breast cancer.

Keywords: Silibinin, Anticancer, MCF7, *GREB1*

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Association between DROSHA rs642321 polymorphism and breast cancer in Iranian women

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Abstract

Backgrounds: Breast cancer is the most common cancer for women worldwide and is main factor of cancer mortality. The incidence rates of breast cancer in the developing countries are increasing. Single nucleotide polymorphisms (SNPs) in microRNA biosynthesis pathways may result in the less or gain of microRNA function that can act as an oncogenic or tumor-suppressive. Dysregulation of microRNA biogenesis pathway genes is involved in the initiation and progression of several human cancers including breast cancer. SNPs in microRNA biogenesis pathway genes are related to breast cancer risk. One of the most important genes in this field is DROSHA. Previous studies have shown that rs642321 is related remarkably to different cancer risks.
Materials and Methods: We performed a case-control examination of 100 breast cancer cases and 100 healthy controls to evaluate the association between rs642321 in DROSHA and breast cancer risk. Genomic DNA was extracted from blood samples. ARMS PCR was performed for detection of the rs642321 by designed primers.
Results: Statistical analysis showed that rs642321 polymorphism located in 3' untranslated region (UTR) of DROSHA gene was related to the enhanced risk of breast cancer.
Conclusion: Altogether, our results indicated that presence of DROSHA rs642321 polymorphism could be proper tumor markers in patients with breast cancer.

Keywords: Breast cancer, DROSHA, rs642321, ARMS PCR, SNP

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Key genes associated with the progression of non-small cell lung adenocarcinoma in smokers and non-smokers

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Abstract

Backgrounds: Non-small cell lung cancer is the most prevalent type of lung cancer, accounting for 85 percent of all cases. It is frequently diagnosed at an advanced stage and has a poor prognosis. Understanding the key genes involved in adenocarcinoma tumor progression in smokers and non-smokers can lead to early identification and multimodal treatments.

Materials and Methods: GSE50081 CEL files were normalized using robust multi-array average (RMA) via the R programming language, and differentially expressed genes (DEGs) of adenocarcinoma stages 1 and 2 were detected in two separate groups of smokers and non-smokers using the following criteria: $|log_2 FC| > 1$ and *P*-value <0.05. The STRING database was used to create a PPI network, and then examined using Cytoscape to track hub genes. Enrichment study was carried using "Enrichr".

Results: In non-smokers and smokers, 358 DEGs (57 up-regulated and 301 down-regulated) and 245 DEGs (43 up-regulated and 202 down-regulated) were identified, respectively. KEGG pathway analysis was enriched in protein digestion and absorption for smokers and phosphatidylinositol signaling system for non-smokers. According to Gene Ontology, Smokers' DEGs enriched significantly in alveolar lamellar body and non-smokers in bone morphogenesis. In smokers, three hub genes were found: CF transmembrane conductance regulator (CFTR), microtubule-associated protein 2 (MAP2), and NEDD4 like E3 ubiquitin-protein ligase (NEDD4L). Non-smokers were found to have erb-b2 receptor tyrosine kinase 4 (ERBB4) and heat shock protein 90 alpha family class B member 1 (HSP90AB1) as hub genes, which could be employed as therapeutic targets.

Conclusion: In summary, identifying discrete hub genes for both smokers and non-smokers and understanding the pathways and ontologies involved can help us better understand the disease progression and provide novel biomarkers for future therapeutics.

Keywords: Non-small cell lung cancer, Lung adenocarcinoma, Gene expression analysis, Bioinformatics

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Creating an Efficient Strain for Purity of TEV-Labeled Recombinant Proteins

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Abstract

Backgrounds: Peptide tags are protein sequences that are used in recombinant proteins mainly in order to increase the solubility or facilitate the purification of the proteins. Generally, the used tags need to be removed accurately and appropriately after the production and purification of the recombinant proteins. Accordingly, in the present study, a plasmid was constructed that exclusively encoded TEV protease using arabinose as the inducer.

Materials and Methods: The constructed final vector was pBAD/GST.TEV/TT/Neo-Kan/p15AOri, which was briefly called pBAD/GST. Also, the accuracy of all cloned sequences was confirmed by DNA sequencing. Finally, pBAD/GST plasmid was used to transform Shuffle T7 Express E. coli cells and the expression of soluble TEV protease was confirmed using SDS-PAGE.

Results: After induction of the recombinant bacterial cells by defined concentrations of arabinose at 30 °C for 4 h, an expected TEV protein with size of 55 KDa was successfully produced. The production of the protein was confirmed by observing the protein band using SDS PAGE. Protease function of TEV inside the bacterial cells was verified by the cleavage of fusion protein TRX IGF1 produced in shuffle E. coli cells. For this, at first bacterial cells are induced by appropriate concentration of IPTG in order to express TRX IGF1. After 1 h, arabinose was added to the media and the culture of the induced cells was continued for 6 h. Total soluble fraction as well as inclusion bodies were isolated and analyzed using SDS PAGE. The results demonstrated that TEV protease cleaved the fusion protein in soluble fraction and inclusion bodies. Finally, purification was performed with Nika resin, which showed an IGF 1 band.

Conclusion: In this study, a new subspecies of Shuffle T7 Express *E. coli* was obtained by transformation of an expression plasmid, which could produce the soluble and active TEV protease. This protease could cleave its specific site between TRX and IGF-1 in the host bacterial cells and separate TRX tag from the recombinant IGF-1, which was expressed by an independent pET vector. Therefore, by this approach there is no need to digest the recombinant fusion protein after extraction from the bacteria. Indeed, in vivo digestion of recombinant fusion protein can have a significant effect on facilitating and reducing the costs of downstream purification process.

Keywords: TEV protease, Protein tag, Recombinant protein, Fusion protein

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Investigation of the subscriptions and association of biologic pathways involved in recurrent acute coronary syndrome

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Abstract

Backgrounds: Atherosclerosis is a chronic inflammatory disease that begins with the formation of a fat layer that is an accumulation of foam cells in the intimal layer of the arteries. Lipid storage is the first step in the pathogenesis of atherosclerosis, where chronic inflammation at the sites of the large arterial walls leads to the formation of fat layer, then leading to the formation of fibroatheromas. Patients with recurrent acute coronary syndrome compared with patients with long-term stable angina have a different atherosclerotic phenotype, including a higher incidence of thin cap fibroathroma and a lower incidence of improved coronary plaques; Suggesting that atherosclerotic features and plaque treatment may contribute to the progression of coronary artery disease. The aim of this study was to evaluate potential pathways in inflammation and recurrence of the disease in PBMCs by bioinformatics.

Materials and Methods: Blood cell transcriptome of patients with recurrent acute coronary syndrome was extracted from *GSE34822* gene expression analysis with GEO2R filtering gene by p-value <0.01. This gene set, along with 20 directly interacting proteins, was analyzed for pathway enrichment in KEGG repository data and analyzed for their connections to each other by ClueGO application.

Results: Among the 53 probes showing a significant increase in the expression of non-recurrent coronary artery disease patients with recurrent coronary artery disease, 19 pathways were enriched from the KEGG repository dataset, the most important of which include FOXO signaling, aldosterone-regulated sodium reabsorption, AGE-RAGE signaling, insulin resistance, type 2 diabetes, and lipolysis.

Conclusion: These pathways share common sites including *INSR*, *IRS1*, *PIC3CB*, and *PIC3R2* genes that can be used for therapeutics, preventive, and diagnostic purposes in the recurrence of this disease.

Keywords: Recurrent acute coronary syndrome, Inflammation, Transcriptome analysis, Biological pathways

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Structural and conformational studies of loop VI in copper–zinc superoxide dismutase by site-directed mutagenesis

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Abstract

Backgrounds: The human superoxide dismutase (hSOD1) is an antioxidant enzyme that catalyzes two molecules of superoxide anion into hydrogen peroxide and water. More than 180 different mutations in the *SOD1* gene have been reported in association with amyotrophic lateral sclerosis (ALS), many of which are due to amino acid replacement. In this study, by substituting leucine to proline (L106P) at position 106, the effect of mutation on activity and structural properties was investigated.

Materials and Methods: The vector pET-28a-hSOD1 was used for mutagenesis by Quick-change PCR methods. The WT- hSOD1 and mutant protein was expressed in E. coli-BL21 (DE3), at 22 °C, 230 rpm for 18h, and purified using Ni-NTA agarose affinity chromatography. Comparative structural study of wild type and mutant was performed by intrinsic and extrinsic fluorescence.

Results: The results of bioinformatics servers showed the destructive effect of mutations on protein structure. The specific activity of wild-type and L106P mutant was 7031.25 and 1942.8 U/mg at a concentration of 0.1 mM pyrogallol, respectively. Increased of mutant intrinsic fluorescence compared to wild-type indicates structural changes and tryptophan exposure in a non-polar environment. The increased ANS fluorescence mutant compared to wild-type, indicating increase the hydrophobic surfaces in the protein.

Conclusion: Overall, our results showed that mutations in loop VI lead to structural changes and implications for initiation of ALS. Further studies on loop VI provided clearer evidence for the pathogenicity and its association with the ALS phenotype.

Keywords: Human superoxide dismutase 1, Amyotrophic lateral sclerosis, loop VI, ANS fluorescence

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Epiregulin gene expression profiling in cumulus cells is reflective oocyte/embryo competence and potentially reliable predictor of embryo developmental competence in PCOS patients

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Abstract

Backgrounds: Polycystic ovary syndrome (PCOS) is a common endocrine and metabolic disorder in women of reproductive age, and has a major impact both on fertility and on long-term health. In mammals, Cross-talk between the oocyte and cumulus cells is critical for oocyte maturation and embryo competence. Cumulus cells (CCs) support oocyte development, while the oocyte influences follicular cell growth and differentiation. Over recent decades, numerous growth factors involved in the bidirectional signals between the somatic and germ cells have been identified. The function and impact of epidermal growth factor (EGF) signaling during ovulation and oocyte maturation has been characterized. However, little is known about the role of EREG in PCOS. The aim of this study was to examine expression and potential functional aspects of epiregulin in cumulus cell proliferation and oocyte competence in women with PCOS.

Materials and Methods: CCs from oocytes in metaphase II (MII) stage of PCOS (n=18) and non-PCOS (n=18) patients who underwent controlled ovarian stimulation were mechanically removed shortly before ICSI. Quantitative real-time PCR (qPCR) was used to analyze changes in gene expression.

Results: Our results demonstrate that consistent with our previous RNA-seq data, EREG was significantly ($P<0.01$) down-regulated in CC samples from the PCOS patients in comparison with the non-PCOS patients.

Conclusion: The study highlights that EREG is differentially expressed in PCOS and non-PCOS patients, in which suggests that EREG could be used as a biomarker to predict oocyte competence or embryo development. Our results may be clinically important as they offer a new potential strategy for the selection of the best oocyte from women with PCOS; and the use of this oocyte to increase in vitro fertilization (IVF) success rates.

Keywords: Polycystic ovary syndrome, Cumulus cells, Epiregulin, qPCR, Non-invasive biomarker

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Critical roles of extracellular matrix genes in the pathogenesis of carpal tunnel syndrome

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Abstract

Backgrounds: Carpal tunnel syndrome (CTS) is the most common peripheral nerve entrapment syndrome, affecting a large percentage of the general population. A recent study of CTS identified a couple of CTS-associated variants within genes implicated in growth and Extracellular Matrix (ECM) architecture, although the causative link has not been established. The aim of this study is to evaluate the differential gene expression among the sample of patients suffering from CTS and normal individuals by bioinformatics analysis.

Materials and Methods: The raw data of RNA-sequencing samples of normal individuals and CTS patients were obtained from the database with the number, GSE108023. Then the steps of sample analysis were performed. Genes with differential expression were isolated with DESeq2 R package. Then, important signaling pathways and the genes involved in the ECM were investigated.

Results: The results revealed that the expressions of 2374 genes were upregulated whereas the expressions of 2474 genes were downregulated in patients. In addition, *TNXB*, *ITGB4*, *LAMC3*, *ITGB3*, *LAMA3*, *TNC*, *DMP1*, *LAMC2*, *HMMR*, *ITGB6*, *LAMB3*, *ITGA3*, *ITGA2*, *LAMB4*, *FN1*, *GP6*, *FRAS1*, *ITGA1*, *COL4A6*, *COL4A5*, *COL6A3*, *SDC1*, *ITGA5*, *FREM2* genes which are upregulated or down regulated involved in the extracellular matrix receptor interaction.

Conclusion: Finally, our analysis proposed the important role of extracellular matrix proteins in the pathology of CTS. However, the accurate molecular experimental studies are needed to confirm the role of ECM genes in the development of CTS.

Keywords: Carpal tunnel syndrome, Extracellular matrix, RNA-sequencing

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ORF8: Promising Target Protein for COVID-19 Treatment

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Abstract

Backgrounds: Recent pernicious COVID-19 pandemic is caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). SARS-CoV-2 accessory proteins are known to play key roles in host immune regulation and immune evasion. Amidst them, Open-Reading Frame 8 (ORF8) as a unique protein, has some prominent roles in disease severity, most striking of them are interaction with Major Histocompatibility Complex-1 (MHC-1) and its down-regulation, Interleukin-6 production and, the antagonistic effect on Interferon Regulatory Transcription Factor-3 (IRF-3). In this study, we explore the molecular features of ORF8 to find the potential hotspot binding sites of the protein for proposing appropriate inhibitors, especially among the natural products (NPs).

Materials and Methods: The X-ray 3D structure of ORF8 was obtained from the Protein Data Bank (PDB). The ligand-binding sites were predicted using sequence features and the I-TASSER server (https://zhanggroup.org//I-TASSER/). The native ligands were then predicted using the I-TASSER server. Potential phytochemical and bacterial NP inhibitors were obtained from the PubChem server (https://pubchem.ncbi.nlm.nih.gov/). All molecular visualization was performed using PyMOL 2.5.1 and Chembiooffice 14.0 softwares. Molecular docking was executed using Autodock vina 1.1.2 software.

Results: The proposed hotspots included the $_{73}$YIDI$_{76}$ motif in addition to R48, E59, L84, E92, K94 and, R101 residues. Through molecular docking it is found that NPs included sesquiterpene lactone phytochemical, Artemisinin, macrocyclic bacterial metabolite, Ivermectin and, the lactose derivative DEG-168 small molecule as potential inhibitors.

Conclusion: ORF8 is a key target for inhibition by Artemisinin, Ivermectin, and lactoside DEG-168.

Keywords: COVID-19, ORF8, Molecular docking, Artemisinin, Ivermectin

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A prion-derived peptide can protect SH-SY5Y neuroblestoma cells against Aβ$_{42}$ oligomer cytotoxicity without interaction between the two peptides

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Abstract

Backgrounds: Alzheimer's disease (AD) is a prevalent and progressive neurodegenerative disease. The cellular prion protein (PrP^C) is a glycoprotein that mostly located at the outer surface of the cell membrane and can act as a high affinity receptor for oligomeric Aβ. Mutation in the *PRNP* gene can change the kinetics of PrP. In present study, neuroblastoma cells were treated with Aβ$_{42}$ oligomers (ADDLs) with and without $PrP_{107-120}$ and the level of viability of cell was investigated. We also assessed the interaction between the two peptides

Materials and Methods: Cell viability was assessed by MTT assay. To investigate the interaction between $PrP_{107-120}$ and Aβ$_{42}$ ADDLs, cells were cultured on glass coverslips then were treated with various sample (Aβ$_{42}$ ADDLs, Aβ$_{42}$ ADDLs + labelled $PrP_{107-120}$ and labelled $PrP_{107-120}$). $PrP_{107-120}$ was labelled with BODIPY TMR-X NHS Ester, Aβ$_{42}$ ADDLs with mouse monoclonal primary antibody 6E10 and secondary antibody, and the nuclei with the Hoechst dye. Cells were imaged using a TCS SP8 confocal microscope.

Results: The present study shows that cytotoxicity of Aβ$_{42}$ ADDLs was strongly reduced when the SH-SY5Y neuroblastoma cells were treated with ADDLs in the presence of $PrP_{107-120}$. Surprisingly, no apparent co-localization between $PrP_{107-120}$ and ADDLs was seen in confocal microscopy images.

Conclusion: These data suggest that viability of neuroblastoma cells exposed to ADDLs with $PrP_{107-120}$ was increased compared to the cells treated with ADDLs alone, although $PrP_{107-120}$ did not show any interaction with ADDLs.

Keywords: Alzheimer's disease, ADDLs, Cellular prion peptide, Receptor, *PRNP* gene

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The effect of crocin on caspase 6 gene expression in breast cancer

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Abstract

Backgrounds: Cancer is one of the leading causes of death in the world. According to statistics published in recent years, twelve million and seven hundred thousand new cases of cancer have been identified in the world. Breast cancer is the most common cancer and the second most common cause of death among women. Crocin with high antioxidants prevents breast cancer by suppressing free radicals and expressing apoptotic genes. Therefore, the aim of this study was to investigate the changes in caspase 6 gene expression in breast cancer.

Materials and Methods: After evaluating the toxicity of Crocin on cancer cells by MTT assay, changes in gene expression after RNA extraction and cDNA synthesis were investigated using Real-time PCR.

Results: The results of real-time PCR showed that the expression of Caspase 6 gene due to Crocin treatment was significantly increased compared to *GAPDH* gene ($p < 0.05$). The amount of fold change in the high dose was 1.4.

Conclusion: The results showed that Crocin due to its antioxidant properties has a significant effect on breast cancer cell mortality and increased expression of caspase 6 gene due to its antioxidant properties.

Keywords: Antioxidant, Crocin, Breast cancer, Real-time PCR

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Novel anticancer peptide derived of Lactoferricin-B inhibits chemo-drug metabolism in cancer cells by blocking GSTP1 factor

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Abstract

Backgrounds: Antimicrobial peptides (AMPs), are essential components of the immune defense of multicellular organisms and are currently being developed as antimicrobial and antitumor drugs. Lactoferricin-B (LfcinB) is an antimicrobial peptide that has cytotoxic activity against cancer cells. Studies have shown that Lactoferricin-B or its derivatives can inhibit tumor growth in vitro and in vivo. Thus, aim of this study is improving the approach for the identification of potential peptide molecule for GSTP1 targeting through bioinformatics analysis.

Materials and Methods: Lactoferricin-B sequence submits to AntiCP server for predict and design of newly anticancer peptides. The 2D and 3D structures of these peptides were drawn with Protean (DNAstar software), Phyre2 and I-TASSER respectively. Furthermore, anticancer property for each peptide expected with iACP software. The 3D structures of peptides were docked with the GSTP1 using docking server HDOCK and the peptide with the maximum binding energy value was identified.

Results: AntiCP server predicts >350 peptides with anticancer property. Peptides with high SVM score were selected. Anticancer activity of new design peptides showed 99% anticancer specificity. Result revealed that among 350 peptides were virtually screened 45 peptides showed greater than 99% anticancer property and among these peptides FKCRRWQWRMKKLGAPSIWCVRR identified as potential sequence for GSTP1 ligand.

Conclusion: Our results indicated that the probability of successful production of new anticancer peptide derived of Lactoferricin-B. These outcomes based on *in silico* analysis may be used in cancer therapy or vaccine design. Therefore, new designed peptide can be used as potential inhibitor agent in for GSTP1 against cancer.

Keywords: Anticancer peptide, Lactoferricin B, Bioinformatics, GSTP1

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Analysis of TCGA data of genes and key pathways indicates potential role of histones in breast cancer

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Abstract

Backgrounds: Protein-protein interactions (PPI) are very important in understanding the regulatory processes involved in cancer.
Materials and Methods: The TCGAbiolinks package was used to obtain RNASeq gene expression data of breast cancer (BC). The data were normalized using the Trimmed Mean of M-values (TMM) normalization approach. Then, limma package was used to find DEGs between tumor samples and normal breast tissues. The STRING database was used for the construction of the PPI network for up-and down-regulated genes separately. MCODE App was used to analysis the networks as well as ClueGo and Cluepedia Apps in cytoscape software were used for functional annotations of networks.
Results: The gene ontology (GO) analysis of up regulated DEGs indicated their prominent roles in mitotic cell cycle and chromosome organization. Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis of up regulated DEGs indicated the involvement of the identified genes in different pathways involved in cell cycle and oocyte meiosis. Two important clusters of PPI were identified. Interestingly, one of the clusters of PPI networks of up regulated genes was found to encode only histone proteins like HIST1H4E, HIST1H1D, and HIST2H4A.
Conclusion: The data from this study suggested that the importance of histones gene expression in breast cancer, which could suggest histone proteins as possible novel prognostic biomarkers in breast cancer therapy.

Keywords: TCGA, Breast cancer, PPI network, Histones

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Reanalysis of exome sequencing data in 20 negative hearing loss samples: efficiencies and benefits

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Abstract

Backgrounds: Hearing loss is the most common sensory defect that affects ~ 1/500 newborns and over 6% of the population worldwide. Approximately 50–60% of hearing loss patients are attributed to genetic causes. With the advancement of Next-Generation Sequencing and bioinformatics tools, exome sequencing (ES) has recently become the most efficient diagnostic test for patients with hearing loss. According to various studies, up to 50% of patients are still undiagnosed; so re-analysis of ES data may improve diagnostic rates in patients who do not have an initial molecular diagnosis.

Materials and Methods: The exome and phenotypic data of twenty undiagnosed hearing loss Iranian patients were re-examined and re-analyzed. ES reanalysis was performed utilizing the most recent GATK and other improved bioinformatics tools to improve variant identification and annotation. The GATK GermlineCNand VCaller was used to perform ES-based CNV analysis.

Results: We found two pathogen variants in the *DIAPH1* and *FGF3* genes in two families after re-evaluating clinical and ES data. These causal variants were not detected in initial ES analysis. The new finding in *DIAPH1* was determined to be due to initially incomplete phenotypic information. A frameshift variation was found in *FGF3* which was missed probably because of mapping error for indels in early versions of analytical pipeline. This is the first reported case in Iranian population with mutation in *FGF3* gene. Also, more clinical evaluations are underway.

Conclusion: Our preliminary analysis resulted in more than 10% increase in diagnostic yield, indicating that periodical reanalysis should be performed in clinical practice.

Keywords: Reanalysis, Whole exome sequencing, Hearing loss, Diagnostic yield

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Virtual high throughput screening: potential inhibitors for SARS-CoV-2 structural and nonstructural proteins

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Abstract

Backgrounds: Pneumonia of unknown cause detected in Wuhan, China was first reported to the WHO Country Office in China on 31 December 2019. The present study aimed to meet the exigent requirement of practicable COVID-19 drug treatment with a computational multi-target drug repurposing approach.
Materials and Methods: Many reports are available with in-silico drug repurposing. However, the majority of them were engrossed on a single target. In the present study, 2371 FDA approved drugs screened with molecular docking approach against COVID-19 protein and extracts the drug combination targeting COVID-19 proteins comprehensively.
Results: The study designated Elbasvir, Ledipasvir, Paritaprevir, promising drug candidates for COVID-19 treatment. The computational analysis also revealed the better potential of the proposed drug combination over the currently used drugs for COVID-19 treatment.
Conclusion: The anticipated drug combination is acting on both non-structural and structural proteins therefore, it can be able to reduce the COVID-19 infection process and also reduce viral multiplication. Moreover, the drugs are safe and well-known so it can be rapidly explored further for the COVID-19 drug discovery process.

Keywords: SARS-CoV2, COVID-19, in-silico, Drug repurposing, qVina

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Over expression of LncRNA DUXAP8 in gastric cancer tumoral tissues

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Abstract

Backgrounds: Gastric cancer remains fifth most common cancer and often diagnosed at an advanced stage and is the second leading cause of cancer-related death worldwide. An increasing number of studies have found that non-coding RNAs including miRNA and LncRNA play important roles in gastric cancer progression. Recent studies highlight pseudogene derived long non-coding RNAs (LncRNAs) as key regulators of cancer process. However, few of them have been well characterized in gastric cancer. Here, we aimed to identify the association between pseudogene derived LncRNA DUXAP8 and growth of gastric cancer cells and also examined the expression level of LncRNA DUXAP8 and its association with clinico pathological characteristic in GC.

Materials and Methods: Total RNA of 100 specimen's tumor tissues and 100 specimens of marginal tissues were extracted by TRIzol reagent. After cDNA synthesis, qRT-PCR was performed to evaluate the expression level of DUXAP8 and the obtained data were analyzed by SPSS 16.0 and Graph Pad Prism.

Results: The relative expression level of DUXAP8 was significantly increased in tumoral tissues as compared with the marginal tissues. The AUC index of LncRNA DUXAP8 was 0.67(P = 0.0001) in tumoral tissue.

Conclusion: The obtained findings suggest that DUXAP8 acts as an oncogene in GC and may be a new target for gene therapy of GC.

Keywords: Gastric cancer, Pseudogene, LncRNA, DUXAP8

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Evaluation of miR-744 expression pattern in the blood of non-small cell lung cancer patients compared with normal individuals

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Abstract

Backgrounds: MicroRNAs (miRNAs) are a group of small non-coding RNAs, which are reported to play crucial roles in repressing downstream targets expressions. Therefore, their changes in expression are assumed to be an important biological marker for diagnosing and prognosing different types of illnesses, including non-small cell lung cancer.
Materials and Methods: In this study, blood samples were collected from 30 normal and 30 non-small cell lung cancer (NSCLC) patients. After the plasmas separation from blood samples, RNAs were extracted and cDNAs for the miR-744 (miRNA of interest) and miR-16 (reference miRNA) were synthesized. The quantitative PCR were performed to compare the expression level.
Results: The results have shown a significant change in miR-744 level in the plasma of NSCLC patients compared with normal individuals.
Conclusion: MiR-744 could be considered as biomarker for diagnostic and therapeutic strategies for NSCLC.

Keywords: MicroRNAs, Non-small cell lung cancer, miR-744, Quantitative PCR, Expression level, Biomarker

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Evaluation of breast cancer cell line due to treatment with vitamin E

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Abstract

Backgrounds: Vitamin E is a fat-soluble vitamin. This vitamin acts as an antioxidant in the body and protects the body's cells against destruction, meaning that this vitamin has a great ability to neutralize free radicals that are naturally produced inside the body's cells. The aim of this study was to evaluate the effect of vitamin E on breast cancer cell line.

Materials and Methods: Breast cell line was treated with different concentrations of vitamin E. The effect of vitamin E on cell mortality was measured by MTT method. In this test, cells were counted with trypan blue and 10,000 cells were cultured in 96-well plates and the cells were treated for 48 hours.

Results: The results of MTT test showed cancer cell mortality at different concentrations of treatment, which increased mortality and decreased survival with increasing concentration of vitamin E treatment ($p < 0.05$). IC50 for breast cancer 45 µg / ml was calculated.

Conclusion: Evaluation of changes in breast cancer cell life due to vitamin E treatment was evaluated using MTT test. The results of the treated cells were analyzed by ELISA reader after reading and the graph was plotted as the percentage of mortality versus concentration. The results showed that 48-hour treatment had a greater effect on cancer cell mortality.

Keywords: Antioxidant, Vitamin E, Breast cancer, MTT

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Aberrant expression of circ-0072309 in breast carcinoma as a promising biomarker for diagnosis

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Abstract

Backgrounds: Breast cancer (BC) is one of the most common cancers and the second highest mortality in women worldwide. Different studies have shown that there is a close correlation between circRNAs and initiation and progression of different cancers and diseases; however, knowledge about the correlation between non-coding RNAs, especially the circRNAs and BC, is not fully explored. In this study, the expression level of circ-0072309 (LIFR) in BC was investigated experimentally and miRNA target genes for it were proposed.
Materials and Methods: BC tissue specimens (twenty-nine causes) and their corresponding adjacent normal tissue were collected during the surgery and has-circ-0072309 expression in breast cancer tissues was analyzed using qRT-PCR. A series of functional experiments were carried out to investigate has-circ-0072309 function in breast cancer development. Additionally, miRNAs that potentially target has-circ-0072309 were predicted by bioinformatics method. miRTargetlink database (https://ccb-web.cs.uni-saarland.de/mirtargetlink) and DIANA database (http://diana.imis.athena-innovation.gr/DianaTools/index.php?r=mirpath/index/) were used to predict interactions of miRNAs with LIFR.
Results: The lower expression levels of circ-0072309 in BC tissues was showed compared to paired adjacent normal tissues with P value (P <0.002). The area under the receiver operating characteristic (ROC) curve was 0.768. In addition, a total 10 miRNAs that can be targeted by candidate circRNA was predicted base on bioinformatics databases. Moreover, miRNAs selection tools predicted that miR-125a-5p and miR-203a-3p can be targeted by circ-0072309.
Conclusion: Our findings revealed that the has-circ-0072309 plays an essential role in BC progression and circ-0072309 could serve as a prognostic biomarker of BC.

Keywords: Circular RNA, microRNA, Breast cancer, DIANA database, miRTargetlink database

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Effects of motility Sperm and prediction of IUI success

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Abstract

Backgrounds: Intrauterine insemination (IUI) is one of the methods of infertility treatment that is used in a wide range of infertility, including infertility with unknown causes, in cases where cervical mucus is the cause of infertility and impotence. Diagnosis of male infertility is often based on semen analysis, the usual parameters of which are: number of sperm per unit volume (concentration), motility and shape of sperm in the ejaculate. Due to the importance of semen analysis in diagnosing the causes of male infertility, the relationship between sperm parameters and success in IUI has always occupied the mind of the researcher and several studies have been conducted in this field.

Materials and Methods: This study is a descriptive analytical type. The sampling method was improbably performed among IUI volunteers. The Statistical Package for the Social Sciences version 19 (SPSS Inc., Chicago, IL, USA) was used in our study.

Results: There was a statistically significant difference between the motility sperm ($p = 0.0001$) and prediction of IUI success.

Conclusion: Given that the first and most accessible test for men is semen analysis, it seems that examining the predictive power of semen analysis is useful in the success of IUI. The number of inoculated motile sperm, sperm morphology, duration of infertility, female age, causes of infertility and treatment method are among the factors that affect the success of IUI.

Keywords: IUI, Infertility, Sperm, Motility, Pregnancy

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To study diabetic neuropathy: using transgenic zebrafish model

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Abstract

Backgrounds: Diabetes Mellitus (DM) is a heterogeneous metabolic disorder that let to hyperglycemia and further to different complications such as retinopathy, nephropathy, delayed wound healing, and. Despite many studies has been conducted on diabetic neuropathy, disease development and drug discovery investigations are yet essential at preclinical stage using appropriate animal models. Zebrafish (*Danio rerio*) because of its features such as transparency at the early developmental stages, easy husbandry and care, regenerative capacity for most organs, along with extremely fast development and similarity in genomic and biological pathways with human in different diseases including diabetes, is an ideal disease model organism.
Materials and Methods: In this study, immersing method was used to induce hyperglycemia and investigate its influence on central nervous system. To induce DM in Zebrafish, adult transgenic Zebrafish (*mbp:(eGFP-NTR)*) that was generated by Tol2 transposase technique, immersed in 220 mM glucose solution for 30 days. In order to measure blood glucose level and evaluate the stability of hyperglycemia and other biochemical parameters for subsequent studies, blood collection performed repeatedly.
Results: All experiment conducted in triplicate and results showed that the average blood glucose level in the treatment group (137mg/dl) increased by 4 times compared to the control group (38mg/dl).
Conclusion: These data suggested that the exposure concentration and time are enough to induce hyperglycemia and impaired peripheral glucose metabolism in adult zebrafish, and this transgenic model could be used to further study the effects of hyperglycemia on neural system.

Keywords: Diabetes Mellitus, Glucose, Hyperglycemia, Transgenic zebrafish, Diabetic neuropathy

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RNA sequencing revealed potential biomarkers in Iranian children with B-cell acute lymphoblastic leukemia

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Abstract

Backgrounds: B-ALL (B-cell acute lymphoblastic leukemia) ranks amongst the most common malignancies in pediatric patients, causing increased proliferation of immature lymphoid cells and resulting in reduction of normal bone marrow cells. As the search for approaches resulting in earlier diagnosis is still ongoing, novel biomarkers present an attractive target for studies as they may help in early detection and improve clinical outcomes. Thus, RNA sequencing (RNA-seq), a powerful technique for transcriptome profiling, presents an ideal tool for biomarker discovery. Here, we utilize the RNA-seq method to obtain a transcriptome profile of pediatric B-ALL patients to identify potential biomarkers.

Materials and Methods: Bone marrow aspiration samples were obtained from 10 newly diagnosed B-ALL patients and 2 Immune thrombocytopenic purpura (ITP) as non-malignant controls. Then, using Ficoll density gradient centrifugation, mononuclear cells were isolated, followed by total RNA extraction. Paired-end RNA sequencing (~100 million reads per sample) was performed on a NovaSeq6000 instrument. Raw RNA-seq data was processed and analyzed using bioinformatics tools. Our raw RNA-seq data are publically available at BioProject under PRJNA589314 accession.

Results: 1216 genes were upregulated and 920 downregulated as compared to the control group ($|\log2FC| \geq 2$, padj < 0.05). Functional analysis and protein-protein interaction networks revealed *ESR1*, *NRIP1*, *MYSM1*, *BCL7A*, *UCKL1*, *SPRING1* and *UBASH3B* may act as suitable biomarkers in pediatric B-ALL patients.

Conclusion: *ESR1*, *NRIP1*, *MYSM1*, *BCL7A*, *UCKL1*, *SPRING1* and *UBASH3B* may act as potential biomarkers in pediatric B-ALL patients. Further studies on larger datasets are necessary for validating results presented in this study.

Keywords: RNA sequencing, Transcriptome profiling, B-ALL

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Effects of DNA methylation on serum triglycerides level: A systematic review and meta-analysis

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Abstract

Backgrounds: Growing body of evidence showed that epigenetic modifications, including DNA methylation might be associated with lipid profile. Inconsistent results exist on the association of DNA methylation and serum triglycerides (TG) levels. This review aims to provide a summary of the literature evaluating the relation between the methylation of specific cytosine-phosphate-guanine (CpG) sites and serum TG levels.

Materials and Methods: A systematic literature search was conducted in Medline database (PubMed), Scopus, and Cochrane library up to September 2020. All observational studies (cross-sectional, case–control, and cohort) on adult populations were included. Studies that assessed the effect of DNA methylation of different CpG sites of *ABCG1*, *CPT1A*, and *SREBF1* genes on serum TG levels were selected. The STROBE checklist was used to assess the quality of included articles.

Results: Overall, ten studies were included in the quantitative synthesis. DNA methylation of *ABCG1* gene had significant positive association with TG levels (β = 0.045; 95% CI = 0.038-0.052, P heterogeneity < 0.001). There was significant inverse association between DNA methylation of *CPT1A* gene and serum TG levels (β = -0.026, 95% CI = -0.031, -0.021, P heterogeneity < 0.001). DNA methylation of *SREBF1* gene was positively and significantly associated with serum TG levels (β = 0.031; 95% CI =0.023-0.039, P heterogeneity < 0.001).

Conclusion: DNA methylation of *ABCG1* and *SREBF1* genes has positive association with serum TG level, whereas this association is opposite for *CPT1A* gene. DNA Methylation of cg06500161 and cg27243685 at ABCG1, cg00574958 and cg17058475 at CPT1A and cg11024682 at SREBF1 affect serum TG levels more than other sites.

Keywords: Triglycerides, Epigenomics, DNA methylation, Meta-analysis, Epigenetics

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Association of genetic polymorphism of 5HTTLPR with temperament in Persian medicine

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Abstract

Backgrounds: Because of its efficacy, accessibility, and affordability, traditional medicine (TM) is the major source of treatment for many people in different part of world. For all its effectiveness, since the science of TM are essentially based on the old since texts and practical experiences, the potency and safety of the curative methods of this system need to be confirmed through modern scientific approaches. One of the main factors in the Persian traditional medicine is temperament, which has important role in diagnosis and treatment of diseases. There is evidence which support the correlation of temperament with individual genetic background.

Materials and Methods: In this study we aimed to examine the association of serotonin transporter polymorphism (5HTTLPR) with hot and cold statuses of temperament in healthy individuals. Two hundred twenty-one males from Fars province, southern Iran were included in the study. Hot/cold status of temperament of volunteers was determined using a standard self-reported temperament identification scale. Polymerase chain reaction (PCR)-based method was applied to determine the 5HTTLPR genotypes.

Results: As the results of $\chi 2$ analysis revealed, the frequency of 5HTTLPR genotypes in the cold temperament group was not significantly differ from that in the warm temperament group ($\chi 2 = 1.04$, df = 2, P = 0.594).

Conclusion: Our data did not support the association of temperament and 5HTTLPR polymorphism. Further research with larger samples is required to clarify the association of temperament and genetic factors.

Keywords: Traditional medicine, Temperament, 5HTTLPR, Polymorphism

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rs10719 polymorphism in DROSHA gene may destroy binding site of has-miR-664a-3p and has-miR-1298-5p

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Abstract

Backgrounds: Breast cancer is the most common cancer for women worldwide and is main factor of cancer mortality. Single nucleotide polymorphisms (SNPs) in microRNA biosynthesis pathways may result in the less or gain of microRNA function that can act as an oncogenic or tumor-suppressive. Dysregulation of microRNA biogenesis pathway genes is involved in the initiation and progression of several human cancers including breast cancer. One of the most important genes in this field is DROSHA. Previous studies have shown that rs10719 is related remarkably to different cancer risks.

Materials and Methods: We performed a case-control examination of 100 breast cancer cases and 100 healthy controls to evaluate the association between rs10719 in DROSHA and breast cancer risk. Genomic DNA was extracted from blood samples. ARMS PCR was performed for detection of the rs10719 by designed primers.

Results: Statistical analysis showed that rs10719 polymorphism located in 3' untranslated region (UTR) of DROSHA gene was related to the enhanced risk of breast cancer. Additionally, this nucleotide substitution may destroy binding site of has-miR-664a-3p and has-miR-1298-5p which can cause high DROSHA protein expression in breast cancer cells.

Conclusion: Altogether, our results indicated that presence of DROSHA rs10719 polymorphism and high expression of DROSHA protein could be proper tumor markers in patients with breast cancer.

Keywords: Breast cancer, DROSHA, rs10719, ARMS PCR, Tumor markers

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Investigation of LNC HOTAIR in renal cell carcinoma and expression of this LNC

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Abstract

Backgrounds: Renal cell carcinoma is one of the most common cancers in the world that causes many deaths every year. Epigenetic changes in non-coding RNAs, including LNC RNA, are a leading cause of cancer. HOTAIR is an LNC RNA which, it causes cancerous growth through an uncontrolled progression of the cell cycle and increased metastasis in some cancers.
Materials and Methods: Our aim in this study was to investigate the role of this LNC RNA in the incidence of renal cell carcinoma. To study, LNC RNA disease 1 and LNC RNA disease 2 databases were selected and the role of this LNC RNA in renal cell carcinoma and its relationship with other LNC RNAs was investigated.
Results: According to Disease Association Statistics, the highest score is related to LNC HOTAIR and this LNC has a significant expression in renal cell carcinoma and also the expression of LNC HOTAIR is higher in people with tumors.
Conclusion: LNC RNA is a long non-coding RNA with a size of more than 200 nucleotides and can't be translated into protein. It also plays an important role in biological processes and regulation of gene expression and is used in understanding the biological sciences, especially diseases. This study is associated with HOTAIR LncRNA uptake and a strong association in kidney cancer and further expression of this Lnc in tumor cells.

Keywords: Lnc, HOTAIR, Renal carcinoma, Gene, Cancer

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Molecular docking study of some antiviral drugs against SARS-CoV-2 RNA-dependent RNA polymerase protein

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Abstract

Backgrounds: In late 2019, the world faced a pandemic called the new coronavirus (SARS-coV-2). Unfortunately, no effective drug has been approved for this disease so far, and the treatment options are very limited. One of the most important coronavirus proteins is RNA dependent RNA polymerase (RdRp). RdRp is responsible for replicating the genomic (+) ssRNA. An alternative way to quickly identify potentially approved drugs is to use a drug repositioning that manages new and emerging diseases.

Materials and Methods: In this study, RdRp was selected as the target and virtual screening was performed. The 3D structure of the RdRp was obtained from the protein data bank (PDB ID: 6M71 resolution 2.90 A) and its energy was minimized. 10 antiviral drugs as inhibitors were selected and their 3D structure was extracted from Drag Bank and their energy was minimized. Autodock 4.2 software was used to evaluate the affinity of antiviral drugs for RdRp. The binding site of the ligands to the RdRp was determined in the gridbox and its dimensions were set in GPF format. Finally, the algorithm was implemented and the results were analyzed.

Results: Among the 10 drugs Lopinavir, Saquinavir, Nelfinavir, Remdesivir, Amprenavir, Indinavir, Dasabuvir, Dolutegravir, Drarunavir, Ritonavir the first three drugs are superior and more effective. Hydrogen bonds, binding energy and inhibition constant (Ki) of these three drugs, including 0, -9.75 kcal/mol, 71.52 nM (Lopinavir), 3, -9.73 kcal/mol, 73.43 nM (Saquinavir), 5, -9.06 kcal/mol, 227.62nM (Nelfinavir) respectively.

Conclusion: Our studies show Lopinavir, Saquinavir, Nelfinavir work very well on RdRp and are recommended that more detailed studies, including animal and human studies, be performed.

Keywords: SARS-CoV-2, Molecular docking, RdRp, Saquinavir

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Bioinformatics evaluation of targetome LncRNA HOTAIR signaling pathways and related function of miR129-5p in breast cancer

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Abstract

Backgrounds: Breast Cancer (BC) is cancer that develops from breast tissue. about 5 to 10 percent of cases are due to genetic predisposition inherited from the individual's parents, including BRCA1, BRCA2, and others. Worldwide, breast cancer is the most advanced type of cancer in women, accounting for 25% of all cases. In 2018, it resulted in 2 million new cases and 627,000 deaths. The disease is more common in developed countries and is more than 100 times more common in women than men. The function of LncRNAs in BC involves RNA binding, degradation, transcription, and translation. They are involved in breast cancer by acting as inhibitors of tumors or tumor genes as well as interacting with DNA, RNA and proteins. Preliminary studies have shown that microRNA expression is characterized by abnormalities in many diseases such as cancer. MicroRNA expression profiles were demonstrated by tumor development, progression, and response to treatment, suggesting their potential use as diagnostic, prognostic, and predictive biomarkers.

Materials and Methods: Based on bioinformatics databases and studies by The Cancer Genome Atlas, LncRNA HOTAIR was selected to study breast cancer, then searched in various databases such as NCBI, mirbase, mirwalk, DAVID to achieve its goals.

Conclusion: Overall, I predict that in people with breast cancer, the expression of LncRNA HOTAIR, should increase, thus inhibiting the miRNA129-5p, and ultimately increase the *PRLR* gene expression and activate the cancer pathways.

Keywords: Breast cancer, LncRNAs, MicroRNAs, *PRLR* gene

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Bioinformatics analysis of Iranian medicinal plants in the treatment of brucellosis

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Abstract

Backgrounds: Brucellosis is a chronic and infectious disease common to humans and animals caused by bacteria of the genus Brucella, which are gram-negative and aerobic microorganisms. Currently, six species of Brucella are known: B. abortus, B. melitensis, B. suis, B. neotoma, B. ovis and B. canis. B. melitensis strain, which is also contagious to humans, is the most common in Iran .Due to the fact that wild pigs are not studied and vaccinated in Iran, and these animals live very close to rural areas, it can be said that controlling the disease through vaccination is almost impossible. Also, apart from the previously known ways of spreading the disease, poachers can cause the spread of the disease in humans and livestock.

Materials and Methods: After receiving the structure of B. melitensis strain catalase protein and its energy minimized, 70 ligands from 12 native Iranian medicinal plants were docked with Brucella bacterial protein catalase by Pyrex software in Autodac 4.2.

Results: The best docking results were related to a ligand called Abietic acid in Ferula assa-foetida with binding energy of -10.11 and Ki = 38.73 nM and also Stigmasterol in Pimpinella anisum with binding energy of -72.72 and Ki = 74.86 nM.

Conclusion: Due to the importance and prevalence of brucellosis in Iran and also the existence of deficiencies in animal vaccination in this disease and its non-eradication, the capacity of Iranian medicinal plants that are available can be used to treat patients and treat animals.

Keywords: Brucellosis, Treatment, Catalase, Iranian medicinal plants

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Significant association of BRCA1, BRCA2 and TP53 gene polymorphisms with breast cancer risk in Khyber Pakhtunkhwa, Pakistan

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Abstract

Backgrounds: Molecular characterization of breast cancer facilitates to understand the disease pathology and genes involvement such as *BRCA1*, *BRCA2* and *TP53*, the tumor suppressor genes responsible for maintaining the genomic stability. Polymorphisms in these genes have been investigated as a risk of breast cancer worldwide, but there is no such evidence from Khyber Pakhtunkhwa, Pakistan. We aimed to investigate the association of *BRCA1* (rs1799950), *BRCA2* (rs144848) and *TP53* (rs1042522) gene polymorphisms with breast cancer risk in the patients of Khyber Pakhtunkhwa, Pakistan.

Materials and Methods: A total of 220 (140 breast cancer patients and 80 healthy controls) were recruited. The genomic DNA was extracted from the peripheral blood cells and genotyping was performed using T-ARMS PCR technique.

Results: Our results indicated that the risk allele of all the selected SNPs showed statistically significant association with breast cancer, $p<0.05$ (*BRCA1*, C- $p = 0.001$); (*BRCA2*, C- $p = 0.000$) and (*TP53*, C- $p = 0.000$). Similarly, all the genotypes carrying risk allele were also significantly associated with the breast cancer risk with $p<0.05$ (*BRCA1*, TC- $p=0.037$, CC- $p = 0.005$); (*BRCA2*, AC- $p = 0.000$, CC- $p = 0.000$) and (*TP53*, GC- $p = 0.000$, CC- $p = 0.000$).

Conclusion: The risk allele and risk allele containing genotypes showed statistically significant association with breast cancer risk in our region. More investigation will be required to disseminate the results with large data sets and using whole genome sequencing.

Keywords: Breast cancer risk, *BRCA1*, *BRCA2*, *TP53*, Polymorphisms

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Investigation of Lnc DA125942 expression in colorectal cancer

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Abstract

Backgrounds: Colorectal cancer (CRC) accounts for 10% of global cancer incidence and 9.4% of cancer mortalities. LncRNAs involved in the tumor formation, angiogenesis, proliferation, migration, and etc. Bioinformatics studies showed that LncDA125942 may be involved in the progression and metastasis of CRC. On the other hand, co-expression of LncDA12594 and vitamin D receptor (VDR) has been demonstrated in the breast cancer. Vitamin D deficiency is associated with high rate of CRC incidence and mortality. The aim of this study was investigation of LncDA125942 expression in CRC tissue samples.

Materials and Methods: The colorectal tumor samples and adjacent normal tissue samples were collected from thirty patients. After total RNA extraction from samples and cDNA synthesis, Real-time PCR was used to measure the LncDA12594 expression. Paired t-test was used for comparison of LncDA12594 expression in tumor and normal samples.

Results: The results of qPCR showed that there is no statistically significant difference in the expression level of DA125942 between normal and tumor samples (p-value 0.8292). Expression of this Lnc in the metastatic patients and patients with higher stages of CRC is lower rather than other patients (p-value 0.0052).

Conclusion: Lnc DA125942 may acts as a tumor suppressor in the CRC and decrease of expression has important role in CRC progression and metastasis. This is suggested that the potential of this LncRNA as a biomarker in the different stages of CRC is evaluated in the large populations.

Keywords: LncDA125942, Colorectal cancer, Vitamin D receptor, Cancer progression, Cancer metastasis

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Comparison study of MeICT expression in pET32-Rh and pET32a cloning vectors

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Abstract

Backgrounds: Production of recombinant toxins with therapeutic applications is a challenging work because of high number of disulfide bonds. Numerous expression systems are currently used to produce recombinant proteins. The pET system is one of the strongest expression systems in *E. coli* that includes different vectors. We previously designed pET32Rh vector to purify recombinant proteins easier.

Materials and Methods: In the present study, the expression of MeICT encoding fragment, which was isolated from Iranian yellow scorpion, was cloned in standard pET32 and modified pET32a-Rh vectors. The vectors were transformed and expressed in *E. coli* (BL21). Different expression conditions such as temperature and time were investigated in this experiment. Then, the expression of MeICT was compared in the soluble and insoluble phases by SDS-PAGE. Finally, with the help of Image J software, the obtained results were quantified and statistically compared.

Results: Our results showed that expression of gene in pET32-Rh vector was comparable with standard vector. The expression of MeICT was detected in high amount in soluble phase of extracted protein for both vectors.

Conclusion: Due to easier purification in pEt32Rh compare to pET32, the high expression of MeICT showed that this vector could be a powerful system for the expression of toxin peptides with multiple disulfide bonds.

Keywords: MeICT, Recombinant toxins, pET32-Rh, pET32

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The effect of Crocin on breast cancer

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Abstract

Backgrounds: Cancers are one of the leading causes of death in the world. DNA damage caused by radioactivity is significantly involved in the development of cancers, and the factors that reduce their formation should reduce the risk of cancer. The role of antioxidants in the prevention and treatment of cancers has been reported by many studies. The aim of this study was to evaluate the effect of Crocin on breast cancer cell line.

Materials and Methods: Breast cell line was treated with different concentrations of Crocin. The effect of Crocin on cell mortality was measured by MTT method. In this test, cells were counted with trypan blue and 10,000 cells were cultured in 96-well plates and the cells were treated for 48 hours.

Results: The test results were evaluated by MTT test. The treated cells had a higher mortality rate than the control group. This mortality was dose-dependent, which increased cell death with increasing dose. IC50 for breast cancer 51 µg / ml was calculated.

Conclusion: MTT test results showed that Crocin dose had a significant effect on cancer cell death and 72 hours of treatment had the best results ($p < 0.05$). The effect of Crocin on cancer cell death was due to its antioxidant effect, which was in line with other researchers.

Keywords: Antioxidant, Crocin, Breast cancer, MTT

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Evaluation of *GAB1* role in pediatric B-cell acute lymphoblastic leukemia

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Abstract

Backgrounds: Acute lymphoblastic leukemia (ALL) is a malignancy in which excessive proliferation of immature lymphoid cells leads to reduction of normal bone marrow cells. It most commonly affects B lymphoblasts where it results in B-ALL and is the most frequent pediatric cancer. A better pathophysiological understanding of this cancer may help create treatment options with less side effects and toxicity. Thus, *GAB1* (Grb2-associated binder 1), an adaptor protein involved in intracellular signal transduction by receptor tyrosine kinases, may be of special interest as it plays an important role in the development of various cancers. However, its role in B-ALL is still unclear. Differential gene expression (DGE) and co-expression analyses may help to explain the role of *GAB1* in this malignancy.

Materials and Methods: RNA-seq raw data samples were obtained from 4 datasets of BioProject at NCBI database. After pre-processing, data normalization and DGE analysis were performed using the DESeq2 package in R. Then, for gene co-expression and correlation analysis of *GAB1*, WGCNA (Weighted correlation network analysis) package in R and GraphPad Prism were utilized, respectively.

Results: *GAB1* was differentially expressed in B-ALL patients compared to the control group (log2FC= 4.90, p< 0.0001). Based on the WGCNA algorithm, *PXDN*, *RN7SL1*, *LEF1*, *NRIP1* and *UBASH3B* genes had the most significantly related co-expression with *GAB1*. Also, their positive correlation confirmed in GraphPad Prism.

Conclusion: Based on our findings, overexpression of *GAB1* may result in upregulation of genes responsible for cell growth and proliferation. Indeed, *GAB1* may play an important role in increasing the proliferation of immature B cells.

Keywords: *GAB1*, RNA-seq, Differential expression, B-ALL

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Alterations in the genes expression profile of hematopoietic stem cell lead to pediatric B-cell acute lymphoblastic leukemia

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Abstract

Backgrounds: Pediatric B-cell acute lymphoblastic lymphoma (B-ALL) is characterized by the lymphoid progenitor cells' exponential proliferation inside the bone marrow. Numerous studies conveyed that the tumorigenesis of B-ALL is associated with several mutations, including ETV6-RUNX1, BCR-ABL-1, RAS, and PI3K, that are leading to cell cycle dysregulation. One of the important things to mention is that perturbation of hematopoietic stem cells (HSCs) homeostasis leads to malignancy. In this study, we analyzed online databases to find novel biomarkers in patients with pediatric B-ALL.

Materials and Methods: The GEO database was searched for pediatric B-ALL, the expression array with accession number GSE128254 was selected. Afterward, via the GEO2R, the data of patients with ALL were compared with normal controls. The genes with altered expression (|logFC| >1) were analyzed by Cytoscape 3.8, and hub genes were demonstrated. Differentially expressed genes (DEGs) were analyzed to reveal the genes ontology and protein-protein interaction.

Results: The KEGG pathway analyses conveyed that DEGs were strongly associated with the proteoglycans in cancer, focal adhesion, and programmed cell death. Interestingly, most of these genes are in the extracellular region part with protein binding function. Nine hub genes were identified from the PPI network in which four genes (*CD44*, *CD34*, *TNF*, and *IL1B*) had a potential impact on the hematopoietic cell lineage differentiation pathway were selected. Ultimately, gene expression analyzes revealed that *CD44 w*as significantly downregulated. On the other hand, *CD34* and *TNF* were significantly upregulated, while the expression of IL1B was not significantly altered in tumoral cells compared to normal cells.

Conclusion: These results revealed that perturbations in the hematopoietic cell differentiation could be one of the main reasons for tumorigenesis in lymphoid progenitor cells and could be served as potential biomarkers.

Keywords: Bioinformatics, Acute lymphoblastic lymphoma, DNA methylation

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Effects of *HAMP* gene polymorphism on iron over load β-Thalassemia Iraqi patients

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Abstract

Backgrounds: β-Thalassemia is an inherited blood disorder. Thalassemia patients need repeated blood transfusion which leads to iron overload. This study aims to investigate the possible association between serum Hepcidin level and the presence of c–582A>G polymorphism (rs10421768) in the promoter of the *HAMP* gene which encoded HAMP protein or the effects of these gene's polymorphisms on iron overload in the thalassemia patients.
Materials and Methods: This case-control study included 200 blood samples (100 patients and 100 controls). The patient was diagnosed with thalassemia syndrome patient was regularly attending the hematology clinic in Thalassemia hematology center in Al Kut women &children Hospital, either for transfusion and chelation and follow up of Hb level and iron status. The β-thalassemia diagnosis was based on clinical presentation, hematological indices, iron overload, and hemoglobin electrophoresis. Hepcidin levels along with iron parameters were measured, DNA was extracted from the blood cells and the polymorphisms were determined using PCR-RFLP.
Results: The genetic analysis of the SNP, for the *HAMP* gene by using the PCR-RFLP technique that there was a significant difference in genotype polymorphisms between patients and control by using the same technique above.
Conclusion: The polymorphism of the *HAMP* gene was associated with patients, but didn't impact physiological parameters.

Keywords: β-Thalassemia, Polymorphism, *HAMP* Gene

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A post-mortem diagnosis of infantile-onset Pompe disease in an Iranian family

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Abstract

Backgrounds: Pompe disease, also called glycogen storage disease type II, is a kind of lysosomal storage disease causes glycogen storage in body cells especially in heart, liver and muscle. The most important features of disease are HCM (hypertrophic cardiomyopathy), respiratory distress and failure to thrive. The frequency of Pompe disease is between 1/9000 and 1/40,000. Pompe disease has autosomal recessive inheritance and caused by mutations in *GAA* gene that codes alpha-glucosidase (α-1,4-glucosidase). The role of this enzyme is degradation of glycogen in lysosome. In the present study, we are reporting a case of infantile-onset Pompe disease in an 18 months' infant.

Materials and Methods: The case is an 18 months' infant with the symptoms of macroglossia and heart disorders. He was clinically diagnosed for Pompe disease. Metabolic enzyme testing was positive for him but negative for his parents. Sometimes later the infant died. The parents' marriage was not consanguineous. The parent's blood specimens were collected and DNA extraction was done. Whole exome sequencing (WES) using Illumina HiSeq4000 platform was performed.

Results: The c.896T>C (p. Leu299Pro) and c.2015G>A (p. Arg672Gln) mutations in *GAA* gene were found in WES analysis in mother and father, respectively. According to American College of Medical Genetics (ACMG), the variants were pathogenic. Both parents were career and the deceased infant was compound heterozygous for *GAA* gene.

Conclusion: In this case, WES as a powerful diagnostic tool helped us to confirm the clinical diagnosis of Pompe disease. PND (prenatal diagnosis) for future pregnancies and genetic counseling for other members of family were suggested.

Keywords: Pompe disease, WES, *GAA* gene, Compound heterozygous, Post-mortem

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Novel frameshift mutation in *SLC12A2* gene associated with severe phenotype of Allan-Herndon-Dudley syndrome (AHDS)

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Abstract

Backgrounds: Allan-Herndon-Dudley syndrome (AHDS) is an X-linked syndrome with neuromuscular involvement characterized by infantile hypotonia, muscular hypoplasia, spastic paraparesis, and cognitive deficiency. It is mostly caused by *SLC16A2* gene (Xq13.2) mutations which encode a transporter protein. Monocarboxylate transporter 8 (MCT8) transports thyroid hormone T3 to nerve. In this study we report a two-and-a-half-year-old boy with AHDS diagnosis and a novel mutation in *SLC16A2* gene manifesting normal level of T4 but high level of TSH hormone.

Materials and Methods: We present a two-and-a-half-year-old boy who was admitted to our clinic for ID evaluation. He was born from unrelated parents. By the time he was 24 days old an increase was observed in SGOT and SGPT levels which can be a sign of brain damage. Sensorineural hearing loss in the right ear (moderate) and left ear (mild) was detected. He was unable to walk, speak and feed independently. Blood sample was collected and whole exome sequencing (WES) using Illumina HiSeq4000 platform was performed.

Results: A rare c.1015dupT (p. P338fs) mutation in *SLC16A2* gene which is hemizygous was detected in WES analysis. We consider this mutation as pathogenic mutation which caused the patient's phenotype. Heterozygous c.344T>A (p. Val 15 Glu) mutation on *UFSP2* gene and heterozygous c.12394delC (p. L4132fs) mutation on *USH2A* gene are reported as incidental findings, these variants were previously reported as pathogenic.

Conclusion: In this case, WES as a powerful diagnostic tool helped us to confirm the clinical diagnosis of Allan-Herndon-Dudley syndrome. PND (prenatal diagnosis) for future pregnancies and genetic counseling for other members of family were suggested.

Keywords: Allan–Herndon–Dudley syndrome, Paroxysmal dyskinesias, Free triiodothyronine, *SLC16A2* gene, Mutation

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Design and cloning of recombinant antimicrobial peptide Melittin-IMekn2

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Abstract

Backgrounds: Today, using of antimicrobial peptides is an important issue due to the antibiotic resistance of pathogenic microbes. Different organisms such as venomous animals produce a wide range of these peptides. Antimicrobial peptides disrupt the integrity of cell membranes and interact with intracellular targets. Peptide 26 amino acids called Melittin isolated from the venom of honey bee, *Apis mellifera* and peptide 13 amino acid called IMekn2 were isolated from the venom of Iranian scorpion *Mesobuthus eupeus* are two antimicrobial peptides that have been proven to have antibacterial properties. IMekn2 is similar to BmKn2 that is an antimicrobial peptide isolated from *Mesobuthus martensii Karsch* scorpion and shows strong antibacterial activities against gram-positive and gram-negative bacteria.

Materials and Methods: The aim of this study was construction and cloning of a fusion fragment containing Melittin and IMekn2. For this purpose, the design and property of fusion peptide was investigated by in silico studies such as ConSSert, RaptorX, ExPASY and HeliQuest servers. IMekn2 and Melittin were amplified with special primers for each fragment and enzymatically digested.

Results: The fusion fragments were ligated together by the ligase and then were amplified by PCR and cloned into prokaryotic expression vector called pET32b (+). The cloning of Melittin-IMekn2 was determined by colony-PCR and sequencing. Bioinformatics studies showed its helical structure and hydrophobicity. In addition, the antimicrobial activities of Melittin-IMekn2 fusion peptide was also increased compare with two separate peptides.

Conclusion: These results suggest that Melittin-IMekn2 fusion peptide may be an effective antimicrobial agent for the treatment of antibiotic-resistant infections.

Keywords: Antimicrobial peptides, Melittin, Bmkn2, IMekn2, PCR

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Meta-analysis of chronic gastritis developing into gastric cancer by gene expression profiles

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Abstract

Backgrounds: Gastric adenocarcinoma is one of the most typical cancers in the world and threatening many lives. The expression and function of genes implicated in the development of chronic gastritis (cGAS) to gastric cancer (GC) remain unclear. Understanding how cGAS develops into GC may lead to novel preventive and treatment approaches.

Materials and Methods: Differentially Expressed Genes (DEGs) from cGAS samples of GSE106656 and GSE55696 compared to primary GC samples of GSE15456 datasets were identified by integrated analysis using R software; following these criteria: $|log_2FC| > 0.5$ and *P*-value <0.05. The protein-protein interaction (PPI) network was built using the STRING database and analyzed by Cytoscape software to discover hub genes. The R package "Clusterprofiler" was used to conduct pathway enrichment analysis.

Results: 237 DEGs (27 up-regulated and 210 down-regulated) were identified. DEGs enriched mainly in cytosolic ribosome according to Gene Ontology (GO); Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis enriched in ribosome, coronavirus disease - COVID-19, maturity onset diabetes of the young, and gastric acid secretion. Ribosomal protein S10 (RPS10), MDM4 regulator of p53 (MDM4), actin alpha 1, skeletal muscle (ACTA1), and tryptophan hydroxylase 1 (TPH1) were identified as four hub genes and could be used as potential therapeutic targets.

Conclusion: In conclusion, we identified four genes associated with the initiation and progression of GC. Analyzing the de-regulation of genes can help us understand how cGAS develops to GC and may provide novel biomarkers for early diagnosis of primary GC.

Keywords: Gastric cancer, Chronic gastritis, Gene expression analysis, Bioinformatics, Meta-analysis

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In-silico analysis of pathogenic SNPs in *JAG1* gene

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Abstract

Backgrounds: The Notch signaling pathway is an important participator in the development and homeostasis of the cardiovascular system. Mutations in Notch receptors and ligands have been identified that impact both the heart and the vasculature. Mutations in the gene encoding the human Notch ligand jagged 1 result in a pleiotropic disorder called Alagille syndrome. Cardiac defects are seen in more than 95% of AGS patients. To identify the structural and functional effects of mutations, various powerful bioinformatics tools are available. The aim of this study is the identification of high-risk non-synonymous single nucleotide variants in the *JAG1* gene via bioinformatics tools.

Materials and Methods: SNPs for the *JAG1* gene were collected from a web-based data source such as NCBI/dbSNP database. Among the identified polymorphisms in this gene, 860 missense variants are retrieved. Deleterious single-nucleotide polymorphisms (SNPs) were screened using the bioinformatics tools such as SIFT, Pplyphen-2, PHD-SNP, PROVEAN, PANTHER and PMut servers.

Results: We found 860 missense mutations in *JAG1* Gene and 16 of 860 mutations were pathogenic. The results obtained from the set of bioinformatics tools identify 8 high-risk mutations in the *JAG1* gene.

Conclusion: Collectively, eight mutations including G274D, R184C, L37S, C693T, C78S, C78Y, C78G and C78R for further studies were identified. A Better understanding of related diseases caused by mutations in the *JAG1* gene was achieved using *in-silico* prediction. All of these mutations organized possible candidates for further genetic studies.

Keywords: Notch, *JAG1*, Gene, SNP, Mutation

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TT genotype at rs4516035 is associated with increased susceptibility to osteoporosis in South-Eastern Iranian people

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Abstract

Backgrounds: Osteoporosis is a wide-spread disease with a major impact on families and society. In addition to calcium and vitamin D deficiency, genetic factors also play a crucial role in the development of this disease. Any reduction in the function of Vitamin D receptor (*VDR*) can lead to osteoporosis.

Materials and Methods: In this study, we selected six SNPs (rs11568820, rs4516035, rs2228570, rs1544410, rs7975232 and rs731236) in the *VDR* gene. The genotype of SNPs was studied by PCR-RFLP, T-ARMS-PCR and sequencing in two groups of osteoporotic patients (n = 40) and control (n = 42). The levels of calcium and vitamin D_3 in patient's blood were also measured. The association between the SNPs and the incidence of osteoporosis was measured by calculating odds ratio (OR).

Results: Despite having osteoporosis, none of the patients had calcium or severe vitamin D_3 deficiency. The results of PCR showed that among the six SNPs, only the TT genotype at the rs4516035 locus significantly increased the chance of disease by 3.061 times (*P* value = 0.007). The presence of C allele at this position adds 50 amino acids to the protein and produces the longer VDRB1 variant with 477 residues. The response to the vitamin D and the activity of VDRB1 is more than the ordinary variant, VDRA which has 427 residues.

Conclusion: Collectively, our data indicates the presence of VDRA variant in peoples which have TT genotype could be the reason for lesser activity of VDR and their greater susceptibility to osteoporosis.

Keywords: Osteoporosis, Single nucleotide polymorphism, VDR, rs4516035, Odds ratio

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The anti-proliferative effect of Moringa olifera aqueous leaf extracts on acute lymphoblastic leukemia cells

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Abstract

Backgrounds: Acute lymphoblastic leukemia (ALL) is the most common hematology malignancy in children. Use of natural compounds in the treatment of ALL has been considered, due to the side effects and toxicity of traditional chemotherapy. The aim of this study was to evaluate the anti-proliferative effect of Moringa olifera aqueous leaf extract in Raji and Jurkat acute lymphoblastic cell lines.

Materials and Methods: After preparing the aqueous leaf extract by soaking, the cells were cultured separately and treated with different concentrations of the extract for 48 hours. Cell viability and growth inhibition were assessed by trypan blue and MTT assay. Changes in P21 proapoptotic gene expression were assessed by real time PCR. Data were analyzed using SPSS 23 and one-way ANOVA method.

Results: Concentrations of 50 to 250 µg/ml of the extract significantly reduced the growth of Raji and Jurkat cell lines ($p<0.001$). The highest growth inhibition rates for concentration 50 µg/ml were 73.4% for Jurkat and 78.5% for Raji cell lines. IC50 was obtained at a concentration of 150 µg/ml. Treatment of cells with this concentration resulted in a 147-fold increase in *P21* gene expression for Jurkat ($p = 0.0091$) and 15-fold increase for Raji ($p = 0.0026$) cell lines.

Conclusion: Moringa olifera aqueous leaf extracts appeared to be able to inhibit growth and increase apoptosis in Raji and Jurkat cell lines. It can be concluded that the use of Moringa leaves as a medicinal or nutritional supplement is useful in the treatment of ALL.

Keywords: Acute lymphoblastic leukemia, Moringa olifera, Jurkat, Raji

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Investigation of changes in the expression of pro-inflammatory cytokines caused by extract Silybum marianum L. in in-vitro and in-vivo

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Abstract

Backgrounds: In the present paper, we effort to inquire the effects of alcoholic extract Silybum marianum L. (AESM) on in vitro and in vivo anti-inflammation and the alleviation of cartilage degradation in the Rabbit model of monosodium iodoacetate (MIA)-induced osteoarthriti. We realize that Silybum marianum L can efficiently and dose-dependently repress the expression of pro-inflammatory cytokines mRNA, including iL-6, iL-1α, iL-18, and TNF-α in LPS-stimulated synoviocytes. Researchers indicate that Silymarin is a compound contains various properties like anti-inflammatory hepatoprotective, antioxidant, heart-protective, hypocholesterolemic, anti-diabetic, anticancer, and cardio-protective activities. Clinical studies have been demonstrated that Silymarin has very rare side effects at high doses (>1500 mg/day).
Materials and Methods: RNA extraction by ®TRIzol method (SinaClon, Iran), Convert RNA to cDNA (Malaysia-Selangor), evaluation of gene expression such as iL-6, iL-1α, iL-18, and TNF-α by RT-PCR, simulation of OA with the help of MIA, extraction with a rotary evaporator vacuum device, the MTT technique, isolation and culture of RFLS.
Results: AESM decreased the expression of iL-6, iL-1α, iL-18, and TNF-α genes in RFLS cells and in cartilage.
Conclusion: AESM can compete significantly with drugs such as dexamethasone and ibuprofen in the treatment of OA. Our experiments indicated that consumption administration of AESM reduces the expression of TNF-α, iL-6, *iL-1α* and *iL-18* genes and can compete well with common drugs in the treatment of OA.

Keywords: Silybum marianum L, MIA, pro-inflammatory cytokines, Osteoarthritis

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Investigation of LincNRAV expression in colorectal cancer

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Abstract

Backgrounds: Colorectal cancer (CRC) is the fourth most common but silent cancer in Iran. Long noncoding RNAs (LincRNAs) involve in the tumor formation, angiogenesis, proliferation, migration, apoptosis and differentiation. Previous studies on role of LincNRAV in several cancers and respiratory diseases showed LincNRAV effects on Rab5c, miR-509-P3, and MAP3K8, directly and indirectly. These genes involve in CRC progression and chemotherapy resistant. Based on these evidences, the aim of this study was investigation of LincNRAV expression in CRC tissue samples and evaluation of its potential as diagnostic biomarker in this cancer for first time.

Materials and Methods: The colorectal tumor samples and adjacent normal tissue samples were collected from thirty patients. After total RNA extraction from samples and cDNA synthesis, Real-time PCR was used to measure the LincNRAV expression.

Results: The qPCR results showed that the expression of LincNRAV was down-regulated in colorectal cancer specimens compared to normal tissue samples (p-value = 0.0038). The AUC of ROC curve was 0.67 and revealed that the expression level of LincNRAV can detect up to 67% of cases of colorectal cancer.

Conclusion: The considerably down-regulation of LincNRAV in CRC tumor samples and its potential as biomarker highlight the need to further investigation of this LncRNA in larger population and cohort studies.

Keywords: Colorectal cancer, Linc RNA NRAV, Rab5c, miR-509-P3, MAP3K8

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Study of *NGF*, *PAX3*, and *NSE* genes expression in bone marrow-derived mesenchymal stem cells after treatment by Glabridin for differentiation into nerve-like cell

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Abstract

Backgrounds: Glabridin extracted from the licorice root. The potential differentiation of BMSCs into nerve-like cells has been approved in the in-vitro, the effectiveness of Glabridin in differentiation of these cells by the mediating role of gene expression to find a solution for improving the nervous system disorders. Changes the expression of the genes NGF, PAX3, NSE in differentiation of BMSCs into the nerve cells by Glabridin were studied.
Materials and Methods: BMSCs with different Glabridin concentrations of 5, 10, 20, 40, 80 µM were induced for 24 hours. The glabridin toxicity was tested by MTT assay. The changes in the expression of *NGF, PAX3, NSE* genes were evaluated by Real-time PCR.
Results: MTT showed that the cells died in 40, 80 µM concentration in 24h treatments, the expression of the genes *NGF, NSE* increased compared to the control group, the expression of gene *PAX3* decreased.
Conclusion: Treatment of BMSCs with Glabridin increased the expression of *NGF, NSE* genes and decreased the expression of PAX3 to these cells into neuron-like cells.

Keywords: Mesenchymal stem cells, Bone marrow, Nerve-like cells, Glabridin

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Investigation of frequency of *VKORC1* gene polymorphisms in Warfarin treated patients in Rafsanjan

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Abstract

Backgrounds: Warfarin is one of the most important oral anticoagulants that are prescribed in the process of preventing blood coagulation based on the needs of individuals. Age, sex, diet, used medications and most importantly genetic factors are important factors in determining the dose of Warfarin. Some *VKORC1* gene polymorphisms, which express the C1 subunit of *VKOR* vitamin K epoxide reductase, are responsible for Warfarin resistance and sensitivity. The present study investigated the frequency of *VKORC1* gene polymorphisms in patients treated with Warfarin in Rafsanjan.

Materials and Methods: In this cross-sectional study, -1369G>A gene polymorphism was determined by PCR-RFLP method on 113 patients taking Warfarin. Statistical analyzes were performed with SPSS software version 25 to investigate the correlation between patients' demographic data and Warfarin dose.

Results: After comparing the mean dose of Warfarin, there was no significant difference statistically in the dose of warfarin with age and sex in relation to this polymorphism, but AA and GG genotype were required the lowest and the highest dose of warfarin in patients, respectively.

Conclusion: It seems that in addition to the mentioned polymorphism, the relationship between Warfarin consumption and alleles of other genes as well as environmental conditions may depend on their effect on Warfarin consumption. It needs to perform more studies.

Keywords: Anticoagulation, Warfarin, Genetic polymorphism, *VKORC1*

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Design of a common vaccine against influenza and SARS-COV-2 viruses by using *In Silico* tools

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Abstract

Backgrounds: Among various infections, acute respiratory tract infections (ARTIs) have the highest incidence and mortality in the world. These infections are caused by various microorganisms such as the influenza virus and SARS-COV-2. The potential effect of influenza alongside COVID-19 on mortality, morbidity and health-service capacity is a main concern, although, recently, little is understood about the interaction between these two pathogenic respiratory viruses. So, there is an urgent need to design and develop efficient vaccines to prevent further cases of these diseases. In this study, we designed a novel multi-epitope vaccine against influenza and SARS-COV-2 infections.

Materials and Methods: HA, M1 proteins from influenza virus and S, E, M proteins from SARS-COV-2 virus were analyzed for use in vaccine structure. The B cell and T cell epitopes identification, energy minimization, prediction of Interferon-gamma response, allergenicity, toxicity was performed using different bioinformatics tools. The best peptides were selected after molecular docking. The selected epitopes were fused by linkers to make the multi-epitope vaccine. 3D model of the vaccine candidate was generated by I-TASSER server.

Results: The results indicated that the designed vaccine candidate is non-allergen, nontoxic with high stability and immunogenicity.

Conclusion: Altogether, the new multi-epitope vaccine can be an appropriate vaccine candidate against Influenza and SARS-COV-2 infections.

Keywords: Influenza, SARS-COV-2, *In silico*, Molecular docking, Peptide

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Protective effect of HLA-E*0101/*0103 genotype in survival of patients after allogeneic hematopoietic stem cell transplant

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Abstract

Backgrounds: HLA-E is located on the non-classical major histocompatibility complex class I and acts as the ligand for natural killer cells. Consequently, it has a main role in the regulation of innate immune responses by involving cell identification by natural killer cells. Differences in expression levels among HLA-E alleles have been suggested to affect transplant outcomes. In this study, we evaluated the effects of different HLA-E genotypes on allogeneic hematopoietic stem cell transplant in southern Iran.

Materials and Methods: We investigated 200 patients who underwent allogeneic hematopoietic stem-cell transplant and 100 normal participants (control group) in a case-control study. Detection of HLA-E polymorphisms was performed using a sequence-specific primer polymerase chain reaction method.

Results: Statistical analyses indicated that genotypes in the transplant group were not distributed in accordance with Hardy-Weinberg equilibrium ($\chi 2 = 76.56$; $P < .001$), whereas genotypes in the control group were distributed in accordance with Hardy-Weinberg equilibrium ($\chi 2 = 0.39$; $P = .53$). No significant differences were observed in cumulative incidence of acute ($P = .76$; hazard ratio = 0.80; 95% confidence interval, 0.19-3.31) and chronic ($P = .75$, hazard ratio = 0.048; 95% confidence interval, 0.00).

Conclusion: Genotypes of the HLA-E molecule did not correlate with acute and chronic graft-versus-host disease in hematopoietic stem cell transplant recipients except for the HLA-E*0101*/*0103 genotype, which was protective in survival of our study patients.

Keywords: Graft-versus-host disease, Human leukocyte antigen E

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Design of a SNaPshot assay for simple and cost-effective detection of six variant related to recurrent pregnancy loss

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Abstract

Backgrounds: Applying karyotyping as conventional approach is still mainly applicable in laboratory but a considerable proportion of RPL (recurrent pregnancy loss) is related to single-gene alteration such as mutation, insertion and etc. Our aim in this study was to design and development a genetically panel using SNaPshot method besides karyotyping.
Materials and Methods: Six specific primers were designed to amplify target region involved in pathogenesis of RPL through multiplex PCR method. Specific single base extension (SBE) designed in order to mini-sequencing six mutation site by the SNaPshot simultaneously. The SBE products were electrophoresed in an ABI 3130xl Genetic TM Analyzer) using POP-4 polymer and 35 cm capillary arrays. The GenMapper v3.2 software was used to analyze the resulting electropherograms.
Results: Our pilot study six mutation sites in 16 women with RPL were previously genotyped by real-time PCR, were used to test the accuracy and reproducibility of multiplex SNaPshot assays. The results were compared with the previously analyzed types.
Conclusion: SNaPshot technique is specific, accurate and inexpensive approach to customized genetically panel and monitoring of frequent pathogenic mutation in RPL.

Keywords: Recurrent pregnancy loss, Multiplex, SNaPshot, Mini-sequencing, Genetically panel

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Identification of prognostic biomarkers in papillary thyroid cancer and developing non-invasive diagnostic models through integrated bioinformatics analysis

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Abstract

Backgrounds: Papillary thyroid cancer (PTC) is the most frequent subtype of thyroid carcinoma, which is mainly detected in patients bearing benign thyroid nodules (BTN). Due to the invasiveness of accurate diagnostic tests, currently there is a need to discover applicable biomarkers for PTC. So, in this study, we aimed to identify the genes associated with prognosis in PTC. Besides, we performed a machine learning tool in order to develop a non-invasive diagnostic approach for PTC.

Materials and Methods: for the purposes of the study, the miRNA dataset GSE130512 was downloaded from the GEO database and then analyzed to identify the common differentially expressed miRNAs in patients with non-metastatic PTC (nm-PTC)/metastatic PTC (m-PTC) compared with BTNs. As well, the SVM was applied to differentiate patients with PTC from those patients with BTN using the common DEMs. A protein-protein interaction network was also constructed based on the targets of the common DEMs. Thereafter, functional analysis was performed. Moreover, the hub genes were determined and survival analysis was then executed.

Results: A total of three common miRNAs were found to be differentially expressed among patients with nm-PTC/m-PTC compared with BTNs. In addition, it was established that the autophagosome maturation, ciliary basal body-plasma membrane docking, antigen processing as ubiquitination & proteasome degradation, and class I MHC mediated antigen processing & presentation are associated with the pathogenesis of PTC. Furthermore, it was illustrated that RPS6KB1, CCNT1, SP1, and CHD4 may serve as new potential biomarkers for PTC prognosis.

Conclusion: RPS6KB1, CCNT1, SP1, and CHD4 may be considered as new potential biomarkers used for prognostic aims in PTC. However, performing validation tests is inevitable in the future.

Keywords: Biomarkers, Machine learning, miRNAs, Papillary thyroid cancer, Prognosis, Protein interaction maps

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The relationship between *eNOS* gene expression and patients with type 2 diabetes and depression

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Abstract

Backgrounds: Type 2 diabetes mellitus (T2DM) is a metabolic disorder caused by hyperglycemia which is the most common form of diabetes and causes impairment in insulin secretion and insulin resistance. Increased inflammatory elements such as eNOS can be associated with type 2 diabetes and depression. Multiple studies show that depression is more common in patients with type 1 and type-2 diabetes than in healthy people. Worldwide, depression in diabetics is linked to the culture or society of countries. It is reported that 26% of patients with diabetes worldwide have depression.
Materials and Methods: After sampling, RNA extraction was performed using TRIzol method and qualitative analysis of RNA extracted by gel electrophoresis and also quantitative analysis of RNA extracted by Nano drop spectrophotometers. GAPDH and eNOS primers were then designed. Then, PCR reaction and cDNA synthesis were performed in order to amplify the desired fragments and finally, Real-time PCR was performed to evaluate the expression of the desired gene. SPSS software was used for data analysis.
Results: In the present paper, it was found that *eNOS* gene expression increased in case group compared to control group, which was not statistically significant ($p>0.05$).
Conclusion: Regarding the increase of this enzyme in the case group, it can be said that the concentration of reactive oxygen or nitrogen species such as superoxide, nitric oxide and peroxynitric can increase in conditions such as inflammation that inhibit the body's natural defense and antioxidant activities.

Keywords: Gene expression, *eNOS*, Type 2 diabetes, Depression, Real-time-PCR

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Pancreatic cancer and the effect of MALAT1 Lnc on it and the level of expression of this Lnc

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Abstract

Backgrounds: In 2015, pancreatic cancers killed 411,600 people worldwide. Epigenetic alterations in non-coding RNAs, especially LncRNAs, are carcinogens. It is an LncRNA that causes cancerous tumors in some cancers through uncontrolled progression of the cell cycle and by increased metastasis as well as cell migration. Our purpose in this study was to investigate the role of this LncRNA in the incidence of pancreatic cancer.
Materials and Methods: LncRNAdisease1, LnRNAcdisease2 and GEPIA 2 databases were used to examine this gene. In this study, the MALAT1 LncRNA and its high association with pancreatic cancer and its expression in healthy and tumor-bearing individuals were investigated.
Results: According to Disease Association Statistics, the highest score is related to MALAT1 Lnc, which has the highest score in pancreatic cancer, and also the expression of MALAT1 Lnc is higher in healthy people than in tumors.
Conclusion: LncRNAs are a long non-coding RNA that contains more than 200 nucleotides and cannot be translated into proteins and play an important role in biological processes and regulation of gene expression, especially in diseases. This study is related to the pathogenicity and strong role of this MALAT1 LncRNA in pancreatic cancer.

Keywords: Lnc, Cancer, MALAT1, Pancreas

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Analysis of *CFTR* gene variants and clinical presentations in children with idiopathic bronchiectasis and unknown etiology

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Abstract

Backgrounds: Idiopathic bronchiectasis is an irreversible abnormal dilation of proximal sub-segmental bronchi. The aim was to survey *CFTR* gene variants in pediatric idiopathic bronchiectasis.

Materials and Methods: All children with idiopathic bronchiectasis confirmed based on signs, symptoms, and HRCT findings and admitted to Tabriz Children's Hospital, Iran were surveyed from 2019 to 2020 duration a cross-sectional study. Demographic and clinical information was gathered by medical records and clinical examination and CFTR variants were investigated by liquid chromatography, direct sequencing, and multiple probe ligations tests. Then children were allocated into two groups based on CFTR variants when CF-causing mutations of varying clinical consequence variants were related to group 1, and polymorphisms related to group 2. Finally, two groups were compared in terms of demographic, clinical, and para-clinical findings. Descriptive statistics, Chi-square tests, and independent samples t-test were used to analyze the data using SPSS software version 22.0.

Results: Out of 21 patients, 10 (47.6%) children were males with a mean age of 9.75 years. Five clinically significant CFTR-related gene variants were identified (group 1). Other patients either had only a single polymorphism or no variants related to CFTR (group 2). Age, FEV1, and sweat tests were lower in group 1 than in group 2.

Conclusion: In this study, the CFTR variants in heterozygote types in pediatric diffuse bronchiectasis with a normal or borderline sweat test. Therefore, it is necessary to determine whether DB is a part of CFTR-related diseases failing to meet the diagnostic criteria of cystic fibrosis or a disease independent of cystic fibrosis.

Keywords: Idiopathic bronchiectasis, Children, CFTR variants, Cystic fibrosis

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Study of *PHOX2B, ELP1* and *MAP2* genes expression in bone marrow-derived mesenchymal stem cells after treatment by Glabridin for differentiation into nerve-like cell

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Abstract

Backgrounds: BMSCs can differentiate into neuron- like cells in vitro conditions. Important genes in this process are *ELP1*, *PHOX2B* and *MAP2*. Glabridin derived from the roots of licorice. Use of Glabridin on cell differentiation was studied. Changes made in the expression of *ELP1*, *PHOX2B* and *MAP2* genes by Glabridin effect in the pathway of differentiation of BMSCs to neuron- like cells was studied in this article.
Materials and Methods: BMSCs was incubated. Toxication levels of Glabridin were determined by MTT Assay test in concentrations of 5, 10, 20, 40 and 80 µM. CDNA was synthesized and the amount of change in gene expression was studied by real time PCR.
Results: Glabridin fatality dosage was tested by MTT in 40 and 80 µM concentrations and based on 24-hour analysis, *ELP1*, *PHOX2B* and *MAP2* gene expression in samples incubated with Glabridin had significant increase compared to the control group.
Conclusion: Results showed that Glabridin of BMSCs cause increased *ELP1*, *PHOX2B* and *MAP2* gene expression resulting in increase in their differentiation into neuron-like cells.

Keywords: Mesenchymal stem cells, Neuron- like cell, Glabridin

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The study of miR-15a and *BACE1* gene expression in patients with Alzheimer's disease

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Abstract

Backgrounds: Alzheimer's disease (AD), the most common form of dementia is a neurodegenerative disorder. BACE1 plays a critical role in AD pathophysiology by generation of Aβ which leads to accumulation of extracellular Aβ plaques. Some miRNAs like miR-15a are dysregulated in AD patients. Furthermore, *BACE1* is a target gene of some miRNAs. The objective of this study was to investigate the relative expression level of *BACE1* and miR-15a genes in Alzheimer patients.

Materials and Methods: Total RNA isolated from whole blood samples were used to synthesize cDNA for quantitative real time polymerase chain reaction analysis. The relative expression of *BACE1* and *miR-15a* were measured using comparative Ct method ($2^{-\Delta\Delta Ct}$) and normalized to *GAPDH* and U6 as internal controls. Statistical differences were analyzed by GraphPad Prism (v. 8.0) statistical software or Student's t-test.

Results: The results showed that *BACE1* was highly expressed in patients as compared to controls and this difference was statistically significant. There was also a significant decrease in miR-15a expression in patients' blood (0.72 ± 0.08) as compared to control subjects (0.95 ± 0.09).

Conclusion: According to our funding so far, a statistically significant increase in *BACE1*, and a decrease in miR-15a expression exist in AD samples. This suggests that an interaction/relation between these two genes may exist in AD patients. Our finding is in line with the previous reports showing the miR-15a expression was altered in AD patients so that both the down and up-regulations were reported in different studies. Furthermore, studies are needed to reveal the alternative underling pathway by which these genes interfere to lead to the AD pathology.

Keywords: Alzheimer's disease, miR-15a, *BACE1*, Neurodegenerative, Gene expression

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Evaluation of high cholesterol rs2967605 and rs6756629 polymorphisms of *RAB11B* and *ABCG5* and *ABCG8* genes in Isfahan population

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Abstract

Backgrounds: High cholesterol, also known as hypercholesterolemia, is a major risk factor for heart disease and stroke. The aim of this study was to investigate the possible association between rs6756629 and rs2967605 polymorphism in high cholesterol in a population of patients in Isfahan.
Materials and Methods: For this study, blood samples were obtained from 40 patients with high cholesterol and 40 blood samples from healthy individuals. Then, by tetra ARMS-PCR method, genotyping was performed using the obtained DNA sample.
Results: After statistical analysis of the relationship between mutant A allele and the risk of high cholesterol, it was concluded that there was a significant relationship between A allele and patients in rs2967605. Also the relationship between minor G allele and the risk of high cholesterol, it was concluded that there was a significant relationship between G allele and patients in rs6756629.
Conclusion: Results predict that the presence of the SNP allele in the *ABCG5* and *RAB11B* gene increases the risk of high cholesterol and can be used as a prognostic factor for high cholesterol.

Keywords: High cholesterol, rs6756629, rs2967605, *ABCG5*, *ABCG8*, *RAB11B*, Single nucleotide polymorphism

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The evaluation of *IRSp53* expression in colon cancer patients

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Abstract

Backgrounds: Colon cancer is the fourth most common cancer, with more than 550,000 associated deaths each year. This cancer is the third most common cancer in Iranian men and the fourth most common in Iranian women. This disease is kind of malignant tumor arising from the inner wall of the colon. Treatment for colon cancer usually includes surgery, radiation therapy, and chemotherapy. In this regard, the identifying new biomarkers or new targets in cancer therapy are considered to be interested for researchers. One of the significant proteins in cell motility, metastasis and invasion is IRSp53. IRSp53 is a key regulator of filopodia formation for cell motility which couples Rho GTPase and kinase signaling pathways with actin cytoskeleton remodeling and membrane tubulation. Implication of its inverse BAR (I-BAR) and other domains in tumor cell growth/ cell motility was shown.

Materials and Methods: In this study, a total of 30 tissue samples from 30 colon cancer patients and 30 healthy controls were collected to evaluate expression of *IRSp53* by using quantitative real-time PCR (qRT-PCR).

Results: Based on our results, we found that IRSp53 expression is a potential gene in diagnose of colon cancer. However, the more experiments will be required to find the molecular mechanism(s) of involvement of IRSp53 in colon cancer.

Conclusion: IRSp53 sounds to be a potential target in cancer therapy.

Keywords: IRSp53, Colon cancer, Biomarker

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In-silico study of rs1801157 and hsa-mir-149-5p single nucleotide polymorphisms related to *CLCX12* gene in patients with leukemia

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Abstract

Backgrounds: Acute myeloid leukemia (AML) is a cancer of the myeloid line of blood cells, characterized by the rapid growth of abnormal cells that build up in the bone marrow and blood and interfere with normal blood cell production. Chemokine-receptor axes are defined as factors involved in AML pathogenesis and prognosis. The chemokine receptor CXCR4 along with its ligand, CXCL12 fit in important players that are actively involved in the cross-talk between leukemia cells and bone marrow microenvironment. The *CXCL12* or *SDF1* gene is an antimicrobial gene that encodes an alpha-derived stromal cell. CXCL12 is produced by the BM microenvironment, binds and activates its cognate receptor CXCR4 on leukemic cells, facilitates leukemia cell trafficking and homing in the BM microenvironment, and keeps leukemic cells in close contact with the stromal cells and extracellular matrix that constitutively generate growth-promoting and anti-apoptotic signals.
Materials and Methods: A gene named is *CXCL12* one of the genes linked with this cancer. MicroRNAs linked to this gene were discovered using the miRNASNP database. A single nucleotide polymorphism called rs1801157 was discovered. The DAVID database of this microRNA picked the corresponding signals for further analysis.
Results: For OC, 1200 genes have been discovered. *CLCX12* genes were shown to have a high level of expression, while hsa-mir-149-5p had up-expression examination of OC signaling pathways, as well as the influence of this miR on gene targets.
Conclusion: These findings imply that CLCX12 could be a potential gene therapy target for gastric cancer. Blocking CLCX12 expression in leukemia cells induces apoptosis, which may provide a novel treatment approach.

Keywords: Leukemia, Cancer, Bioinformatics, *CLCX12* gene, MicroRNA (hsa-mir-149-5p), Single nucleotide polymorphism (rs1801157)

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Potential biomarkers and signaling pathways involved in helicobacter pylori-induced gastric cancer: A network-biology approach

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Abstract

Backgrounds: Gastric cancer (GC) is the second most frequent malignancy-related death worldwide. The 5-year survival rate of patients remains fragile. There is a requirement to discover biomarkers for prognosis approaches. Chronic infection with *Helicobacter pylori* (*H. Pylori*) is closely associated with the progression of GC. We aimed to identify the genes associated with poor/favorable prognosis in *H. Pylori*-induced GC.

Materials and Methods: The tissue miRNA dataset GSE54397 was obtained from the GEO database and analyzed to identify differentially expressed miRNAs (DEMs) in patients with *H. Pylori*-induced GC compared to *H. Pylori*-positive patients with non-cancerous tissue. A protein-protein interaction (PPI) network was built and analyzed. The biological processes (BPs) and pathways associated with genes involved in the main clusters were studied. The hub genes in the PPI network were identified, and the survival analysis was performed.

Results: A total of five DEMs were found with the criteria of $P < 0.01$ and the absolute value of Log2 fold change > 1. The most significant pathways and BPs affected in patients with *H. Pylori*-induced GC were primarily associated with the ubiquitination, neddylation, and ciliary process. Survival analysis illustrated that the overexpression of DOCK4, GNAS, CTGF, TGF-b1, ESR1, SELE, TIMP3, SMARCE1, and TXNIP was associated with poor prognosis, while increased expression of MRPS5 was associated with favorable prognosis in GC patients.

Conclusion: DOCK4, GNAS, CTGF, TGF-b1, ESR1, SELE, TIMP3, SMARCE1, TXNIP, and MRPS5 may be considered as prognostic biomarkers for *H. Pylori*-induced GC. However, confirmation is required in the future.

Keywords: Biomarkers, Helicobacter. Pylori, Prognosis, Protein interaction maps, Stomach neoplasms, Survival analysis

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Biological connections between *AHR* gene and the genes involving in human skin aging

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Abstract

Backgrounds: The skin acts as a protective barrier between the internal organs/body the environment. Skin properties such as hydration, elasticity, and antioxidant capacity play a key role in the skin aging process. *AHR* (aryl hydrocarbon receptor) is one of the involving genes in skin aging. Exposure of keratinocytes and skin fibroblasts to ultraviolet radiation, tobacco smoke *etc*. increases the expression and activity of MMP-1(matrix metalloprotease) in an AHR-dependent manner. As a result, activation of the *AHR* signaling pathway and increased CYP activity, leads to the formation of free radicals (ROS), collagen breakdown and the formation of wrinkles**.**
Materials and Methods: A systematic literature review was performed to collect the genes related to skin hydration, elasticity, and antioxidant capacity. GeneMANIA algorithm was used to recognize the biological connection among the genes. The gene network was created based on protein-protein interaction, genetic interaction, co-localization and pathway.
Results: We found 55 genes associated with skin aging. Systematic analysis showed that *AHR* gene has a biological relationship with *NFE2L2*, *IL6*, *PTGS2*, *CYP1B1*, *ALDH1A1* genes through co-localization and physical interaction. Likewise, we observed *JUN* gene has the most biological connections with the other skin aging genes.
Conclusion: This study shows that the *AHR* gene may be involved in the aging process of the skin by its antioxidant activity, elasticity, and its association with the other related genes. It introduces *JUN* gene as an important gene in skin aging. Our study provides insights about the prioritization of the genes are involving in skin aging.

Keywords: Skin aging, AHR gene, GeneMANIA, gene network

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Gene Cloning of Omega 6 Fatty acid as an Effective Dietary Supplement in Cancer Prevention in Yeast host

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Abstract

Background: γ-Linolenic acid (GLA), is a prominent omega6 polyunsaturated fatty acid that has a structural role in lipid membranes ingredients. In humans, GLA is metabolized to produce prostaglandins and eicosanoids such as leukotrienes which have many health and medicinal roles in cardiovascular disorders, cancers, inflammatory disorders, diabetes, and some other diseases by regulating the levels of expression in various genes. Some microorganism such *Mucor rouxii* is a typical oleaginous filamentous fungus has been widely used to investigate GLA production. The production of GLA in yeas is cost-effective than fungi as the present study focused on overexpression of delta-6 desaturase gene from *M. rouxii* to *Pichia pastoris*.

Materials and Methods: Fungus RNA was extracted by RNX- PLUS Kit and cDNA was synthetized. Purified products were ligated into pTZ57R/T vector according to the manufacturer's instructions and transformed using the heat shock method into *E. coli* DH5α competent cells prepared by chemical $CaCl_2$ method. After TA cloning gene was transformed to expression vector pPICZC.

Results: After transformation into *E. coli* DH5α, positive clones were selected with direct colony PCR screening. Finally, pPICZC - delta-6 desaturase plasmid was additionally confirmed by restriction enzyme digestion and sequencing. The GC assay of lipid combination was also evaluated and revealed 46% lipid production with 72.3 mg GLA in recombinant**.**

Conclusion: Recombinant yeast may provide an opportunity for the development of the method for industrial-scale GLA manufacturing.

Keywords: Omega 6, Cancer, Cloning, yeast

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Study of ZNF804A and DISC1 Genes in Iranian Patients with Schizophrenia

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Abstract

Background: The aim of this study was to investigate the relationship between polymorphism of ZNF804A and DISC1 genes in patients with schizophrenia in Iran.

Materials and Methods: In this case-control study, 50 patients with schizophrenia and 50 healthy controls were evaluated. The PCR-RFLP method was used to evaluate single nucleotide polymorphism in both groups of patients and control. For enzymatic digestion of PCR products, rs1344706 and rs6675281 were amplified and digested using MboI and BseLI enzymes at 37 ° C for 16 hours, respectively.

Results: The frequency of TT, GT and GG genotypes for ZNF804A gene in rs1344706 was 26%, 52%, and 22%, respectively, and in healthy subjects 46%, 42%, and 8%, respectively. In the DISC1 gene, the frequency of TT, CT and CC genotypes in the rs6675281 region was 2%, 14%, and 84%, respectively, and 2%, 14%, and 80%, respectively, in healthy subjects or controls, respectively.

Conclusion: Frequency of homozygous GG and heterozygote GT genotypes was 8% and 14% higher than healthy subjects, but the frequency of homozygous TT in healthy subjects was 22% higher than those with schizophrenia for ZNF804A gene in rs1344706 region. However, in case of DISC1 gene, the frequency of TT, CT and CC genotypes in the rs6675281 region was very similar in healthy and healthy subjects, and there was no significant difference between homozygous and heterozygous genotypes. Therefore, the result of our study can be a way to providing suitable information about the disease in order to prepare patients and family and to program adjusted treatment to prevent major injuries.

Keywords: Heterozygote; genotype; PCR-RFLP; schizophrenia.

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The importance of NFATc1 in endometriosis: a case-control study

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Abstract

Background: Endometriosis is a common, chronic inflammatory disease characterized by the presence of extrauterine endometrial tissue mainly on pelvic organs and tissues. It has been shown that the immune system has an important role in the development and increases the severity of the disease. NFAT (Nuclear Factor of Activated T Cells) proteins are transcription factors that are integral for the development and function of the immune system. The aim of this study was to evaluate the expression level of NFATc1 in endometriosis compare to eutopic endometrial tissue samples.

Materials and Methods: The case group consisted of 48 patients with pathological confirmation of endometriosis. Fifty endometrial specimens from patients who underwent laparoscopic examination for simple ovarian cysts were used as a control group. We performed quantitative real-time polymerase chain reaction (qRT-PCR) to determine the RNA expression changes in endometriotic and eutopic endometrial tissue samples. Total RNA was isolated from gastric tissue with TRIzol reagent. The purity and concentration of total RNA were assessed with a Nanodrop UV-Vis spectrophotometer at 260 and 280 nm. Quantitative measurements were performed in triplicate and relative expression was measured using comparative Ct method ($2^{-\Delta\Delta Ct}$) and normalized to *GAPDH* as internal control.

Results: In this study *NFATc1* expression in the ectopic endometria of endometriosis patients was significantly lower than that in the normal endometrium (1.01±0.05 vs 2.15±0.34, $p<0.05$).

Conclusion: Altered expression levels of NFATc1 were observed in the tissues of the ectopic endometrium. This is a first report of importance of NFATc1 in endometriosis. However, more research is needed to fully elucidate the underlying molecular mechanisms of endometriosis susceptibility.

Keywords: NFATc1; gene expression; endometriosis; real time PCR

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Investigation of *Ins2* gene expression change in polycystic ovary syndrome in mouse model

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Abstract

Background: Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women. The pathophysiological causes of this disease and the genetic inheritance pattern of PCOS are not yet known. One of the prevalent the disease is hyperinsulinemia, leading to increased production of androgen. Based on the studies of the genes involved in insulin production and function, it has been shown that insulin affects the pathogenesis of hyperandrogenism in PCOS.
Materials and Methods: In this study, the disease was induced by injecting of Estradiol valerate into female NMRI mice for 25 days and their ovarian tissue was removed. *Ins2* gene expression changes were evaluated by qRT-PCR technique using specific primers. The *GAPDH* gene was used as internal control.
Results: Analysis of qRT-PCR results was performed using GraphPad prism8 software. The Analysis showed that the relative expression level of *Ins2* gene in sick mice was significantly higher than the control group ($P < 0.05$).
Conclusion: We indicated that *Ins2* gene expression has correlation with PCOS, so we suggest the gene expression control maybe useful in PCOS treatment. Although it necessary to study the relationship between *Ins2* gene and PCOS in human.
Keywords: Polycystic ovary syndrome, Estradiol valerate, *Ins2* gene

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PARP1 expression in sporadic triple-negative breast cancer using bioinformatics analysis

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Abstract

Background: Poly (ADP-Ribose) Polymerase 1 (*PARP1*) expression as a target for PARP inhibitors has been under great attention in hereditary ovarian and breast cancer. However, *PARP1* expression status, as a target for these new inhibitors, is uncertain in sporadic triple-negative breast cancer (TNBC), which is a poor prognosis subtype of breast cancer without any targeted therapy. In this study, the *PARP1* expression status was investigated as a potential treatment target in sporadic TNBC tumours compared with non-TNBC or normal breast tissue samples using bioinformatics analysis.

Materials and Methods: Three gene datasets (ID: GSE65194, GSE76275 and GSE45827) with breast cancer and healthy breast tissue samples data (in total 280 TNBC tumours in comparison with 67 non-TNBC tumours and 22 normal breast tissue) were downloaded from the Gene Expression Omnibus (GEO) database. The GEO2R online tool was used to screen DEGs in which genes with adjusted *P*-value <0.05 and |log fold change (FC)| > 0 were considered as DEGs. Finally, the expression profile of *PARP1* was determined among DEGs in all datasets.

Results: Our results revealed significant overexpression of *PARP1* in the TNBC tumours compared with non-TNBC and healthy breast tissue samples (adjusted *P*-value <0.05 and logFC > 0) according to bioinformatics investigation in gene expression datasets.

Conclusion: It seems that the *PARP1* is overexpressed in sporadic triple-negative breast tumours compared with non-TNBC and healthy breast tissue samples. This finding can suggest further investigation concerning the potential application of *PARP1* inhibitors for the treatment of the TNBC subtype of sporadic breast cancer in future clinical trials.

Keywords: *PARP1* expression, TNBC, Bioinformatics, GEO

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Identification of crucial genes and pathways associated with esophageal squamous cell carcinoma based on weighted gene correlation network

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Abstract

Background: Esophageal squamous cell carcinoma (ESCC) is already a frequent and severe cancer around the world. The current study aimed to investigate mRNA expression profiles associated with ESCC in order to identify important hub genes involved in the cancer's development.

Materials and Methods: A weighted gene co-expression network analysis was performed using the GSE161533 dataset from the Gene Expression Omnibus (GEO) collection (WGCNA). The biological roles of the core gene modules were then discovered by enrichment analyses using Gene Ontology (GO) and the Kyoto Encyclopedia of Genes and Genomes (KEGG). A search for differentially expressed genes (DEGs) led to identification of genes with substantial variance (FDR of 0.05 and |log2FC| 2). Finally, to confirm the study's findings, an online database analysis was performed using XenaBrowser and GEIPA to analyses hub-gene expression and evaluates its diagnostic significance.

Results: The blue module (2197 genes) was the most important contributor to ESCC (r = 0.93, p-Value = 5e-25). This module's genes were discovered to be abundant in cytokine-cytokine receptor interaction, the IL-17 signaling pathway, and the TGF-beta signaling pathway, all of which are linked to cancer development. We found and confirmed five novel hub genes associated with ESCC (*KRT78, ENDOU, AIF1L, GYS2* and, *SFTA2*), all of which were validated by the databases provided.

Conclusion: In conclusion, these observations provide new visions into the mechanisms underlying the initiation, diagnosis and treatment of ESCC.

Keywords: Diagnosis, Esophageal squamous cell carcinoma, Molecular Pathogenicity, Transcriptome Analysis, WGCNA.

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Investigating the relationship between gene expression level of *MYC* gene and non-coding RNA lnc-mycbp-1-3 in Acute Lymphoblastic Leukemia

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Abstract

Background: In recent years, an increasing trend in the incidence of acute lymphoblastic leukemia (ALL) has been reported. However, the molecular mechanisms involved are not fully understood. Because of the importance of c-*MYC* in ALL pathogenesis, it is important to consider the associated lncRNAs in identifying the molecular mechanisms involved in disease progression. Therefore, the present study aimed to investigate the role of *MYC* gene and related LncRNAs as a potential target for the treatment of acute lymphoblastic leukemia.

Materials and Methods: This case-control study was performed on 40 ALL patients and 40 healthy controls in the years 2020-2021. For this purpose, total RNA was extracted from blood samples and after cDNA synthesis, *MYC*, lnc-mycbp-1-3 expression were measured using Real Time PCR. Statistical analysis of the results was performed using SPSS software and appropriate tests.

Results: The results of the gene expression study showed that in patients with ALL, *MYC* expression and related lncRNA lnc-mycbp-1-3 compared to controls had significant increases ($P < 0.05$). These expression changes were not significantly different in age, sex, MRD and T-ALL and B-ALL categories ($P > 0.05$). lncRNA lnc-mycbp-1-3 correlated with the *MYC* gene, and the ROC curve indicated their strong biomarker potential.

Conclusion: Using lncRNAs as diagnostic, prognostic and therapeutic markers can be a appropriate option that needs further research. According to the results of the present experiment, it is reported for the first time that lnc-mycbp-1-3 has increased expression in patients with ALL and can be used as strong biomarkers

Keywords: Acute lymphoblastic leukemia, *MYC* oncogene, lnc-mycbp-1-3, MRD

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Bioinformatics evaluation of hsa-miR-205-5p signaling pathways and related function of tp53 in patients with pancreatic cancer

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Abstract

Background: Pancreatic cancer is among the deadliest cancers and more than 331,000 deaths a year, making it the seventh leading cause of cancer death in both sexes combined. Pancreatic cancer develops when cells in the pancreas the glandular organ behind the stomach generate multiply uncontrollably and form a mass. The Tp53 gene is located on chromosome 17, and it is a tumor suppressor gene that encodes a transcriptional activator protein that responds to apoptosis. The aim of this study was to find more bioinformatics information.

Materials and Methods: General information about Tp53 was obtained from NCBI database. The microRNA was chosen through miRwalk database. More data was achieved from miRbase database, and DAVID made the acquire sortment of pathways connected to Tp53 gene. In addition, KEGG showed carcinogene pathways associated with Tp53 gene.

Results: the bioinformatics prediction showed that the tumor suppressor role of the tp53 gene is responsible for the microRNA's binding location.

Conclusion: Previous bioinformatics studies have shown that, hsa-miR-205-5p is predicted to target the tp53 gene and activate the apoptotic pathway, which helps to inhibit cancer. According to the negative regulatory function of microRNAs, the expression of hsa-miR-205-5p is expected to be increased and makes the expression of target gene to downregulate and cause cancer.

Keywords: pancreatic cancer, tp53 gene, hsa-miR-205-5p

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The elevation of *Pinkbar* expression in samples of Iranian patients with colon cancer

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Abstract

Background: Pinkbar (planar intestinal- and kidney-specific BAR domain protein)/BAIAP2L2 is a member of inverse BAR (I-BAR) domain protein subfamily that contains an I-BAR domain and a SH3 domain. The members of this subfamily have participated in the cell motility and cell shape changes by regulation of actin filaments and formation of plasma membrane protrusion. Moreover, colon cancer is one the most causes of death worldwide. To identify the novel and more effective platform with low side effects in cancer therapy was remained unknown. Therefore, the identification of new biomarkers in treatment of cancer seems to be interested for researchers.
Materials and Methods: In order to evaluate the expression of a possible new target in colon cancer therapy, a total of 30 tissue samples from 30 colon cancer patients and 30 healthy controls was collected. Next, the total RNA was extracted by using Trizol reagent based on the manufacturer-provided protocol followed by reverse transcription into cDNA. Finally, we evaluated the expression of *Pinkbar* by using quantitative real time PCR (qRT-PCR) method.
Results: Our finding indicates that the expression of *Pinkbar* was elevated in samples of patients with colon cancer. So, it seems that *Pinkbar* may be a potential target in colon cancer therapy. However, to identify the details of the molecular mechanisms, more experiments will be required.
Conclusion: The results from our study support this idea that *Pinkbar* may to be a novel target in colon cancer therapy.

Keywords: *Pinkbar* expression, Colon cancer therapy, Biomarker

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Expression of HAND2-AS1 in Colorectal Cancer Is Under Control by DNA Methylation

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Abstract

Background: DNA methylation and long non-coding RNAs (lncRNAs) are the epigenetic mechanisms that numerous investigators studied. Genetic and epigenetic alterations, lead to disruptions in the cellular hemostasis that lead to carcinogenesis. The changes in DNA methylation, rationally, are not a random process and can accurately characterize the cancer status. Recently, the function of lncRNAs has been focused on, and numerous studies try to decipher the potential roles of lncRNAs in cancer biology. This study investigated the correlation between DNA methylation and RNA expression of colorectal cancer (CRC).

Materials and Methods: The data were investigated at the GEO database, including the methylation array and the expression array of the CRC. Afterward, via the GEO2R, data was analyzed. Consequently, data were evaluated by statistics tests, including Spearman, Pearson, one -way Anova.

Results: This bioinformatic-based study found that *HAND2-AS1* was markedly downregulated in CRC tissues (p= 8.52E-05). This downregulation is correlated with the hypermethylation of the HAND2-AS1 promoter (Spearman: -0.42 (p = 5.85E-17), Pearson: -0.40 (p = 1.36E-15)). Noteworthy, HAND2-AS1could sponges numerous miRNAs, which potentially promote cancer progression.

Conclusion: In this study, the importance of DNA methylation was emphasized. Also, these data showed that the expression of *HAND2-AS1* is controlled by DNA methylation, which is altered in cancer creation.

Keywords: lncRNA, bioinformatics, HAND2-AS1, DNA methylation

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Identifying novel biomarkers in hepatocellular carcinoma by weighted gene co-expression network analysis

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Abstract

Background: A better comprehension of the genetic basis of hepatocellular carcinoma (HCC) is required to forecast a patient's prognosis and create new targeted gene therapies. The goal of this study is to find critical genes linked to HCC.

Materials and Methods: WGCNA and DEG analysis were utilized to study the relationship between gene sets and clinical characteristics, as well as the interactions underlying the co-expression modules. The Kyoto Encyclopedia of Genes and Genomes (KEGG) and Gene Ontology (GO) were then utilized to investigate the biological functions of the discovered dysregulated genes. Finally, to validate the study's findings, an online database analysis was performed using XenaBrowser and GEIPA to analyses hub-gene expression and determines its diagnostic significance.

Results: The pink module was found as the most significant module in the co-expression network linked with the progression of HCC (r = 0.84, p-Value = 2e-07) in the GSE114564 dataset. This module was linked to the positive regulation of the non-canonical Wnt signaling pathway, the regulation of lipolysis in adipocytes, and the positive regulation of the Wnt signaling pathway, planar cell polarity pathway. According to the Venn diagram constructed between the pink module and DEGs, the top seven genes, including *MND1, FCN2, CLEC4G, CLEC4M, PTH1R, VIPR1, and AKR1B10*, were also associated with HCC patient progression. Among these shared hub-genes, *MND1* was found as a novel biomarker and validated by the mentioned databases.

Conclusion: The current study identified important modules and *MND1* as a hub-gene related to HCC, which could provide references to understand the genesis and could be considered as a novel candidate for HCC target-therapy

Keywords: hepatocellular carcinoma, Molecular Pathogenicity, Transcriptome Analysis

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Comparison of two computational online tools for sgRNA designing in gene editing experiments by CRISPR/Cas9

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Abstract

Background: CRISPR/Cas9 system is a specific genetic manipulation method that causes the specific double stranded break (DSB). The sgRNA sequence plays a fundamental role to success with high efficiency through limiting off-target cutting. There are several softwares that can be used to predict sgRNA primers with different efficiency and specificity for cutting target sites. Each software has some advantages and limitations that should be considered in sgRNA design. Here, we compared two standard tools with different algorithms, EuPaGDT and CRISPOR, which are common software in eukaryotic cells.

Materials and Methods: First, we found more than 10 leishmanial specific gene sequences from different species from tritrypDB database and then, we tried to predict the best sgRNA sequences through two different algorithms.

Results: Both softwares identified common specific sgRNA sequences but their efficiency score and off-target sites predicted with very different. CRISPOR was able to detect both intergenic and intragenic off-targets with more power than EuPaGDT. In spite of the number of predicted primers were equal in both software but CRISPOR put the almost 70% of itself prediction sgRNA primers in high score cluster but EuPaGDT high score data contain nearly 60% of all primers and just about 40% of high efficiency score primers were similar in both of them for all genes.

Conclusion: Both softwares are strong approach for prediction of sgRNA. Nevertheless, using of several software to determine the best sgRNA for gene knockout or tagging, and also, sometimes using of more than one guide primers with high scores is recommended.

Keywords: CRISPR/Cas9, sgRNA, CRISPOR, EuPaGDT

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Association between catalase gene (*CAT*) and other involving genes in human skin ageing

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Abstract

Background: The elasticity of the skin and collagen fibers in the epidermis and dermis gradually decreases which is called aging. The characteristics of aging include wrinkles, dryness and pigmentation. Generally, three groups of the genes are involved in skin aging including antioxidant capacity, elasticity, and hydration. Defects in any of these genes cause wrinkles on the skin. Oxygen free radicals in the skin cause oxidative stress, one of the main causes of collagen and elastin destruction, which ultimately leads to wrinkles and sagging skin. One of the antioxidant genes is the catalase gene, which plays an important role in converting free radicals into inert molecules. In this study we exhibited the association among the genes involving the human skin aging as well as their connections with *CAT* gene by creating a gene network.

Materials and Methods: The genes related to hydration, antioxidant capacity and skin elasticity were systematically collected by literature review. The gene network was created by GeneMANIA algorithm based on protein-protein interaction, genetic interaction, co-localization and pathway.

Results: We found 55 genes related to skin aging. Catalase is connected to *MNSOD2, ALDH1A1, PCNA and CYP1A1* genes. Likewise, we observed *JUN* gene has the most biological connections with the other skin aging genes.

Conclusion: This study shows catalase gene in addition to antioxidant activity may also involve in skin aging and introduce *JUN* genes as important gene in skin aging. Our study provides insight about the prioritization of the genes is involving in skin aging.

Keywords: Skin aging, GeneMANIA, Catalase, gene network

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Investigation of the Association of FOLH1 rs61886494 and DISC1 rs12133766 loci in Iranian Schizophrenia Patients

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Abstract

Background: The aim of this study was to identification of polymorphisms of FOLH1 and DISC1 genes in Iranian patients with schizophrenia.
Materials and Methods: In this case-control study, 50 patients with schizophrenia and 50 healthy controls were evaluated. PCR-RFLP and Tetra-ARMS methods were used for detection of FOLH1 and DISC1 gene respectively in both of patients and control groups.
Results: The frequency of CC, CT, and TT genotypes for FOLH1 gene in rs61886494 locus in schizophrenic patients was 92%, 8%, and 0%, respectively, and in healthy subjects, 94%, 0%, and 6%, respectively. The frequency of DISC gene in GG genotype was higher than that of normal people and frequency of GA genotype was lower than normal subjects. In addition, the genotype AA was identified only in patients.
Conclusion: For FOLH1 gene in rs61886494 locus, the frequency of CC and TT genotypes in patients was 2% and 6% lower in healthy people, while CT genotype in patients was 8% higher in healthy people. Interestingly, TT genotype was not observed in patients and CT genotype in healthy people was not observed. Regarding the DISC1 gene, the results showed that the frequency of homozygous GG and GA homozygote genotypes in the patients was higher in the rs12133766 locus, while the heterozygote GA was high in healthy subjects and was not observed in patients. Therefore, the result of this study in our country can provide suitable method for diagnosis and prevention of schizophrenia patients.

Keywords: Schizophrenia; polymorphism; DISC1 gene; FOLH1 gene

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The expression analysis of has-circ-0000284 in breast carcinoma: Looking for a diagnostic biomarker and a possible therapeutic target

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Abstract

Background: Breast cancer (BC) is one of the most common cancers among women around the world as well as in Iran. Non-coding RNAs play a key role in the development of BC, their use as biomarkers in diagnosis and prognosis is becoming increasingly useful. In recent years, they pay more attention to circularRNA(circRNA) due to its high stability and the possibility of early detection moreover the discovery of their roles in the pathogenesis of the disease, and their high therapeutic and diagnostic potential have opened new horizons for research.

Materials and Methods: 29 BC tumors and their adjacent normal tissues were collected from Motamed institute of breast cancer research (Tehran, Iran). The samples were snap-frozen and stored at −80 ◦C. Before sample collection, circHIPK3(has-circ-0000284) expression in breast cancer tissues was analyzed using qRT-PCR. CircInteractome (https://circinteractome.nia.nih.gov) was performed to detect circRNA/miRNA targeting relationship. Additionally, potential miRNAs that can be targeted by circHIPK3 were predicted by the bioinformatics method. miRTargetlink database (https://ccb-web.cs.uni-saarland.de/mirtargetlink) and DIANA database (http://diana.imis.athena-innovation.gr/DianaTools/) were used to predict interactions of miRNAs with circHIPK3. circHIPK3 has carcinogenic or anti-tumor effects on different cancers.

Results: The lower expression levels of circHIPK3 in Her2+ BC tissues were shown compared to paired adjacent normal tissues and Her2- tissues with P-value (P <0.0054). In addition, 10 miRNAs can be targeted by candidate circRNA, which was predicted based on bioinformatics databases. Moreover, miRNAs selection tools predicted that miR-192, miR-326, and miR-365 can be targeted by circHIPK3.

Conclusion: Our findings revealed that circHIPK3 facilitates BC development and progression, providing a novel therapeutic target for BC and could serve as a prognostic biomarker of BC.

Keywords: circular RNA, microRNA, breast cancer, DIANA database, miRTargetlink database, CircInteractome

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Study of BDNF gene expression in Alzheiemer´s patients

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Abstract

Background: Alzheimer's disease is one of the most destructive neurodegenerative disases. It is mostly seen in people over 65 years old, and is associated with the loss of neurons in specific areas of the brain. Brain –derived neurotrophic factor(BDNF) is involved in the development of neural survival and the synaptic process of memory. BDNF level vary according to the severity of the disease.BDNF can be involved as an important biomarker in the diagnosis of Alzheimer´s disease.we can suggest a treatment for alzheimer´s disease by adjusting the amount BDNF and suppressing the amyloid beta peptide.

Materials and Methods: RNA was isolated from blood of sick and healthy individuals using TRIZOL reagent. cDNA synthesis was done by anchored olig-dTs and RT-PCR was carried out by using BDNF specific primers. We used GAPDH gene as internal control gene. Then qRT-PCR performed to assess of BDNF gene expression level.

Results: Our results indicated that there is a significant relationship between the levels of expression of BDNF with alzhemier´s disease. Real-time PCR results showed that BDNF gene expression is significantly increased in the early stages of the disease and is almost two fold higher than healthy subjects.

Conclusion: Overall, we found that BDNF circulating amount can be used as an important biomarker to diagnosis of Alzheimer´s disease. However, future additional researches are necessary to confirmation of these results.

Keywords: BDNF, Alzheimer, biomarker, gene expression

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Evaluation of the association of XRCC7 rs7003908 gene polymorphism in children with lymphoid cancer

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Abstract

Background: Today, cancers are one of the leading causes of death in children, the most common type of which is leukemia. Acute lymphoid leukemia (ALL) was formed in the bone marrow due to the high accumulation of underdeveloped lymphocytes. The XRCC7 genome is one of the genes in the DSB repair system and also, its repair pathway is NHEJ. The aim of this study was to investigate the XRCC7 gene polymorphism in children with acute lymphoid cancer.

Materials and Methods: XRCC7 genome polymorphism have compared between 70 children and adolescents under 18 years of age with lymphoid leukemia and 140 healthy children and adolescents under 18 years of age using RFLP and PCR methods. And statistical analysis has performed using SPSS25 software, too.

Results: The findings show that among the blood groups with ALL, the O^+ blood group had the highest frequency and out of 70 patients, 33% had the O^+ blood group. The frequency of TT, TG, GG genotypes in two groups of patients were 10%, 42% and 48%, respectively, and in the healthy group was 63%, 22% and 15%. According to (P = 0.001), genotypic distribution in this polymorphism shows a significant relationship with ALL disease.

Conclusion: Comparative analysis done on XRCC7 gene polymorphism at rs7003908 position in two healthy and affected groups indicates that there was a significant relationship between XRCC7 gene polymorphism and lymphoid cancer in GT genotype. Also, the results of some of the studied factors such as parental addiction to smoking, gender and family history of the disease indicate that the presence of these factors is significantly associated with the risk of having a variety of leukemias, including lymphoid cancer.

Keywords: children, leukemia, polymorphism.

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In-silico analysis of Rac1 gene and hsa-mir-182-5p and its related target gene of Liver Cancer

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Abstract

Background: Liver cancer (LC) is one of the most invasive malignancies and may derive from different types of liver cells with an estimated more than 781000 deaths in 2018. The Rho-family GTPase Rac1 plays a key role in carcinogenesis and inflammatory responses. Epidemiological studies demonstrated a relation between chronic inflammation and cancer. Most cases of hepatocellular carcinoma (approximately 80 %) are associated with cirrhosis related to chronic hepatitis following viral infections.

Materials and Methods: Based on bioinformatics analysis, hsa-mir-182-5p was selected. Using by Mirwalk database, Prediction data of genes was collected. Then in the NCBI database, at UniGene, we have checked genes expression. Functional annotation analysis has been parsed with David database. Pathways relations were collected at KEGG in David database.

Results: 415 genes were identified for LC. Information of gene expression shows that Rac1 genes were down-expression in normal livers. In the other hand, hsa-miR-182-5p had up-expression.

Conclusion: These results suggest that Rac1 may be a new gene therapy target for LC. Blocking Rac1 expression in LC cells induces apoptosis of these tumor cells and may thus represent a new therapeutic approach.

Keywords: Liver Cancer, microRNA, RAC1, has-miR-182

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Introducing a recurrent mutation in a patient affected with Methylmalonic academia by Whole Exome Sequence

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Abstract

Background: Methylmalonic Acidemia (MMA) is a rare autosomal recessive metabolic disorder, result from genetic defect in methylmalonyl-CoA mutase (MCM) enzyme. This enzyme is necessary in the catabolism of branched chain amino acids (BCAA) for the degradation of odd-chain fatty acids, the amino acid valine, isoleucine, methionine, and threonine, and cholesterol. MMA has wide range of clinical manifestations varying from no signs or symptoms to severe lethargy and metabolic crisis in newborn infants. This disease is caused by mutation in five mainly genes (*MUT, MMAA, MMAB, MMADHC, MCEE*). In this study we reported a recurrent MMA causative mutation in 2 years old boy.

Materials and Methods: We performed whole exome sequencing method (WES), followed by Sanger sequence in our patient. *In silico* analyses of the identified variant was performed using web-based bioinformatics programs.

Results: WES identified the missense mutation c.A976G (p.R326G) in the *MUT* gene which affects the stability and enzymatic activity of MCM. The results of the Sanger sequence showed that our patient is homozygous and his parents are carriers. Bioinformatics software programs such as Polyphen, SIFT have predicted that this variant will be damaging.

Conclusion: This pathogenic mutation has previously been reported in Iran and Ukraine. Considering that our patient is from the northern Iran and this mutation has been already reported the same region; Therefore we can conclude that this mutation is recurrent and prevalent in north of Iran. Additionally, our finding would be beneficial for prenatal diagnosis of MMA as well as establishing a local variant database.

Keywords: Methylmalonic Acidemia, Whole exome sequencing, Iran, Mutation, Metabolic disorder

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Association between rs9344 polymorphism of cyclin D1 gene (CCND1) on breast cancer in Iran

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Abstract

Background: Cell cycle regulator cyclin D1 (CCND1) is a pivotal regulator for G1/S phase transition, a critical part of carcinogenesis initiation. Breast cancer comprises a very heterogeneous group of cancer cells, but little is known about what is wrong in the genome of these patients. This study investigated contribution of CCND1 (rs9344) in the breast cancer susceptibility.
Materials and Methods: Blood samples were collected from 50 patients diagnosed with Breast cancer and 50 people as controls. Genomic DNA was extracted from whole-blood samples using Triton-X100 and genotyped by tetra-primer amplification refractory mutation system PCR (T-ARMS-PCR). Specific oligonucleotide primers for amplification of the CCDN1 were designed by Oligo7 software. Finally, the statistical analysis was performed by MedCalc software.
Results: The results of this study showed a significant difference in genotype distribution of rs9344 CCDN1 polymorphism between breast cancer patients and controls (p=0.03).we indicated GG genotype frequency in breast cancer patients is significantly higher than controls.
Conclusion: Our study suggests that the polymorphism rs9344 in cyclin D1 gene has association with cancer risk in Guilan population, indicating that CCND1 rs9344 may be an important biomarker to prediction of breast cancer risk. However, future studies with more patients and controls are needed to confirm the results. Also, additional evidences are necessary to further clarify the findings of this research.

Keywords: rs9344, CCND1, breast cancer, Gene polymorphism

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Bioinformatic analysis and Protein Properties of Delta 6 desaturase Enzyme Cloned in *Pichia pastoris*

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Abstract

Background: Fungi are the best microorganism to production of essential fatty acids, but due to the high-volume industrial production, gene cloning in the yeast was used commonly.
Materials and Methods: In this study, cloning of delta 6 desaturase gene obtained from fungi *Mucor rouxii* DSM1194 in the yeast *Pichia pastorisGS115* was performed and the expression of GLA production as omega 6 fatty acid in the recombinant strain was confirmed. The complete sequence of the cloned delta 6 desaturase protein was examined using Expasy browser and the phylogenetic tree of the delta 6 desaturase gene was plotted by CLC software. The final recombinant vector map was drawn by Snap gene viewer software and the Delta 6 desaturase gene, which is located between the restriction enzymes *EcoRI* and *XhoI* was confirmed.
Results: By using the CFSSP server, the second structure of cloned protein was predicted. Investigations performed on the PDB server revealed that the crystallographic structure of the delta 6 desaturase enzyme had not yet been studied or recorded. Study showed the cloned delta desaturase enzyme containing 556 amino acids. The protein alignment of this study with the reference protein in the NCBI gene bank shows that these two proteins are different in three positions 84, 111 and 271.
Conclusion: According to the studies, it was found that the parts that have been altered in this protein are all related to extracellular sequences, and the sequences that pass through the membrane and inside the cell are quite similar to the reference protein.

Keywords: Cloning, Delta6 desaturase, *Pichia pastoris*, Bioinformatic analysis

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Pathogenic Analysis of R414C Mutation in the *APC* Gene in FAP Cancer

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Abstract

Background: Familial adenomatous polyposis is one of the colon cancer syndromes with the autosomal dominant disorder. Patients with this syndrome suffer from multiple polyps, mainly in the colorectal area, which, at an average age of 35 to 40 years, have an almost inevitable progression to colon cancer. These patients mainly have a mutation (Germline) in the gene (Adenomatous polyposis coli, APC) on chromosome 5q21. The main mutation in patients with this disease is missense. In this effect, a single nucleotide polymorphism (SNP) in NCBI was selected as a missense mutation in the *APC* gene for investigation.

Materials and Methods: In (rs137854567 C> T), the effect of conversion of arginine (acidic and hydrophilic amino acid) to cysteine (polar amino acid and hydrophobicity) on codon 414 on protein structure was investigated using bioinformatics sites SIFT, PROVEAN, POLYPHEN.

Results: In the SIFT database, Amino acids with probabilities LESS THAN 0.05 are predicted to be deleterious. in this STUDY, Substitution at pos 414 from R to C is predicted to AFFECT PROTEIN FUNCTION with a score of 0.00. Also in the PROVEAN database, Variants with a score equal to or below -2.5 are considered "deleterious, PROVEAN predicts R414C variant DELETERIOUS with SCORE = -7.916. Also, POLYPHEN-2 showed this mutation is predicted to be PROBABLY DAMAGING with a score of 1.000 (sensitivity: 0.00; specificity: 1.00).

Conclusion: The R414C variant of the *APC* gene is likely to be a potentially pathogenic SNP. However, further investigation is needed to clarify this issue.

Keywords: *APC* Gene, FAP Cancer, SNP, pathogenic Variant.

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Case-Control Analysis of rs937301 Polymorphism in *GIP* Correlated to Type 2 Diabetes in Iranian Population

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Abstract

Background: Glucose-dependent insulinotropic polypeptide (GIP) is one of the incretins, which is an important amino-acid peptide hormone that is secreted from the gut and then binds to glucose-dependent insulinotropic polypeptide receptors (GIPRs) after a meal and plays a crucial role in the secretion of insulin upon food stimulus and in the regulation of postprandial glucose level. It also exerts an effect on the synthesis and secretion of lipoprotein lipase, from adipocytes, important for lipid metabolism. The aim of our study was to do a case-control association analysis of rs937301 (SNP) in *GIP* with type 2 diabetes in Iranian patients and healthy people.

Materials and Methods: A total of 277 subjects which includes 183 (101M/94F) cases with type 2 diabetes and 94(45M/ 49F) normoglycemic control subjects belonging to Yazd from Iran were recruited to assess the frequency of single nucleotide polymorphism (SNP) in *GIP* (rs937301) in a case-control manner. The SNP was genotyped by using tetra primer amplification refractory mutation system PCR (ARMS PCR). Association analysis was carried out using the chi-square test.

Results: No significant difference in the allele frequency and genotype distribution of rs937301 in *GIP* were observed between cases and controls ($P > 0.001$).

Conclusion: No statistically significant association was observed between SNP rs937301 and type 2 diabetes in our population.

Keywords: Type 2 diabetes. ،SNP،rs937301 ، *GIP* gene،ARMS-PCR

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Investigating the Pathogenic Single Nucleotide Polymorphisms of *MT-ND5* Gene by Bioinformatics Tools

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Abstract

Background: Mitochondrial is one of the most essential organelles in cells that play important roles in numerous biological processes For example, it has been confirmed that mitochondrial take charge of supplying cellular energy through generating adenosine triphosphate (ATP) in cells. The Mt-nd5 (mitochondrial encoded NADH: ubiquinone oxidoreductase core subunit 5) Gene offers instructions for growing a protein referred to as NADH dehydrogenase 5. This protein is part of a huge complicated enzyme referred to as complicated I. Mutations in the MT-ND5 gene are responsible for cases of the disease such as lactic acidosis, mitochondrial encephalopathy, stroke-like episodes (MELAS), and Leber. This study aimed to investigate the one single nucleotide polymorphism (SNP) in genes MT-ND5 using tools in Silico and predict their pathogenicity.
Materials and Methods: In this study with a search in the NCBI database among the recognized polymorphism in this MT-ND5 gene, 829 missense variants are fined. Then, analyzed the pathogenicity of SNP using bioinformatics tools including sift, poly phen, I-Mutant2.0.
Results: According to the Sift, poly phen result A236T, F124L, E145G could be disease-causing. I-Mutant2.0 predicted decreased stability A236T, F124L, E145G alteration.
Conclusion: According to the results, it can be said that these changes in amino acids cause probably damaging and pathogenic SNP and also affect the polarity and solubility of amino acids.

Keywords: Mitochondrial, MT-ND5 genes, SNP**,** Bioinformatics

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Identification of Potential Substrates for the Enzyme Sortase in the Human Genome

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Abstract

Background: Sortase is a bacterial enzyme which ligates a protein to the membrane. The bacterial surface proteins are produced as immature proteins in the cytoplasm and contain a signal peptide and a soratase-recognition motif (LPXTG) at the amine and carboxyl terminals, respectively. After expression, the proteins directed out of the cytoplasm by the Sec secretory system. After cleavage of the signal, proteins remain attached to the membrane by the hydrophobic motif. By identifying the LPXTG sequence, the enzyme sortase breaks down some bonds and makes new bonds that results in the protein binding to the cell surface. The aim of this study is to find out the presence of an LPXTG motif in human proteins. These proteins can potentially be sortase substrates.
Materials and Methods: To find out all putative sortase substrates for our future investigations, genome-wide screening was done in the resource of "scan prosite" in the www.expasy.org website. The search for proteins with this motif was done separately for each amino acid in the X position.
Results: We extracted 184 human protein types with LPXTG motif in their sequences. These proteins were classified via their subcellular locations and 13 membrane protein types were selected in which the motif was located on the extracellular surface.
Conclusion: In previous works it was shown that glutamic acid (E) is the most frequent amino acid presented in the X position in the bacteria but in the human genome the frequency of argenin (A) in this position is more than other amino acids.

Keywords: sortase, human genome, surface protein

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LC3B as a novel marker for diagnosis of cancer

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Abstract

Background: Worldwide, cancer is the most common malignancy and the most common cause of deaths in the past few decades. Early diagnosing of cancer by novel biomarkers is a public and policy priority. A prognostic biomarker provides information on the likely outcome of the disease in an untreated individual and is helpful in identifying patients for adjuvant systemic therapies. Recently, autophagy genes and proteins have attracted the attention of many researchers as diagnostic biomarkers. One of them is the microtubule-associated protein 1 light chain 3B (MAP1LC3B, or LC3B), has long served as an autophagy marker in multiple in vitro assays. The expression levels of LC3B gene and protein have also been examined by new molecular methods and immunohistochemistry in many cancers. The results of recent studies showed that high gene and protein expression of LC3B predicted adverse overall survival in cancers. Thus these data suggest that LC3B could be a clinically useful biomarker as a diagnostic and/or prognostic tool in cancer.
Materials and Methods: The current review has been achieved by using an organized search of the scientific data published on molecular biology of LC3B from various databases, including PubMed, ScienceDirect, Scopus, Scielo, SciFinder and Google Scholar.
Results: The results of the gene and present study showed LC3B could be a good candidate as a prognostic factor to diagnosis of cancer.
Conclusion: LC3B has been reported to be a potential biomarker of cancers. Given the dire need for tumor markers, only further studies can establish the utility of LC3B in the detection and treatment of cancer and provide irrefutable evidence for its diagnostic and/or prognostic use as a new weapon against human cancer.

Keywords: cancer, autophagy, LC3B, biomarker

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Alignment and phylogenetic tree analysis of CCNE1 and CCNE2 cyclic protein partial gene sequences in human

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Abstract

Background: CCNE cyclic protein is the limiting factor for G1 phase progression in to S phase in cell cycle associated with high genome ploidy in breast cancers. Cyclin E1 is one the most promising biomarkers in estrogen receptor positive breast cancer for response to the new standard of care drug class, CDK4/6 inhibitors. Because of its strong predictive value, cyclin E1 expression may be used in the future to triage patients into potential responders and non-responders. Importantly, cyclin E1 is highly related to cyclin E2, and both cyclin E1 and cyclin E2 are estrogen target genes that can facilitate anti-estrogen resistance and can be highly expressed in breast cancer.

Materials and Methods: The nine nucleotide and protein sequences were taken from National Center for Biotechnology Information GenBank. The alignment of nucleotide sequences was done by Multalin software. Phylogenetic tree was drawn using protein sequences by neighbor-joining method.

Results: Part of sequence alignment result revealed that CCNE1 and CCNE2 variants sequences are 53.3 percent similar. The phylogenetic tree shows some differences between protein sequences.

Conclusion: Some protein sequences in phylogenetic tree are near and some far from each other but their nucleotide sequences are very similar and it shows differences in the CCNE cyclic protein translation and post-translation. Although both play a role in the development of disease, cyclins E1 plays a more prominent role and is more pathogenic.

Keywords: Alignment, Phylogenetic tree, CCNE cyclic protein, Human, partial gene

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Application of gene expression sequencing in COVID-19 pandemic diagnostics

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Abstract

Background: In late December 2019, an outbreak of an unknown disease called coronavirus occurred in Wuhan, Hubei Province, China, leading to a sharp increase in global mortality. Therefore, the need for early prevention through the accurate and timely diagnosis of the disease is needed to control and prevent its recurrence as a powerful and cost-effective tool for high-power transcription analysis.

Materials and Methods: In this study, applied diagnostic methods were proposed, which, based on research by next-generation sequencing technology (NGS), provided a powerful tool for studying emerging pathogens/diseases, including whole-genome sequencing, RNA-Seq, and single-cell sequencing. Gene expression pattern analysis and pathogen detection are used. In this study, the RNA-Seq platform for rapid detection of the COVID-19 epidemic was examined by the Galaxy instrument.

Results: Traditional approaches challenge the detection of complex and massive interactions between viruses and host/cell. There are many diagnostic methods, but the main advantage of NGS is that it can detect viral agents without prior notice and provides reports from laboratories around the world for high-volume COVID-19 tests.

Conclusion: With this tool, cells containing active viruses can be identified, several viruses can be combined in one cell, and expression can be distinguished between infected and non-infected cells. This helps us understand how viruses play a role in stimulating or modifying disease development in specific diseases and developing new therapies to target viruses. Identifying a wide range of pathogens using NSG technologies is also essential in controlling viral infections caused by a new pathogen.

Keywords: Covid19, Diagnosis, RNA-Seq, Gene expression, NGS sequencing.

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Evaluation of DNA expression of nuclear factor kB (NF-kB) in oral squamous cell carcinoma patients using RT-PCR

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Abstract

Backgrounds: Cancer is a fatal disease caused mainly by environmental factors that mutate genes encoding critical cell-regulatory proteins. Oral cavity squamous cell carcinoma (OSCC) is the sixth most common cancer in the world. Degradation of the cell cycle and the proliferation of malignant cells results in the loss of control mechanisms that ensure the normal function of tissues. Traditional risk factors of oral cancer include tobacco and alcohol abuse. The nuclear factor kB (NF-kB) comprises a family of transcription factors regulates the expression of genes involved in many processes that play a key role in the development and progression of cancer such as proliferation, migration and apoptosis and growing evidences support a major role in oncogenesis. Aberrant or constitutive NF-kB activation has been detected in many human malignancies. In the present study, we evaluated the expression of the *NF-kB* genes in OSCC patients and normal controls

Materials and Methods: Samples included 19 paraffin embedded case and 20 biopsy control. RNA from case samples was extracted using high pure FFPE RNA micro kit (ROCHE) and RNA from control sample was extracted using Cinnapure RNA tissue kit. RNAs exchange to cDNA by RevertAid First Strand cDNA Synthesis Kit (fermentase). To evaluate the expression of NF-kB real-time PCR was performed.

Results: Results showed significant differences between OSCC patient and healthy groups for expression of *NF-kB* gene ($p < 0.036$) and we saw up regulation of this gene.

Conclusion: Our results, for the first time, provide methylation profiles of *NF-kB* gene in a sample of patients with OSCC in a Southeast Iranian population. Up-regulation of *NF-kB* gene has significant function in oral squamous cell carcinoma. This may provide another promising target for drug development.

Keywords: OSCC, *NF-kB*, Oncogenesis

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Study of effect of extract of Capparis on expression genes of self-renewal in MCF7 cells

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Abstract

Backgrounds: Several drugs have been proposed for the treatment of breast cancer, but none has fully treated the disease so far. Extensive effort is being made to find new high-potency medications. In this study, we have evaluated the effect of aqueous-alcoholic extract of unripe Capparis fruit as an anticancer agent an MCF7 cells line on the expression pattern of important genes of the self-renewal pathway (*OCT4*, *NANOG* and *SOX2*).

Materials and Methods: The MCF7 cells were cultured in RPMI1640 medium contained aqueous-alcoholic extract of unripe Capparis fruit (125- 5000 µg/mL) for 48 and 72 h. The fold changes of OCT4, NANOG and SOX2 were determined by real-time-PCR technique. Data were analyzed by one-way ANOVA.

Results: The hydro-alcoholic extract of the unripe fruit of Capparis caused time- and concentration-dependent cell death in MCF7 cells. Real-time PCR results showed that in Capparis extract treated cells, the mean expression of *OCT4*, *NANOG* and *SOX2* genes decreased after 48 and 72 hours of incubation with IC50 concentration of Capparis extract as compared to the control group.

Conclusion: The results of this study suggest that Capparis plant species is able to alter the expression of the desired genes. Therefore, based on the results of this study, it is possible that the fruit of this plant can be used as a potential candidate for the treatment of human breast cancer after clinical trial studies.

Keywords: Breast cancer, Capparis plant, MCF-7 cells, Medical herbs

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In-silico analysis predicting the status of pathogenic SNPs of the human *PAX3* gene

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Abstract

Backgrounds: The paired box protein (PAX-3) is a transcription factor encoded by *PAX3* gene. PAX3 belongs to the family of *PAX* gene. They have a crucial role in developing tissues and organs during embryogenesis. PAX3 has two DNA binding sites and it can bind to DNA as a homodimer or a heterodimer with PAX7. Mutation in *PAX3* caused some diseases such as Waardenburg syndrome that involved abnormality in pigmentation, arms, hands, and hearing loss. Craniofacial-deafness-hand syndrome is characterized by distinctive facial features, severe hearing loss. Rhabdomyosarcoma caused by chromosome aberration. It is the most common soft tissue carcinoma in childhood (5-8% of all malignancies in children). In this study, 24 single nucleotide polymorphisms (SNP) for isoform *PAX3* are analyzed which are identified as missense changes in the National center for biotechnology information (NCBI) on the SNP database.

Materials and Methods: In NCBI/SNP database 47,256 SNPs were found for *PAX3*. Pathogenic and missense filters were applied and the result showed 18rs (rs758136826, rs1380858784 rs267606931,…). Their effect on the final protein product was checked.

Results: The result of this research with bioinformatics tools (SIFT, PROVEAN, PANTHER, SNP&GO, FATHMM) shows that Reference SNP for instance rs1228590199 causes change R (Arg) to S (Ser) in 270th amino acid residue in PAX3 transcript, can produce an abnormal protein that has a terrible effect on patients with this polymorphism.

Conclusion: Based on the results were obtained these SNPs most probably deleterious and only rs769650688 in the SIFT and SNP & GO databases were declared neutral.

Keywords: *PAX3*, DNA-binding protein, SNP, Bioinformatics

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The effect of Composol Medium on platelet microRNAs expression during blood bank storage

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Abstract

Backgrounds: Platelet additive solutions, such as Composol-PS, are good choices for extending the storage time of platelet concentrates (PCs) in blood banks. Platelets express high levels of various microRNAs (miRs). We aimed to investigate platelet miR-16, miR-127 and miR-320a expression during storage and the effect of Composol medium on miRs expression.

Materials and Methods: Ten PC bags from healthy volunteers were collected and each bag was divided equally into two separate bags, with or without Composol, bags were stored for seven days and tested for platelet functional tests and miRs expression analysis. Statistical analysis and miRs expression interpretation were fulfilled by SPSS and REST. A $P<0.05$ was considered statistically significant.

Results: All miRs expression was elevated during the storage in both plasma and Composol medium, but only the results of miR-16 were statistically significant ($p<0.05$). The most obvious up-regulation were reported for day 5 of storage in both plasma (mean fold change = 5.02, $p = 0.002$) and Composol (mean fold change = 5.42, $p = 0.026$) groups. Furthermore, PCs stored in Composol medium showed better results according to the platelet functional tests and miRs expression. Despite the overt increased expression of miR-16 in both groups, its expression significantly decreased in the Composol samples (mean fold change =0.339) compared with the plasma samples ($p<0.05$). Results for miR-127 and miR-320a were less obvious and not significant.

Conclusion: We concluded that Composol might be a good additive solution for extending platelet storage time, compared with conventional plasma environment. This may be as a result of miR-16 down-regulation in Composol medium.

Keywords: Platelet storage, Additive solutions, Composol, MicroRNAs

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Psammplysin F increased chemotherapy sensitivity to Doxorubicin by reducing the number of Stress Granules

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Abstract

Backgrounds: Doxorubicin (DXR) is an antibiotic derived from the bacterium Streptomyces peucetius. Since the 1960s, it has been widely used as a chemotherapeutic agent in the anthracycline class. DXR is commonly used in chemotherapeutic regimens with other agents because of its effectiveness in destroying malignant cells. DXR's anti-tumor properties are mediated by DNA intercalation and topoisomerase inhibition. Cancer cells alone can withstand much stress due to maximal growth conditions; DXR also imposes increased ER stress and pro-apoptotic processes on the treated cancer cell, promoting the development of Stress Granules (SGs). An established cell mechanism for reducing the damage of stress and increasing cell survival involves the formation of SGs. Ribonucleoproteins is formed due to the cell's stress caused by a break in translation. DXR, in particular, increases the number of SGs by directly affecting eIF2α phosphorylation and results in its chemotherapy resistance.

Materials and Methods: The number of SGs in doxorubicin-resistant cancer cells was determined using the protein markers G3BP1 and TIA-1. Psammplysin F, which reduces eIF2α phosphorylation, was used to reduce the number of SGs. The sensitivity to the chemotherapy drug DXR was measured before and after the use of Psammplysin F.

Results: Psammplysin F reduced the number of SGs in DXR-resistant cells while increasing sensitivity to this chemotherapeutic drug when used in combination.

Conclusion: Psammplysin F reduced the number of SGs in DXR-resistant cells while increasing sensitivity to this chemotherapeutic drug when used in combination. Psammplysin F can be used as the primary compound to improve DXR efficiency in cancer-resistant cells.

Keywords: Doxorubicin, Stress granule, Psammplysin F, Cancer, G3BP1

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In-silico analysis of single nucleotide polymorphisms (SNPs) in human *ALK* gene

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Abstract

Backgrounds: The Anaplastic Lymphoma Kinase (ALK) oncogene is a receptor tyrosine kinase known to be oncogenically activated either by point mutations or by chromosomal translocations found in some cancers like Neuroblastoma, non-small cell lung cancer, and anaplastic large cell lymphoma. ALK receptor tyrosine kinase, which is part of a family of proteins called receptor tyrosine kinases (RTKs), RTK transmits signals from the cell surface into the cell through a process called signal transduction. Some mutations and abnormalities in ALK may lead to Neuroblastoma (this cancer kills children under five years old). In this study, we checked some single nucleotide polymorphisms (SNP) that were identified as missense changes in the National Center for Biotechnology Information (NCBI) on the SNP database. These changes may increase the growth of cancer cells

Materials and Methods: The information was extracted from NCBI/SNP database and discovered 321862 SNPs in various parts of ALK. The results are then narrowed down to 2338 missense SNPs using filters. These SNPs include 15 pathogenic SNPs. Then the result was checked for finding the SNP which makes the abnormal protein.

Results: The result of this study with bioinformatics tools (e.g. SIFT, POLYPHEN-2, PHD-SNP, GO, and PROVEAN) shows that five types of these SNPs like rs113994087 (R>L) can produce an abnormal protein and cause cancer cells to grow and spread.

Conclusion: According to this result, we predict with a high probability that these SNPs are damaging and pathogenic.

Keywords: ALK, SNP, Neuroblastoma, RTK, Cancer

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Analysis of pathogenic SNPs of *NOTCH1* gene using bioinformatics tools

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Abstract

Backgrounds: T-cell acute lymphoblastic leukemia (T-ALL) is an aggressive cancer that affects children and adults. More than 50% of T-ALLs is caused by activating mutations in NOTCH signaling pathway, and this has made NOTCH1 the most prominent T-ALL specific oncogene. *NOTCH1* gene encodes a Class-I membrane receptor that is crucial for differentiation of progenitor pluripotent cells to committed T-cells. NOTCH1 receptor is a ligand-activated transcription factor and so it directly transmits the information of extracellular signals to the nucleus and changes the gene expression. Also, this protein has two subunits of NEC and NTM that ligands bind to NEC subunit.

Materials and Methods: Information about nucleic acid and amino acid sequences of *NOTCH1* were taken from NCBI database. From variation viewer section of this database and limiting the results to pathogenic and missense mutations, 11 cases of SNPs were obtained. Using databases such as PATHER, POLYPHEN, PhD SNP, PROVEAN and SNPs&GO, the pathogenesis of SNPs was investigated. The effect of SNPs on protein stability was also investigated by I-Mutant database.

Results: According to the results, the SNPs were predicted by 4 databases as pathogenic mutations and were identified by one database as neutral. The results of the I-Mutant database also showed a decrease in protein stability due to mutations.

Conclusion: In this study, the effect of 11 cases of SNPs on NOTCH1 protein was investigated and it was found that these SNPs were pathogenic and reduced protein stability. So, it can be said that these SNPs are directly related to the incidence of T-ALL in children.

Keywords: NOTCH1, SNP, Bioinformatics

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Evaluation of point mutation of T54R superoxide dismutase enzyme using bioinformatics methods

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Abstract

Backgrounds: Amyotrophic lateral sclerosis (ALS) is a progressive and fatal neurological disorder caused by mis-folding and aggregation of superoxide dismutase (SOD1). Considering the relationship between ALS and mutations in the gene encoding SOD1, investigate enzyme structure of mutation at position 54 enzyme (T54R) of the Zinc loop in SOD1 and identify methods for the prevention or treatment of ALS using bioinformatics' studies. Mutations in this position cause the spatial deformation of the enzyme and cause the mis-folding that was associated with pathogenesis
Materials and Methods: Using Chimera software and Project hope server, enzyme structure, i-stable and DUTE servers, enzyme structural stability and with Predic-SNP server, the stability of wild and mutant enzyme activity were studied. Finally, the predisposition to mutant amyloid accumulations was investigated using PASTA and AGGRESCAN servers.
Results: The T54R replacement mutation, by changing the charge and spatial shape of the enzyme, causes instability of the enzyme structure, and with a high confidence level of %72, is classified as destructive mutations. Also, the number of points of amyloid fibrils was 14, the best energy of amyloid points was -6.773894, and the number of hot spots of aggregation formation was 6, which is similar to wild enzyme.
Conclusion: The mutated residue is located in a domain that is important for binding of other molecules and in contact with residues in a domain that is important for the activity of the protein. The mutation might affect this interaction and thereby disturb signal transfer from binding domain to the activity domain and interaction between these two domains and as such affect the function of the protein. Studies reveal that the T54R mutation has destructive effects upon SOD1 T54R dimer stability due to increased fuctuation of mutation-residing loop distant from the dimer interface (Ghosh, D. K., 2020).

Keywords: Amyotrophic lateral sclerosis, Superoxide dismutase1, Zinc loops, T54R mutant

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Bioinformatics evaluation of expression *CK19* gene with miR-30a in breast cancer

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Abstract

Backgrounds: Breast cancer is the most commonly occurring cancer in women, comprising almost one third of all malignancies in females. It is second only to lung cancer as a cause of cancer mortality and it is the leading cause of death for American women between the ages of 40 and 55.1. Twenty-five percent to 30% of women with invasive breast cancer will die of their disease. About 5 to 10 percent of cases are due to genetic predisposition inherited from the individual's parents, including BRCA1, BRCA2. MicroRNAs (miRNAs) are a class of short, non-coding RNAs with endogenous function that control gene expression after transcription by suppressing translation or mRNA degradation. It is clear that miRNAs play an important role in regulatory mechanisms in various organisms, including the time of evolution and host-pathogen interactions, as well as cell differentiation, proliferation, apoptosis, and tumorigenesis.
Materials and Methods: Therefore, finding more bioinformatics information we used NCBI, miRbase, miRWALK2.0, Target scan, DAVID database and KEGG pathway.
Results: By examining the KEEG pathways, we predict that the *CK19* gene will be overexpressed due to an increase in miR-30a function, which increases the risk of breast cancer.
Conclusion: Considering the effect of Mir-30a and CK19 on each other, therefore, to have targeted treatment of breast cancer in patients whose increased expression of CK19 has caused cancer, we can use the pattern of reduced expression of Mir-30a as a result of reduced gene expression and ultimately cancer treatment.

Keywords: Breast cancer, CK19, KEEG, miR-30a, MicroRNAs

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Profiling the expression of LncRNAs involved in colorectal cancer progression in search for suitable diagnostic biomarkers

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Abstract

Backgrounds: Colorectal cancer (CRC) is among the most lethal cancers in both women and men, worldwide. This high mortality rate can be prevented by early diagnosis and thus more efficient treatment strategies. To that end, introducing more effective and clinically relevant biomarkers would be very important. Recent comprehensive transcriptome studies highlighted the importance of differentially expressed LncRNAs (DELs) in the tumorigenesis pathways of CRC. In this study, we aimed to construct networks of co-expressed genes (modules) involved in CRC in search for novel LncRNAs that can serve as diagnostic biomarkers.

Materials and Methods: This project has been carried out using public RNA-seq data sets of NCBI (bio project: PRJEB27536). Data from 62 samples (tumor and adjacent normal tissue) in fastq file format were retrieved from SRA. Differential expression analysis was performed by DESeq2 package in R and by utilizing WGCNA algorithm. Genes that exhibit a similar expression pattern were classified into a number of modules.

Results: We found 251 upregulated and 192 downregulated LncRNAs in our analysis of CRC samples. WGCNA clustered all the genes into 20 distinct modules. Our gene of interest, *APOBEC3A* (LFC = -3.2) was highly co-expressed with these novel DELs: RP11-638I2.6, RP11-109D20.2 and RP11-342H21.2.

Conclusion: Our results revealed many unannotated LncRNAs that might be crucial in progress and/or prognosis of colorectal cancer. We speculate that RP11-638I2.6, RP11-109D20.2 and RP11-342H21.2 may have key roles in biological pathways related to RNA editing due to their tight association with APOBEC3A. Further functional analysis is required for clarifying the potential roles of these candidate LncRNAs as potential diagnostic markers or druggable targets in CRC.

Keywords: Colorectal cancer, Diagnostic biomarkers, Transcriptome analysis, Differential expression, Long non-coding RNAs

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Production of optimized AAVs carrying the *RPGR* gene for X-linked retinitis pigmentosa type-3 gene therapy

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Abstract

Backgrounds: The most common form of X-linked retinitis pigmentosa is caused by mutations in the *RPGR* gene, leading to photoreceptor degeneration and loss of vision. Gene therapy using adeno-associated viral (AAV) vectors has proved its safety in clinics and AAV serotype-2 (AAV2) has been widely used for gene delivery into the retina. The aim of this study is to evaluate photoreceptor transduction efficiency of two rAAV2-RPGR vectors with mutant capsids following intravitreal and sub-retinal delivery in mice.

Materials and Methods: We synthesized codon-optimized human $RPGR^{ORF15}$ gene cloned into an AAV vector with CMV promoter. $RPGR^{ORF15}$ transgene expression was analyzed by transfection into cells followed by western blotting using an anti-RPGR antibody. The transgene was cloned into an AAV vector under the control of photoreceptor-specific GRK1 promoter. AAV2-(7m8) and AAV8 capsid vectors were used to introduce tyrosine to phenylalanine mutations by site-directed mutagenesis. To evaluate the function of mutant AAVs, we produced an AAV2 shuttle plasmid encoding an EGFP reporter.

Results: The recombinant AAV (7m8-YF)-EGFP particles were produced in HEK293T cells, purified from cell lysates by Heparin affinity chromatography, concentrated and stored. The activity and titer of the AAV (7m8-YF)-EGFP variant has been assessed by transduction of cultured cells showing a high transduction activity *in vitro*. We are now analyzing AAV-$RPGR^{ORF15}$ mutant variants and will test the transduction efficiency of these mutant viruses in the mouse retina.

Conclusion: AAVs harboring capsid surface tyrosine mutations display increased stability and penetration compared with the wild type counterparts.

Keywords: Retinitis Pigmentosa, *RPGR*, Gene therapy, Adeno-associated virus

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Evolutionary Trade-offs during tumor progression using Pareto Task Inference (ParTI) analysis

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Abstract

Backgrounds: Recent advances have enabled powerful methods to type tumors into diagnosis and treatment groups. Here, we applied a framework based on multi-task evolution theory, using the fact that tumors need to perform multiple tasks that contribute to their fitness. This approach relies on Pareto optimality concerning multiple evolutionary tasks. It predicts that cells that require performing multiple tasks have phenotypes that fall on low dimensional polytopes, phenotypes optimal for every task, known as archetypes.
Materials and Methods: For each cancer type, we downloaded the gene expression data from the TCGA data portal. Then we downloaded the clinical data of cancers from the cBioPortal. We focused our analyses on adenocarcinoma of three cancers (Colorectal, Breast, and Prostate). To find polyhedra and archetypes in tumor cells, we used the Pareto Task Inference (ParTI) package in MATLAB software.
Results: There are trade-offs between cancer cells for proliferation and survival. In the early stages, tumors have more of a cell division archetype for proliferation, but as the tumor progresses to the higher stages of malignancy, their tasks change, and they have an archetype such as invasion to survive.
Conclusion: As tumors progress from adenoma to carcinoma, their tasks change from general to specialize because of changes in trade-offs.

Keywords: ParTI, Archetype, Multi-task evolution, Phenotype, Cancer

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Differential gene expressions of *CALM1*, *PSMD6*, and *AK124742* long non-coding RNA in Cumulus cells from PCOS patients vs. normal control women

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Abstract

Backgrounds: One of the well-known causes of subfertility is polycystic ovary syndrome (PCOS). Genetic components play a critical role in the etiology of PCOS. The recognition of differentially expressed genes in PCOS patients might provide a better understanding of the pathophysiology of this syndrome and paves the way for novel therapeutics. Gene expression profiles in cumulus cells could be used as biological criteria for embryo competence and their analysis might lead to important molecular information about embryo quality. *CALM1*, *PSMD6*, and *AK124742* are three well-known genes associated with embryo development. Therefore, the objective of this study was to compare the expression of *CALM1*, *PSMD6*, and *AK124742* genes in the cumulus cells of infertile PCOS patients with their expression in the cumulus cells of the donor fertile group.
Materials and Methods: Cumulus cells were collected from the follicular fluid of 33 patients with PCOS as the experimental group and 33 cumulus donor women who referred to the infertility center for egg donation as the control group. Cumulus cells were frozen until genetic testing. The expression of *CALM1*, *PSMD6*, and *AK124742* genes was detected by real-time PCR.
Results: *CALM1* and *AK124742* gene expressions significantly increased (*CALM1* P = 0.003) (*AK124742* P = 0.000) and *PSMD6* expression significantly decreased (P = 0.002) in the PCOS group compared to the cumulus donor group.
Conclusion: Therefore, our findings suggested that may be the impact of PCOS on fertility is because of the changes in the expression levels of genes affecting the reproductive process including *CALM1*, *AK124742*, and *PSMD6*.

Keywords: *AK124742*, *CALM1*, *PSMD6*, Infertility, PCOS

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The evaluation effects of estrogen on *DLGAP5* gene expression in prostate cancer-3 (PC3) cell

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Abstract

Backgrounds: Benign Prostatic Hyperplasia and Prostate cancer are common clinical complications in urology. Estrogen receptor signaling pathways may be important in the development and maintenance of BPH and Prostate cancer. Estrogen and Selective Estrogen Receptor Modulators (SERMs) have shown a potential role in promoting or inhibiting prostate proliferation in Prostate cancer. The aim of this study is to investigate the effect of estrogen on *DLGAP5* gene expressions in Prostate Cancer-3 (PC3) cell lines.

Materials and Methods: In this study, prostate cancer cells of the PC3 cell line were cultured in DMEM medium with 10% bovine serum and treated at 24, 48 and 72 hours' intervals. The cells were exposed to concentrations of 60, 80, 100 nμ of Estrogen hormone. Apoptosis and cell growth were assessed by flow cytometry with Annexin-PI kit according to the kit instructions. Then expressions of *DLGAP5* gene in cells exposed to 100 nμ Estrogen hormone concentration were investigated by Real Time RT-PCR.

Results: By increasing the concentration of Estrogen hormone, and time-dependently, while increasing the induction of apoptosis, the expression level of *DLGAP5* gene decreased. The maximum Effect was gained by 100 nμ of Estrogen hormone and 72 hours after treatment of the cells.

Conclusion: Estrogen hormone, in a dose-dependent and time-dependent manner, decreases cell growth, increases induction of apoptosis and reduces the expression of these genes examined in PC3 cells. According to the current evidence, estrogen hormone can act as an anti-cancer agent.

Keywords: Estrogen hormone, Prostate cancer, PC3 cell line, *DLGAP5* gene

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The effect of alpha lipoic acid on cell survival and *fis1* gene expression in a Parkinson's disease cell model

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Abstract

Backgrounds: Mitochondria are known as semi-independent and dynamic organelles. Rotenone was used as an inhibitor of mitochondrial complex I to induce the Parkinson's disease model. In the present study, to further understand the role of mitochondrial dynamics in PD, it was determined to investigate the effective rotenone concentrations in SH-SY5Y neurons viability as well as the effect of alpha lipoic acid on cell survival in stress condition induce by rotenone. Genomic expression level of fis1 gene, in SH-SY5Y cell line treated with rotenone and alpha-lipoic acid was evaluated.

Materials and Methods: The effect of rotenone toxicity on SH-SY5Y cell growth in presence of rotenone and alpha-lipoic acid was evaluated by MTT method. The expression of *fis1* gene was then evaluated by real-time PCR.

Results: Based on IC50 calculations, the toxicity of rotenone was determined at concentrations higher than 1 µM. Toxicity effect of two concentrations of 2.5- and 5- µM rotenone for 24 and 48 hours' treatment showed a significant decrease in SH-SY5Y cells survival ($P < 0.0001$). Improved cell viability was observed in presence of 20 µM alpha-lipoic acid in SH-SY5Y cells treated by rotenone ($P = 0.04$). The qPCR results of *fis1* gene expression indicated a significant increase in SH-SY5Y cells treated with 5 µM rotenone ($P < 0.002$).

Conclusion: The results of this study show that the expression of a mitochondrial fission gene is altered in rotenone-treated SH-SY5Y cells in culture medium. Thus, mitochondrial dynamics may involve in the pathogenesis or control of Parkinson's disease.

Keywords: Rotenone, Parkinson, SH-SY5Y, Alpha-lipoic acid, Fission

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Pathogenicity prediction of PTS: c.70C>G (p.H24D) variant, identified recently in an Iranian PTPS patient

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Abstract

Backgrounds: BH4 is known as an essential cofactor for phenylalanine hydroxylase enzyme (PAH). Genetic mutations occurred in the genes related to this cofactor, including PTS, may lead to hyper-phenylalaninemia (HPA). In the present study, we used multiple in silico tools to predict the pathogenicity of *PTS*: c.70C>G (p.H24D), a variant recently identified in an Iranian patient with PTPS deficiency. Subsequently, it was classified based on ACMG-AMP guidelines.

Materials and Methods: To predict the nature of deleterious or neutrality of *PTS*: c.70C>G (p.H24D), a total of 10 in silico tools including: CADD, Mutation Taster, Polyphen-2, I-Mutant disease, PROVEAN, SIFT, SNPs&GO, FATHMM-XF, PhD-SNPg, and PANTHER PSEP were used. To assign the ACMG-AMP criteria related to this variant, a literature search was performed in multiple online databases.

Results: All predictive tools used in this study showed deleterious effects for *PTS*: c.70C>G (p.H24D) variant. Therefore, PP3 criterion was applied for this variant. Two other criteria including PM2 and PP4 were also assigned. Based on these observations, *PTS*: c.70C>G (p.H24D) was classified as a VUS variant.

Conclusion: *PTS*: c.70C>G (p.H24D) has only recently been identified in an Iranian PTPS patient in homozygous form and has not been reported in public mutational databases. Therefore, its classification as a VUS variant was not unexpected. Considering that so far only two studies, with a total sample size of 60 cases, have been performed in the field of identifying *PTS*-gene mutations among Iranian PTPS patients, it is possible that this variant will be seen again in Iran in the future.

Keywords: BH4, PAH, hyper-phenylalaninemia (HPA)

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Evaluation of alternations in *Akt* Gene expression in the T98G cell line treatment (Ni)

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Abstract

Backgrounds: GBM is the most aggressive diffuse glioma of astrocytic lineage. GBM is still an incurable disease with a 15-month median survival rate. The purpose of this study was to evaluate alternations in *Akt* gene expression in the Glioblastoma T98G cell line under treatment with thiosemicarbazones complexes (Ni).

Materials and Methods: Ni-thiosemicarbazones complexes were prepared in 57 and 61µM. The T98G cell line, was purchased from Pasteur Institute of Iran at passage 1, and then treated by Ni-thiosemicarbazones complexes in two groups after cell passage in 48h. Then RNA extraction and cDNA synthesis were performed and the expression of *Akt* gene and GAPDH were evaluated by Real-Time PCR. Finally, the results of Real-Time PCR were analyzed.

Results: Evidence showed that after treatment of the cell line with thiosemicarbazones complexes of Ni, *Akt* gene decreased in both concentrations of 57 and 61 µM in 48 hours, which was statistically significant. The rate of reduction in *Akt* gene expression treated with thiosemicarbazones complexes of Ni at concentrations of 57 and 61 µM was 0.001 and 0, respectively.

Conclusion: The results of T98G cell line treatment with Ni-thiosemicarbazones complexes and comparison with GPDH control gene showed that Ni- thiosemicarbazones complexes can be effective in reducing the expression of *Akt* gene as an oncogene. Changes in *Akt* gene expression showed that with increasing concentration, the greatest reduction in expression was observed, so the optimal effect of the drug depended on its concentration.

Keywords: Glioblastoma multiforme, Thiosemicarbazones, T98G, *AKT*, Ni

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The potential effect of miR-17-5p on RRMS through inhibition of PTEN in CD4^{+} T-cells

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Abstract

Backgrounds: Relapsing Remitting Multiple Sclerosis (RRMS) is the most common type of Multiple sclerosis (MS) which is a chronic autoimmune disease of the central nervous system. Up-regulation of miR-17-92 cluster in lymphocytes contributes to development of autoimmunity. The expression of miR-17-5p, a member of miR-17-92 cluster increases in CD4+ T-cells in RRMS patients. The aim of this study was to investigate the target genes of miR-17-5p in T-cells, the affected pathways and its relationship with RRMS.

Materials and Methods: The experimentally validated targets of hsa-miR-17-5p were obtained from miRTarBase database. The target genes with significant expression in T-cells were selected through DAVID database and their most related pathways were analyzed.

Results: Based on the achievements through bioinformatics and KEGG investigation, two signaling pathways including "T cell receptor signaling pathway" and "Toll-like receptor signaling pathway" were the most statistically related pathways with targets of miR-17-5p in T-cells.

Conclusion: Information from above signaling pathways indicates that miR-17-5p may inhibit 4 genes including CD28, MAPK1, MAP3K8 and IRAK1. It restricts proliferation, differentiation, and immune response, pro-inflammatory, chemotactic and antiviral effects of T-cells. According to previous researches, CD4+ T-cells are significantly increased in RRMS patients. Up-regulation of miR-17-5p in these cells causes down-regulation of Phosphatase and Tensin homolog (PTEN), which can lead to autoimmunity. Considering that PTEN is among experimentally validated targets of miR-17-5p, it can be concluded that miR-17-5p may causes RRMS through inhibiting PTEN instead of its 4 main targets in CD4+ T-cells.

Keywords: Multiple sclerosis, RRMS, miR-17-5p, PTEN, CD4+

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The application of gene expression analysis by ART in the selection of competent genes for pregnancy prediction

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Abstract

Backgrounds: In human assisted reproductive techniques (ART), selecting high-quality embryos for transferring is usually based on morphological criteria. Analyzing gene expression of Cumulus cells might lead to important molecular information about the embryo quality. CALM1. One of the well-known causes of infertility is polycystic ovary syndrome (PCOs). The number of retrieved oocytes with high implantation potential in PCOs patients is limited; therefore the process of selecting a good embryo in PCOs patients receiving ART is very important.

Materials and Methods: Granulosa cells were collected from 33 infertile patients with PCOs as an experimental group and 33 patients who referred to an infertility center for egg donation as a control group.

Results: Expression of all three genes *CALM1*, *PSMD6*, and *AK124742* in the pregnant group was higher than the non-pregnant group. Although the increase was not significant for the *CALM1* gene, it was significant for the other two genes: *PSMD6* ($p < 0.001$) and *AK124742* ($p < 0.05$). The expression of *CALM1* and *AK124742* genes increased significantly and the expression of *PSMD6* decreased significantly in PCOs group compared to the control group ($p < 0.05$).

Conclusion: If our prediction model is based on differences in gene expression levels between pregnant and non-pregnant groups then all three genes will be proper markers for predicting embryo competence due to increased expression levels in pregnant groups. If our prediction model is based on comparison of gene expression levels between control and PCOs groups, these three genes cannot be introduced as proper markers for predicting embryo competence due to ineffectiveness of gene changes on fertility outcomes in PCOs group.

Keywords: *AK124742*, *CALM1*, *PSMD6*, Infertility, PCOS

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Investigation of LincMTX2 expression in colorectal cancer

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Abstract

Backgrounds: Colorectal cancer (CRC) is the third most common type of cancer in the world due to the lack of noninvasive and accessible prognostic and diagnostic biomarkers for early detection of this disease. Long noncoding RNAs (LncRNAs) are of paramount importance in the underlying molecular mechanisms of CRC initiation and progression, and can be as a potential biomarker in it. According to the previous studies, MTX2 acts as a tumor suppressor by binding to miR-574-5p and increase SMAD4 expression in esophageal squamous cell carcinoma, cervical and stomach cancers. On the other hand, decrease of SMAD4 expression is associated with CRC metastasis and chemotherapy resistant. For these reasons, the aim of this study was investigation of MTX2 expression in CRC tissue samples and evaluation of its potential as diagnostic biomarker in this cancer for first time.

Materials and Methods: The colorectal tumor samples and adjacent normal samples were collected from thirty patients. After RNA extraction and cDNA synthesis, Real-time PCR was used to measure the LincMTX2 expression.

Results: The qPCR results showed the expression of LincMTX2 was down-regulated in thirty paired colorectal cancer specimens (*P*-value = 0.0001). The AUC of ROC curve was 0.7305 and revealed that the expression level of LincMTX2 can detect up to 73% of cases of colorectal cancer.

Conclusion: The considerably down-regulation of LincMTX2 in CRC tumor samples and its potential as biomarker highlight the need to further investigation of this LncRNA in larger population and cohort studies.

Keywords: LincMTX2, CRC, SMAD4, miR-574-5p, Biomarker

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The *KLK2* gene function in prostate cancer through informatics study

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Abstract

Backgrounds: The *KLK2* gene encodes a member of the grandular kallikrein protein family. Kallikreins are a subgroup of serine proteases that are clustered on chromosome 19. The protein encoded by this gene is a highly active trypsin-like serine protease that selectively cleaves at arginine resides. This protein is primarily expressed in prostatic tissue and is responsible for cleaving pro-prostate-specific antigen into its enzymatically active form. The *KLK2* gene is highly expressed in prostate tumor cells.

Materials and Methods: The GEPIA2 database was used to explain the gene and gene expression in normal and tumor tissues. Since *KLK2* gene is one of the CCDS sets, the NCBI site helped to identify members of the CCDS suite. The interactions between proteins were studied through STRING database. Ensemble and GeneCards databases were also used for genomic sequence information and their interpretation.

Results: The results we obtained include the following: The *KlK2* gene is highly expressed in prostate tumor cells. This gene is located on chromosome 19 and is responsible for protease cleavage. Bonding results in both coding and non-coding transcripts.

Conclusion: *KLK2* gene expression is higher in people with prostate cancer than in healthy ones. According to the results, it can be stated that *KLK2* gene can be considered as an effective and involved factor in prostate cancer. The upregulation in this gene is associated with the progression and development of the disease.

Keywords: *KLK2* gene, Prostate cancer, Tumor, Genomics

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A bioinformatics analysis of A168D Substitution in the *DMD* Gene in Duchenne muscular dystrophy

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Abstract

Backgrounds: Duchenne muscular dystrophy is a progressive neuromuscular disease that leads to difficulties in movement and premature death. This disease is a X-linked recessive disorder. DMD disease is caused by mutations in *DMD* gene (encoding dystrophin) that destroy the production of dystrophin in muscle. Muscles without dystrophin are sensitive to damage, that cause progressive loss of muscle tissue and function. In this study, a single nucleotide polymorphism (SNP) in NCBI was selected in the *DMD* gene for investigation.

Materials and Methods: In (rs128626236 G>T), the effect of conversion of alanine, a hydrophobic amino acid to aspartic acid, a hydrophilic amino acid on protein structure was assessed using SIFT, PROVEAN and I-Mutant databases.

Results: In this study, the SIFT database showed that Substitution at pos. 168 from A to D is predicted to AFFECT PROTEIN FUNCTION with a score of 0.01. The variant was then examined in the PROVEAN database. According to the PROVEAN database, the A168D variant with PROVEAN score = -4.513 (cutoff = -2.5) is predicted to be a DELETERIOUS variant. Finally, the variant was assessed using the I-MUTANT database [this database is Predictor of Protein Stability Changes upon Mutations] and DDG = -0.52 was obtained (DDG less than 0: Decrease Stability.

Conclusion: These results suggest that the A168D variant in the rs128626236 region of the *DMD* gene probably is a Deleterious variant and affects protein function. However, more investigation is needed to clarify this.

Keywords: *DMD* Gene, Duchenne muscular dystrophy, SNP, Pathogenic variant

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A novel missense mutation (c.215G>A) in two Iranian siblings with combined oxidative phosphorylation defect type 7: A case report

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Abstract

Backgrounds: Combined oxidative phosphorylation defect type 7 (COXPD7) is a rare mitochondrial disease resulting from the malfunction of the translational termination factor c12orf65 (MTRF-R), which leads to the disrupted mitochondrial protein synthesis. COXPD7 is characterized by several phenotypes, include early onset of failure to thrive and psychomotor regression, as well as vision issues and global muscle atrophy. The prevalence is < 1 in 1,000,000. So far, ten mutations have been reported in the literature to cause the disease.
Materials and Methods: The proband demonstrated intellectual disability, global developmental delay, visual impairment, strabismus and scoliosis. Whole exome sequencing and further Sanger sequencing were carried out to confirm the mutations in the proband and additional family members. Assessing the variant against databases such as VarSome and HGMD shed light on this novel variant.
Results: The WES data identified the variant in the proband as likely pathogenic. The results were consistent with that of the exome sequencing, confirming the segregation of c.215G>A with the phenotypes.
Conclusion: Here we report c.215G>A as a novel homozygous variant in C12orf65. It is the first missense mutation to cause c12orf65-related diseases, suggesting a loss of function mechanism might have led the multi-systemic phenotypes.

Keywords: COXPD7, C12orf65, WES, Missense mutation, Mitochondrial disorder

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Frequency of MRPA, PGP gene in drug resistance in Leishmania tropica and Leishmania major

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Abstract

Backgrounds: The aim of this study was to investigate the presence of two PGP and MRPA Efflux pumps related to ABC transporters and investigate the frequency and function of two MRPA (*pgpa* gene) and PGP (*mdr1* gene) pumps in drug resistance in clinical strains of Leishmania tropica and Leishmania major in cutaneos leishmaniasis and study of Leishmania resistance to antimony compounds.

Materials and Methods: In this study, 40 volunteers with leishmaniasis were randomly selected after Sampling of wound with a light microscope amastigotes examining, then inoculated into a specific two-phase NNN culture medium, Then DNA extraction was performed by phenol-chloroform method and then primers were identified with specific primers in ITS region, and the frequency of these two pumps involved in drug resistance was determined by PCR and specific primers.

Results: The results of the study of selected samples showed the frequency of *mdr1* gene was higher than of *mrpa* gene.

Conclusion: Probably the reason for the increase in the frequency of MDR pump compared to MRPA pump is the presence of MDR pump on the surface of plasma membrane, which transfers materials and drugs from the internal layers of the lipid bilayer membrane to the outer layers, reducing the concentration of the drug inside the cell and causing resistance. While the MRPA pump is in the cell organelle membrane.

Keywords: ABC transporter, Glucantim, Leishmaniasis, *mdr1* gene, *pgpa* gene

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Expression oscillation of natural antisense transcripts in the circadian clock

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Abstract

Backgrounds: Circadian clock enables organisms to perceive regular environmental changes and acquire proper adaptations. This system is essential for synchronizing biological processes with day/night cycles. So, misalignment of environmental and endogenous circadian rhythms is associated with different diseases. Noncoding transcripts including antisense RNAs are substantial components of the molecular clocks. Generally, the antisense transcripts participate in the regulation of gene expression. *PER2AS* and *CRY1AS* are the only identified Natural Antisense Transcripts (NAT) related to the core clock genes, which overlap with the *PER2* and *CRY1* genes, respectively. In this research, we hypothesized that *PER2AS* and *CRY1AS* like the other clock genes, display the oscillatory pattern in a 24-hour period and affect the expression of *PER2* and *CRY1*.

Materials and Methods: Initially, the A549 cell line was grown under standard conditions. The horse serum shock method was applied to stimulate the clock genes expression oscillation. In the next step, RNA extraction and cDNA synthesis was performed. Then, the expression fluctuations of *PER2AS*, *CRY1AS*, *PER2*, and *CRY1* were evaluated with real-time PCR technique.

Results: Our findings indicated that *PER2AS* and *CRY1AS* had similar oscillatory behaviors with their sense strand during 24-hour period.

Conclusion: We suggested that *PER2AS* and *CRY1AS* transcripts possibly by preventing the interaction of miRNAs with *PER2* and *CRY1* mRNAs influence their expression, positively. Therefore, more studies are needed on the pathological and biological significance of these antisense transcripts.

Keywords: Natural antisense transcripts, *CRY1*, *PER2*, *CRY1AS*, *PER2AS*

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Study of the effect of PRKDC knockout on the function of ectodermal genes in mouse embryonic stem cells

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Abstract

Backgrounds: Stem cells are characterized by their ability to self-renew and differentiate to numerous cell lines. PRKDC encodes the catalytic subunit of the DNA-dependent protein kinase (DNA-PKcs) playing a key role in non-homologous end-joining pathway. Also, it has been shown that PRKDC is modulated in disorders with mental retardation. Due to the differentiation of ectoderm to central and peripheral nervous system, we aimed to study the potential role of PRKDC on the expression of ectoderm genes.
Materials and Methods: TT1 stem cells in the form of $PRKDC^{-/-}$ and wild-type were cultured in defined medium. RNA and protein were extracted and then, the expression of NOG, BMP4 and FGF8 was quantitatively evaluated by real-time PCR and western blotting.
Results: Our data showed that FGF8 and NOG were upregulated in $PRKDC^{-/-}$ cells rather than wild-types. However, BMP4 was downregulated in the absence of PRKDC.
Conclusion: Collectively, the results demonstrate the role of PRKDC in the function of ectoderm genes.

Keywords: PRKDC, CRISPR/Cas9, Ectoderm, CNS

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Construction of an LncRNA-miRNA-mRNA network reveals functional Circulating miRNAs in pancreatic cancer

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Abstract

Backgrounds: Pancreatic ductal adenocarcinoma (PDAC) is the 7th cause of cancer mortality. Uncovering possible plasma biomarkers are necessary to set effective therapeutic strategies at the early stages of PDAC. MicroRNAs (miRNAs) are easily detectable biomarkers with delicate sensitivity and specificity in various cancers. This study introduces serum miRNAs expression profiles to find the most significant miRNAs in PDAC diagnosis.

Materials and Methods: The plasma miRNA expression profile of fifteen cases was obtained from the GEO (GSE114778). Differentially expressed miRNAs (DEMs) extraction was accomplished between healthy, pancreatitis, and PDAC samples using the limma package in R. $|\log2FC| \geq 0.58$, and p-value< 0.05 cutoff were set to identify the significant DEMs. MiRNet tool was used for target genes prediction of DEMs, including miRNAs and xeno-miRNAs. Gene Ontology and pathway enrichment analyses were performed using the Pathview and ClueGO. Survival analysis by the Kaplan-Meier plot was also conducted to validate critical miRNAs and target genes.

Results: A total of 132 miRNAs showed significant up/down-regulation in PDAC samples compared to healthy and pancreatitis samples. Our analyses introduced four novel key miRNAs with high node degrees in the network (miR-378c, miR-500a-3p, miR-1270, and miR-3605-5p). The NEAT1 and KCNQ1OT1 were identified as important shared lncRNAs for the regulation of these potential diagnostic miRNAs. These potential markers of PDAC were classified as miRNAs in cancer, PI3K-Akt pathway, Hippo pathway, focal adhesion, regulation of cell cycle, and apoptotic pathway. The candidate miRNAs are also important in regulating critical genes, including *bcl2*, *klhl15*, *gls*, *akt1*, and *fyn* which are downregulated in PDAC.

Conclusion: In conclusion, our study demonstrates new insights into the significant miRNA signatures of the PDAC prognosis and diagnosis. Identifying key miRNAs as candidate players in PDAC may be reflected as potential new targets to improve treatment strategies in PDAC.

Keywords: Pancreatic ductal adenocarcinoma, miRNA, Serum biomarkers, Bioinformatics, Survival rate

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The significant expression of P450 drug metabolism pathway between untreated tumors and normal-adjacent tissues in breast cancer patients

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Abstract

Backgrounds: The cytochrome P450 (CYP) family is a group of enzymes that contribute to the cell proliferation, progression and drug metabolism of breast cancer (BC). This pathway is affected in the metabolism of pro-carcinogens and response to the treatment as well, so their role remains controversial. Nowadays, with the advent of bioinformatics analysis and high-throughput-based methods, it is possible to study and describe the expression profile of tumors and determine the genes' functions and their pathways toward diagnosis, prognosis and therapeutic targets. Our study aims to detect the significant genes and pathways involved between cancerous and non-cancerous breast tissue by analysis of microarray datasets.

Materials and Methods: Based on our inclusion and exclusion criteria, six microarray studies were obtained from Gene Expression Omnibus (GEO). Finally, four datasets "GSE139038, GSE22384, GSE31589 and GSE24124" were chosen among them. We analyzed raw data with "R" software, "limma" and "AgiMicroRna" packages, then normalized by "SVA" package. At the next step, Gene Set Enrichment Analysis (GSEA) was performed to determine the key pathways.

Results: The result based on GSEA was performed between untreated tumor and adjacent-normal samples and finally P450 drug metabolism circumscribed through Kyoto Encyclopedia of Genes and Genomes (KEGG) database. Finally, 28 top genes were determined to confirm the vital role of P450 pathway among downregulated ones in cancer.

Conclusion: This study manifested the reduction expression of P450 Drug Metabolism pathway in BC and its association as biomarkers in this malignancy.

Keywords: Bioinformatics analysis, GEO, GSEA, Breast cancer, P450 Cytochrome Pathway

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The evaluation effects of estrogen on *BAX* gene expression in prostate cancer-3 (PC3) cell lines

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Abstract

Backgrounds: Prostate cancer is the commonest cancer in men, affecting 214 per 1000 European men. It is the second commonest cause of cancer death. Estrogens play a role in proliferation in the prostate, but interestingly are capable of stimulating as well as inhibiting growth. Recent studies have demonstrated that estrogen receptor signaling pathways may be important in the development and maintenance of BPH and Prostate cancer. The aim of this study is to investigate the effect of estrogen on *BAX* gene expressions in Prostate Cancer-3 (PC3) cell lines.

Materials and Methods: In this study, prostate cancer cells of the PC3 cell line were cultured in DMEM medium with 10% bovine serum. Cells were treated at 24, 48 and 72 hours' intervals. The cells were exposed to concentrations of 10, 20, 30, 40, 50, 60, 70, 80, 90, 100 nμ of Estrogen hormone and the cell growth was measured by MTT colorimetric method. Then expressions of *p53* and *BAX* genes in cells exposed to 100 nm Estrogen hormone concentrations were investigated by real-time PCR

Results: By increasing the concentration of Estrogen hormone, and time-dependently, while increasing the induction of apoptosis, the bioavailability of the cells and the expression level of *BAX* gene decreased. The maximum Effect was gained by 100 nm of Estrogen hormone and 72 hours after treatment of the cells.

Conclusion: The prostate is an estrogen target tissue and estrogens directly and indirectly affect growth and differentiation of prostate.

Keywords: Estrogen hormone, prostate cancer, *BAX* gene

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Experimental verification and bioinformatics analysis of miRNAs for the differentiation between HER2 positive and HER2 negative Breast cancer

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Abstract

Backgrounds: Breast cancer is the most frequent malignancy cancer among women. Clinically, breast cancers are classified by hormone receptor status including estrogen receptor (ER), progesterone receptor (PR), and human EGF-like receptor 2 (HER2) receptor expression. HER2 is over-expressed or amplified in 30% breast cancers which are associated with poor prognosis among all subtypes of breast cancer. microRNAs are a class of short non-coding regulatory RNAs that can be proposed to be used as biomarkers for cancers. Several studies showed that microRNAs could be considered as potential biomarkers for early detection of breast cancer.
Materials and Methods: The Gene Expression Omnibus database (GEO, http://www.ncbi.nlm.nih.gov/geo/) in the National Center for Biotechnology Information (NCBI) is currently the largest fully public gene expression resource. In the study, several bioinformatics tools were utilized to investigate the most important biomarkers. Microarray data set GSE68085 was downloaded from GEO. Differentially expressed miRNAs were obtained by using R package "limma" in microarray datasets. The expression levels of miRNAs were confirmed by real-time PCR.
Results: Bioinformatics algorithms are predicted signature miRNAs as biological markers in breast. Real-time PCR confirmed that the expression level of these miRNAs ware significantly different in HER2 positive breast cancer tissues compared to HER2 negative breast cancer tissues.
Conclusion: However, it is not clear whether the changes in miRNA expression are a cause or effect of the disease for many miRNA species, they could be potential biomarker in cancers because many studies on the expression of various miRNAs. This study demonstrate that optimized high-throughput microRNA expression profiling offers novel biomarker in HER2 positive breast cancer and Her2 negative ones.

Keywords: Breast cancer, HER2, microRNAs, Biomarkers, Bioinformatics

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Significance of circulating miR-107 in type2 diabetes mellitus

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Abstract

Backgrounds: MicroRNAs (miRNAs) are involved in various biological processes, such as cell development, proliferation, differentiation, apoptosis and metabolism. It has been shown that there is selective expression of circulating miRNA that may correlate with diabetic conditions. Here, we evaluated the expression of circulating miR-107 by quantitative PCR in blood from patients with type 2 diabetes (T2D) and healthy controls.

Materials and Methods: In this case-control study, miR-170 expression was evaluated in 30 blood samples from patients with T2D and 30 controls. Total RNA was extracted using Trizol reagent. The integrity and quality of RNA was evaluated gel electrophoresis and spectrophotometry. Quantitative real-time polymerase chain reaction (qRT-PCR) was performed following synthesis of complementary DNA (cDNA). Specific primers were designed using the Oligo 7 software and were subsequently synthesized. Each run of qRT-PCR was completed with a melting curve analysis. Quantitative measurements were performed in triplicate and relative expression was measured using comparative Ct method ($2^{-\Delta\Delta Ct}$) and normalized to U6 snRNA as internal control. Statistical analyses were performed using GraphPad Prism 8.0. $P < 0.05$ was considered statistically significant.

Results: A single peak was observed in all the dissociation curves and a single band was seen on the gel at the correct product size for each gene. miR-107 expression in patients was significantly higher than that in the controls (1.94 ± 0.04 vs1.01 ± 0.02 $p < 0.0001$).

Conclusion: According to the data of this study, miR-107 expression level appear to be effective in the emergence of T2DM.

Keywords: T2DM, β cell, ncRNA, miR-107, Gene expression

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Nurr1/GPX1-expressing adipose-derived stem cells cultured on PCL/MWCNT scaffolds differentiate into dopamine-secreting cells: A new approach for Parkinsons's disease cell therapy

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Abstract

Backgrounds: Parkinson's disease (PD) is a progressive neurological ailment with a wide range of motor and non-motor symptoms. It is the second most prevalent neurodegenerative disease after Alzheimer's disease. The destruction and death of dopamine-producing neurons in the substantia-nigra of the midbrain is the characteristic pathology of Parkinson's disease. Intrastriatal transplants of foetal mesencephalon-derived dopaminergic neurons have shown that the cell replacement technique works and that the denervated striatum can be reinnervated. However, the use of prenatal dopaminergic neurons as a source for cell therapy in Parkinson's disease has been halted due to ethical, technological, and practical difficulties. Adipose-derived stem cells have emerged as a promising treatment option because of their ability to multiply and create dopamine-producing neurons.

Materials and Methods: In this work, Adipose-derived Stem Cells were created that could co-express Nurr1 (an important transcription factor in dopaminergic neuron development) and GPX-1 in a stable manner (a neuroprotective enzyme against oxidative stress). Nurr1/GPX-1-expressing Adipose Derived Stem Cells (Nurr1/GPX-1-AdSC) were developed into dopaminergic-like cells in a three-dimensional culture environment made up of Poly—Caprolactone/Multi-Wall Carbon Nano Tube (PCL/MWCNT) Nano fibrous scaffolds and particular signaling molecules.

Results: AdSC-derived dopaminergic neurons grown and developed on PCL/MWCNT scaffolds have a high expression of dopaminergic neuron-specific genes. The Nurr1/GPX-1-AdSC differentiated on PCL/MWCNT electrospun scaffolds could effectively and selectively produce dopamine in response to stimulation, according to reverse-phase HPLC. Finally, our findings showed that Nurr1/GPX-1-AdSC cells could be successfully supported and promoted by PCL/MWCNT Nano fibrous scaffolds, resulting in the production of functioning dopaminergic-like cells.

Conclusion: The findings of this study might have an influence on future tissue engineering for Parkinson's disease cell treatment.

Keywords: Dopaminergic neurons, Adipose derived stem cells, Nano fibrous scaffolds, Parkinson's disease

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Classification of a *PTS* gene variant, c.400G>A (p. E134K), based on ACMG-AMP criteria

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Abstract

Backgrounds: Defects in the enzymes involved in the BH_4 de novo synthesis or its recycling pathway may lead to hyperphenylalaninemia (HPA). PTPS is one of the enzymes participated in the BH_4 de novo synthesis and encodes by *PTS* gene. To date, about 200 *PTS* gene variants have been identified and recorded in BioPKU database (http://www.biopku.org/home/pnddb.asp). The aim of this study was to predict the pathogenicity of a variant recently reported in an Iranian patient with PTPS deficiency, c.400G>A (p. E134K), and classify it based on ACMG-AMP guidelines.
Materials and Methods: Ten predictive tools including: CADD, Mutation Taster, Polyphen-2, I-Mutant disease, PROVEAN, SIFT, SNPs&GO, FATHMM-XF, PhD-SNPg, and PANTHER PSEP, were used. In addition, a literature search was performed in multiple online databases to assign the ACMG-AMP criteria related to c.400G>A (p. E134K) variant.
Results: c.400G>A (p. E134K) variant showed a deleterious effect in all ten predictive tools. Therefore, we applied PP3 criterion (defined as: multiple lines of computational evidence support a deleterious effect) for this variant. Three other criteria including PM3_strong (detected in trans with a pathogenic variant), PM2 (absent/rare in controls), and PP4 (patient's phenotype or family history is highly specific for a disease with a single genetic etiology) were assigned. Based on these observations, c.400G>A (p. E134K) was classified as a likely pathogenic variant.
Conclusion: Our findings in this study on the likely pathogenic nature of c.400G>A (p. E134K) will be a good reference for physicians who advise couples carrying this variant.

Keywords: PTS, ACMG-AMP, hyperphenylalaninemia

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Bioinformatics study of the important role of S100A8/9 and inhibition microRNA-223 in acute myeloid leukemia inflammation and secondary injuries

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Abstract

Backgrounds: Acute myeloid leukemia (AML) is a hematopoietic stem cell malignancy characterized by ineffective hematopoiesis and excessive proliferation of immature myeloid cells. The role of pro-inflammatory cytokines, chemokines, adhesion molecules, and inflammatory enzymes has been linked with chronic inflammation. S100A8 and S100A9 are calcium-binding proteins predominantly expressed by neutrophils and monocytes and play key roles in both normal and pathological inflammation. Both proteins were found to promote tumor progression through the establishment of premetastatic niches and inhibit antitumor immune responses. MiR-223 is an evolutionarily conserved anti-inflammatory microRNA primarily expressed in myeloid cells. MiR-223 post-transcriptionally regulates many genes essential in inflammation, cell proliferation, and invasion. Chronic inflammation has been found to mediate a wide variety of diseases, including cardiovascular diseases, cancer, diabetes, arthritis, Alzheimer's disease, pulmonary diseases, and autoimmune diseases.

Materials and Methods: In this study, Raw data associated to miRNA-223, S100A8/9 were extracted from databases TCGA, UCSC Xena, String and GEPIA. Then it was analyzed and evaluated with bioinformatics techniques and software such as cytoscape, MCODE and SPSS26.

Results: Inhibition of microRNA-223 and expression of S100A8/9 main causes of inflammation in leukemia. According to this study, In the FEB category, category M3 shows the lowest expression of miRNA-223, and the expression of S100A8/9 in the age of 61-80 years has the most expression (respectively 1341.14 and 1087.84 Read per million). The P(-value) of patient survival in the graph (miRNA-223, S100A8/9) is equal to 0.075, 0.081 and 0.085, respectively

Conclusion: Bioinformatics analysis shows the importance of the effect of the cancer group and the patient s age was clearly demonstrated. With targeted control of biomarkers, the severity of inflammation can be informed in a timely manner, the patient can be treated correctly, and secondary lung and kidney damage can be prevented. It will greatly help the patient, family and medical staff, increase the success rate of the struggle for survival in AML inflammation and secondary injuries.

Keywords: Inflammation, Acute myeloid leukemia, miRNA-223, S100A8/9, Bioinformatics

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Predicting of miR-149 Regulatory Network and hub genes in breast cancer: an *in silico* study

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Abstract

Backgrounds: Breast cancer (BC) is the most common cancer among women and one of the leading causes of death among women worldwide. Frequent studies have demonstrated the role of miRNAs in BC. miRNAs, are small noncoding RNA, that regulate gene expression through target mRNAs. Bioinformatics analysis is a valuable tool in predicting miRNA target genes involved in BC. Among them, miR-149 was confirmed to be deregulated in various tumors including BC. Studies showed that miR-149 as a tumor suppressor, repressed migration, and invasion of BC. Therefore, we aimed to identify regulatory mechanism associated of miR-149 in BC.

Materials and Methods: Targetscan, Mirmap, mirwalk and mirdb databases were used to predict miR-149 target genes. The potential prediction of 50 common miR-149 targets and the discovery of their potential roles in BC were performed by GEPIA. The STRING database was then used to identify and establish a protein-protein interaction network (PPI) and the Cytoscape tool was used to analyze the network pathway and hub genes.

Results: The target genes and pathways potential by miR-149 were analyzed using integrated enrichment prediction tools (Enrich R). KEGG pathway analysis suggested the role of miR-149 target genes in cancer pathway and Ras, MAPK, Rap1 signaling pathways. It also GO pathway enrichment showed regulation of apoptosis and transcription in *FOS*, *SMAD2*, *SRC*, *Bcl2L11* and *FASLG* genes.

Conclusion: This study, using bioinformatics approaches, showed that the function of miR-149 and its target genes could provide new insights into the treatment of BC.

Keywords: Breast cancer, miR-149, Bioinformatics analysis

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Bioinformatics analysis Identified miR-487a-3p in human dilated cardiomyopathy

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Abstract

Backgrounds: Dilated cardiomyopathy (DCM) is a common type of non‑ischemic cardiomyopathy, which causes heart failure and sudden cardiac death worldwide. MicroRNAs (miRNAs) are small noncoding RNAs that play crucial roles in post-transcriptionally regulating gene expression, by targeting 3'UTR of their target mRNAs. Recently, they are introduced as promising biomarkers in cardiovascular disease. The present study aimed to predict and candidate circulating miRNAs, as potential biomarkers for DCM.

Materials and Methods: Data from the National Center for Biotechnology Information Gene Expression Omnibus were employed to investigate the differential expression of miRNAs in a serum of DCM patients versus normal ones. Then, the gene targets of miRNAs were determined through the miRWalk database. Consequently, the GTEx portal database was used to attain the expression of gene in tissues.

Results: Our bioinformatics analysis demonstrated that hsa-miR-487a-3p is differentially expressed in serum samples of DCM patients. According to miRWalk data, this miRNA could possibly target 3'UTR of *MYPN* and *TPM1* which have high expression in heart tissues as well as mutation in DCM.

Conclusion: Altogether, our analysis suggests that there is correlation between hsa-miR-487a-3p, *MYPN* and *TPM1* genes expression and DCM. With performing functional analysis along with bioinformatics analysis, this miR-487a-3p appeared as a potential diagnostic biomarker for DCM.

Keywords: Dilated cardiomyopathy, miR-487a-3p, *MYPN*, *TPM1*

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REG4, CEACAM5 and OLFM4 are among the most recurrently fused genes in patients with colorectal cancer

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Abstract

Backgrounds: Colorectal cancer (CRC) is one of the leading causes of cancer-related deaths in both men and women, all around the world. Since current treatments are not really effective, molecular targeted therapy would be advantageous for CRC therapy. Next generation sequencing technologies provide new insight into the dynamics of cancer development. In this work, we focused on molecular dynamics of mRNAs at transcription level to identify some of the recurrent fusion genes in colorectal cancer.

Materials and Methods: This study was carried out using RNA-seq data from NCBI data bank (PRJEB27536 bio project). For this purpose, a total of 60 matched samples were analyzed with FusionCatcher V.1.20. A list of fusions was then constructed for all the cancer samples, and finally the frequency of recurrent fusions was evaluated.

Results: REG4, CEACAM5 and OLFM4 were the most recurrently fused genes present in cancer samples in comparison with their normal counterparts. REG4 is a very hyperactive mRNA in terms of transcriptional dynamics and is involved in the most frequent fusions in cancer such as PIGR-REG4, MUC2-REG4 and KRT8-REG4. Other recurrent fusions were CEACAM5-MUC2, CEACAM5-KRT8 and OLFM4-PIGR.

Conclusion: Our study revealed that REG4, CEACAM5 and OLFM4 are among the most frequent fusions found in our cancer data. The oncogenic role of these fusions can be investigated with further functional analysis. Some of these fusions can be druggable and might be good candidates for molecularly targeted therapy.

Keywords: Colorectal cancer, Transcriptome analysis, Fusion transcripts, Recurrent fusion

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Occupation of ACE receptor by SARS-CoV-2 and male infertility risk: An *in silico* analysis

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Abstract

Backgrounds: SARS-CoV-2 has a single-stranded RNA-plus genome (~30 kb) with five major open reading frames, which is encode nonstructural replicase polyproteins and structural proteins: Spike (S), Envelope (E), Membrane (M), and Nucleocapsid (N). Spike protein as known a causative ligand for mammalian cell's angiotensin-converting enzyme 2 (ACE2) receptor which transmits the virus in to host cells. Due to the high expression of ACE and ACE2 receptor in various organs, the aim of this study is to investigation of correlation between ACE and ACE2 receptor with other proteins, which involved in the male infertility using by *in silico* analysis.
Materials and Methods: In this study free web databases such as NCBI (https://www.ncbi.nlm.nih.gov) and MalaCards (https://www.malacards.org) and online proteins interaction data analyzer *e.g.*, GeneMANIA server (https://genemania.org) were used.
Results: Our studies showed that ACE and ACE2 receptors have a higher expression in testicular tissue. In other hand interaction between proteins showed these receptors have co-expression with Protamine 1/PRM1 and Protamine 2/ PRM2.
Conclusion: Since Protamines are a special protein in the sperm cells, so defective of this protein cause the sperm abnormalities and affects in male infertility. We recommend, occupation of ACE and ACE2 receptors by SARS-CoV-2 may cause to verity of protamine expression level, which effect on male infertility risk.

Keywords: Angiotensin-converting enzyme (ACE), *In silico* analysis, Male infertility, Protamine, SARS-CoV-2

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Molecular evaluation of exon 28 von willebrand factor gene in the diagnosis of type 2B VWD in patients referred to the Iranian Blood Transfusion Organization

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Abstract

Backgrounds: Von willebrand disease (VWD) is most common inherited bleeding disorder with a prevalence of 1% in the global population. Type 2VWD includes four types (2A, 2B, 2M, 2N). Type 2B VWD is rare subtype consisting about 5% of all VWD. Laboratory diagnosis of type 2B VWD is challenging and needs a complex phenotype and genotype analysis.

Materials and Methods: In a 3 years period of time all cases referred to the IBTO reference coagulation lab, cases who referred for VWD and showing a minimum criteria as response to low-dose RIPA test selected for the study. VWF: Rco, VWF: Ag, FVIII: C and RIPA tests were performed. Cases suspected for type 2B VWD were evaluate for exon 28 molecular testing.

Results: 7 case suspects for type 2B/platelet type VWD found. Our results were Age (*median:* 18y, *range:* 3–56y), Sex (men: 6, female: 1), VWF: Ag (*median:* 57, *range:* 44–117) VWF: Rco (*median:* 28, *range:* 2–91) FVIII:C (*median:* 66, *range:* 2-148) VWF: Rco / Ag (*median:* 0.6, *range:* 0.04–0.77). We were detected the variants c.3946G>A p. V1316M; c.3735G>A p. V1245V; c.3789G>A p. S1263S; c.3797C>T p. P1266L. Molecular testing of exon 28 was for 3 cases as type2B VWD. The other 4 cases (member of a family) not approved for type 2B by molecular testing, however platelet type VWD should be excluded in this family.

Conclusion: A panel of testing included molecular analysis to needed for confirmation or exclusion of type 2B VWD.

Keywords: Von willebrand disease, Type 2B von willebrand disease, Molecular analysis

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Bioinformatically design of potential cyclooxygenase-1 (Cox-1) inhibitors

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Abstract

Backgrounds: Cyclooxygenase is a key enzyme in the conversion of arachidonic acid to prostaglandins. It is found in many cells in the body, such as white blood cells, the immune system, stomach, kidneys, and brain cells. Cyclooxygenase-1 is mainly produced in non-inflammatory cells such as stomach cells and its production is a continuous process. The Cox-1 gene has 22 kb, 11 exons, and lacks TATA-box. Numerous studies revealed serious side effects by using enzyme inhibitors of Cox-1. In this research, to decrease the side effects and enhance their efficiency, a novel in silico-based inhibitor was designed.

Materials and Methods: First, 20000 compounds similar in structure of aspirin inhibitor were extracted from the ZINC database with the files related to the structure of Cox-1 from RCSB (Research Collaboratory for Structural Bioinformatics). After ligands preparation, all compounds were docked to Cox-1 for the selection of 10 potent inhibitors.

Results: 10 inhibitors were selected based on Gibbs free energy (least ΔG). According to the docking findings, inhibitors bound to Cox-1 lead to conformational changes in enzyme, potential energy reduction, and enhancing the inhibitor-enzyme stability.

Conclusion: Based on the findings, the inhibitors can decrease the inflammation and pain in various inflammatory diseases, by insertion to the active site on the basis of more specificity and consequently less toxicity.

Keywords: Cyclooxygenase-1, Docking, Prostaglandins, Gibbs free energy, Aspirin

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Comprehensive meta-analysis and differential network analysis of breast cancer

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Abstract

Backgrounds: Breast cancer is the most common cancer known among women and is the leading cause of cancer death in women worldwide. Various molecular markers were suggested in numerous studies, but they were limited by one study and its experimental design. The aim of this project was to validate suggested prognostic and therapeutic markers using an integrative analytical approach in breast cancer.

Materials and Methods: We performed meta-analysis of 21 gene expression microarray studies and differentially expressed genes (DEGs) were identified using LIMMA Package of R. Weighted gene co-expression network analysis (WGCNA) was used to construct free-scale gene co-expression networks to explore the associated modules and identify candidate biomarkers. Quantitative real-time PCR (qPCR) was performed to evaluate the expression of hub genes in tumor and healthy breast tissues in Iranian women.

Results: The results demonstrated that the blue and tan modules have the lowest module preservation between tumor and healthy networks. The hub genes of above mentioned modules were identified based on intramodular connectivity. A total of 1911 differentially expressed genes (DEGs) were screened out which among these DEGs, the 33 genes were common with hub genes. The *FOXA1* and *ERBB2* genes with the most intramodular connectivity were selected for experimental validation. Two above mentioned genes were found to be significantly higher expressed in tumor samples compared to paired normal tissues.

Conclusion: The *FOXA1* and *ERBB2* genes can be used as biomarkers for early detection of breast cancer and the appropriate treatment.

Keywords: Meta-analysis, WGCNA, DEGs, Breast cancer, qPCR

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Molecular docking of secondary metabolites in the plants of apocynaceae family to inhibit P-Glycoprotein (Pgp) for cancer treatment

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Abstract

Backgrounds: This study was performed to investigate the anti-cancer properties of the secondary metabolites of the plants of Apocynaceae family and their abilities to inhibit P-Glycoprotein (Pgp) drug resistance through molecular docking.
Materials and Methods: The homology modeling of the crystal structure of Pgp (PDBID: 3G5U) was conducted by using the SWISS-MODEl ExPASy server. Upon drawing the Ramachandran plot, we saw that 98.4% of the residues were in the favored and allowed areas. Flexible docking study on Pgp by using a group of secondary metabolites, whose properties were demonstrated via the Way2Drug server, proved to be able to inhibit Pgp. As a result, Pgp was energy-minimized by applying UCSF Chimera package. After identifying the active sites, the M-site and R-site showed to have the highest roles in the interaction between the ligand and protein, while the H-site displayed the least role in this interaction. The greatest roles of residues in the M-site, R-site, and H-site were related to Phe, Ser, Val, Met, and Gln residues, Ser, Phe, and Gln residues, and Leu, Ser, and Gln residues, respectively. Gln691 residue generally played a key role in all the interactions.
Results: The most effective secondary metabolites in the Apocynaceae family were identified to be related to Oleandrin, Oleandrigenin, Neriine, Vindoline, Vincristine, Vinblastine, Serpentine, Tabersonine, Tetrahydrosecamine, and Vallesiachtamine plants, which demonstrated the ability to inhibit Pgp.
Conclusion: We found that, secondary metabolites in the Plants of Apocynaceae Family increase the chance of treatment after reducing the dose of chemotherapy.

Keywords: Molecular docking, Multi-drug resistance, P-glycoprotein (Pgp), Anti-cancer, Apocynacea

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Association between common HLA alleles and GVHD occurrence after allogeneic hematopoietic stem cell transplantation

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Abstract

Backgrounds: Graft-versus-host disease (GVHD) in its acute (aGVHD) and chronic (cGVHD) form remains one of the most serious complications of allogeneic hematopoietic stem cell transplantation (allo-HSCT). There are several risk factors known to be associated with GVHD development. Some reports suggest that certain human leukocyte antigen (HLA) variants may influence the incidence of GVHD.

Materials and Methods: The aim of our study was to analyze possible association between individual HLA alleles (HLA-A & HLA-B) and the occurrence of aGVHD in patients following allo-HSCT from HLA-identical sibling donors. We analyzed 234 patients with acute myeloid leukemia (AML) in Iran population who had received a first matched-sibling allogenic HSCT between March 2008 and March 2021. HLA genotyping was performed serologically and using the polymerase chain reaction with specific primer sequence (SSP-PCR).

Results: Cumulative incidence of acute GVHD was 32.5% (76 patients). Recipients carrying the HLA-A*01, HLA-A*24, HLA-B*07, and HLA-B*35 alleles was associated with a higher incidence of aGVHD. While, HLA-A*32 and HLA-B*18 alleles showed a statistically significantly lower incidence of aGVHD.

Conclusion: The findings of this study may by implication suggest the possibility that the effects of specific HLAs on transplant outcomes may reflect inherent biological features, and may be helpful to predict risk and clinical outcomes after allo-HSCT and to develop optimal treatment strategies. More extensive studies are warranted to identify the effect of specific HLAs/HLA alleles on clinical outcome and to elucidate its biological features in populations of other ethnicities.

Keywords: Hematopoietic stem cell transplantation, Human leukocyte antigens (HLA), Graft-versus-host disease (GVHD)

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An Iranian long chain-3-hydroxyacyl-CoA dehydrogenase deficiency patient with HADHA mutations: case report

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Abstract

Backgrounds: Mitochondrial trifunctional protein (M-FTP) deficiency, as a rare metabolic disorder, classified into three phenotypes including lethal phenotype which begins in the neonatal period. The M-FTP protein catalyzes the oxidation of long chain fatty and composed of 8 subunits such long-chain 2,3-enoyl-CoA hydratase (LCEH) and long-chain 3-hydroxyacyl CoA dehydrogenase (LCHAD). LCHAD deficiency inherited as an autosomal recessive trait and associated with HADHA gene mutations (OMIM: 600890). These cause a clinical spectrum of symptoms such as progressive peripheral neuropathy, hypoketotic hypoglycemia, hepatopathy, cardiomyopathy, myopathy and pigmentary retinopathy.

Materials and Methods: We report an Iranian girl with an initial diagnosis of LCHAD deficiency using tandem mass spectrometry (MS/MS) who unexpectedly died on the 70th day after birth. The parents were first cousins, with one healthy son, and a history of two previous miscarriages.

Results: When an AR disorder occurs in a family without familial history, the whole exome sequencing (WES) is an option to identify the genetic causal mutation in the parents of deceased child and then further confirmed by Sanger sequencing. The mother, with sectoral heterochromia, had heterozygous missense mutation "c.2026C>T (p. Arg676Cys)" mutations in the *HADHA* gene, diagnosed by WES. According to ACMG guideline and several prediction tools, this mutation is known as likely pathogenic mutation. Furthermore, she had 2 other heterozygous missense mutations in *CFTR* and *PLEKHG2* genes. Then, these 3 mutations were examined in her husband by Sanger sequencing and the heterozygosity for "c.2026C>T (p. Arg676Cys)" mutations in the *HADHA* gene was detected.

Conclusion: Due to the validation of carrier state for mutant alleles in both parents and pathogenicity of c.2026C>T mutation in *HADHA* gene, this is the cause of the disease in deceased affected child. Moreover, it is important to perform genetic counseling and prenatal diagnosis (PND) for next pregnancy to prevent the birth of another affected child.

Keywords: LCHAD deficiency, Metabolic disorder, M-FTP deficiency, Genetics

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A network-based approach to uncover the potential genes, microRNAs and pathways in colorectal cancer pathogenicity

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Abstract

Backgrounds: Colorectal cancer (CRC) is one of the most prevalent malignancies worldwide. Despite various conducted surveys and experiments around the CRC, the pathogenicity of this disease is not clear enough. The present study aimed to apply a systematic approach to make valuable insight into the involved genes and their regulatory layers that can shed light on CRC pathogenicity.

Materials and Methods: In the current survey, GSE126095 microRNA profiles, and gene microarray dataset GSE113513 re-analyzed through $P<0.05$ |log fold change (FC) |≥ 1 parameter to recognize differentially expressed genes (DEGs) and MicroRNAs (DEMs). The quality of datasets was analyzed by principal component analysis (PCA). Using the EnrichR database, the DEGs related kinases (KEA) and transcription factors (ChEA) were retrieved. Following, by using Cytoscape application, a multi-layer network composed of DEGs, KEA, and ChEA was constructed and analyzed. Then functional and pathway enrichment analyses by Cytoscape ClueGO plugin were applied.

Results: Top 10 hub genes, miRNAs, TFs and kinases extracted from multilayer network, Module 1 of the merged network was chosen for further investigation, most of the edges and nodes were connected with RHO GTPase effectors, Cdc20-mediated mitotic protein degradation, rRNA processing and the senescence-associated secretory phenotype, based on GO and pathway enrichment analysis. Most DEGs are related to import and biological pathways such as Wnt/β-catenin, flavonoids metabolism pathway and UDP-glucuronosyltransferases pathway. Moreover, top-most central *TP53*, *AR*, *CTNNB*, *POU3F2*, *FOXA1*, *NR3C1*, *PIAS1*, *PPAR* were identified as genes in the network that play a significant role in CRC.

Conclusion: We have here followed a systematic approach to exploring the underlying molecular mechanisms of CRC.

Keywords: Colorectal cancer, microRNAs, GSE126095

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Investigation of LincFOXF1 expression in colorectal cancer

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Abstract

Backgrounds: Colorectal cancer (CRC) is the third most common cancer in the world. Long intergenic noncoding RNAs (LncRNAs) are of paramount importance in the underlying molecular mechanisms of CRC initiation and progression. According to the recent bioinformatics studies, lincFOXF1 may be involved in the CRC progression and metastasis via induction of epithelial-mesenchymal transition (EMT). For this reason, the aim of this study was investigation of lincFOXF1 expression in CRC tissue samples and evaluation of its potential as diagnostic biomarker in this cancer for first time.

Materials and Methods: The colorectal tumor samples and adjacent normal tissue samples were collected from thirty patients. After total RNA extraction from samples and cDNA synthesis, Real-time PCR was used to measure the LincFOXF1 expression. Paired t-test was used for comparison of LincFOXF1 expression in tumor and normal samples and receiver operating curve (ROC) was used to assess the diagnostic value of LincFOXF1.

Results: The qPCR results showed that the expression of LincFOXF1 was down-regulated 3/76 times in thirty paired colorectal cancer specimens (p-value = 0.0423). The AUC of ROC curve was 0.6883 and revealed that the expression level of LincFOXF1 can detect up to 68.83% of cases of colorectal cancer and can be used as a diagnostic biomarker.

Conclusion: Finally, the authors suggest that the considerably down-regulation of LincFOXF1 in CRC tumor samples and its potential as biomarker highlight the need to further investigation of this lncRNA in larger population and cohort studies.

Keywords: LincFOXF1, CRC, Cancer progression, Cancer metastasis, LncRNA

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Identification of the distinctive genes in the development of very early and late relapsed childhood ALL

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Abstract

Backgrounds: Acute lymphoblastic leukemia (ALL) is the most common type of leukemia diagnosed in children. Between 15 and 20 percent of ALL patients who are received initial treatment and achieved complete remission will experience the disease return. even very late relapses in childhood ALL occurs 5-20 years after diagnosis. The distinctive gene expression pattern of these prognostic factors remains poorly understood. Very early relapse of ALL is characterized by an increased proliferative capacity of leukemic blasts and up-regulated mitotic genes.

Materials and Methods: We first extracted all the genes involved in an ALL disease from the GEO database (FDR≤0.05) then we obtained all the miRNAs-mRNAs interactions from the mirDIP database. And finally, by using Cytoscape to find the most critical differentiation genes. also by GO, we apply enrichment analysis for these genes.

Results: We identified a set of top 10 genes (*CBX5*, *KAT6A*, *PLCB1*, *ABI2*, *C16orf72*, *CBFB*, *TNS1*, *SSX2IP*, *ZFP36L2*, *TIMP3*) differentially expressed in very early relapsed ALL compared to late relapsed disease and also we find that the most key microRNAs in this regard. The majority of genes had a function in mitosis.

Conclusion: This study suggested that The distinguishing feature of early or late onset of the ALL disease can be the key role of these top 10 genes that involved cell cycle pathways and cell adherence junctions or in the mitotic phase so can regulation of cell growth and transformation. We also find the most critical microRNA in diseases onset and progression.

Keywords: Acute lymphoblastic leukemia (ALL), GEO database, mirDIP database, microRNA, Genes

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Investigating the effect of *MMP-1* gene and its rs1799750 polymorphisms on endometriosis disease in an Iranian women population

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Abstract

Backgrounds: Endometriosis is clinically defined as the presence of endometrial-like tissue found outside the uterus, resulting in a chronic, inflammatory reaction. It is a complex disease that is influenced by genetic and environmental factors. Recently several candidate genes have implicated in the pathogenesis of endometriosis, including genes involved in inflammation, cell cycle regulation and adhesion molecules. Matrix metalloproteinases (MMP) are a family of proteolytic enzymes that can degrade extracellular matrix Components. Importantly, these groups of enzymes have been also implicated in the pathogenesis and diffusion of endometriosis.

Materials and Methods: One hundred endometriosis patients and 100 healthy controls were enrolled in this study. DNA was extracted from whole blood samples. PCR-RFLP technique was used to investigate the relationship between endometriosis and rs1799750 [-/G] polymorphism on *MMP-1* gene in Iranian population.

Results: Distribution of genotypes was not significantly different between case and control groups ($p = 0.618$). Frequencies of the --, -G and GG genotypes were 32.6%, 44.2%, 23.2% in patients and 35.8%, 46.7%, 17.5% in controls, respectively.

Conclusion: Our results provide no evidence of a relationship between the rs1799750 polymorphism and susceptibility to endometriosis in Iranian patients. However, these findings should be confirmed in studies with larger sample sizes.

Keywords: *MMP-1* gene, rs1799750, Endometriosis, Polymorphism

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In-silico screening of bio-antimicrobial peptides as potential drug for inhibiting CYP51 in Aspergillus fumigatus, Candida albicans and Leishmania infantum

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Abstract

Backgrounds: Aspergillus fumigatus, Candida albicans and Leishmania infantum are three widespread fatal skin disease producers so controlling these diseases is important. Cytochrome P450 protein (CYP51) is common among these three microorganisms. It's a hemoprotein enzyme and its duty is catalyzing oxidation of organic compounds cycle so blocking this protein can be effective in treating of diseases caused by these microorganisms. It's clear that natural remedies are more reliable so using natural remedies is more effective and has less side effects. bio antimicrobial peptides(bio-AMP) are one of the natural agents that we can use them in the treatments of diseases. Bio-AMPs are made in bacterias' body and we use them against bacterias with the closest kinship.

Materials and Methods: In this study we use RCSB PDB database in order to find PDB codes by using PDB database (https://www.rcsb.org/). StraPep (http://isyslab.info/StraPep/) and PhytAMP (http://phytamp.hammamilab.org/main) database were used to figure out AMPs. HADDOCK 2.2 (https://alcazar.science.uu.nl/services/HADDOCK2.2/) was used to check binding affinity between protein and peptide.

Results: After checking and comparing it was proved that 2KUY has the highest score of binding affinity for all of the target proteins and can be a Comprehensive treatment for skin diseases caused by A.fumigatus, C.albicans and L.infantum. 2KEG from bacteria microorganism for Candida albicans, 1Z64 with hookworm source for Aspergillus fumigatus and 2MWT from snake venom microorganism for Leishmania infantum can be used as exclusive treatments.

Conclusion: According to the results using 2KUY, 2KEG, 1Z64 and 2MWT and change it to eliminate possible side effects it can be a good way to control these microorganisms. It's a bioinformatics study and need to be confirmed by experimental researches.

Keywords: CYP51, Aspergillus fumigatus, Candid albicans, Leishmania infantum, Bio-antimicrobial peptides

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Correlations of mRNA-miRNA interaction between tumor and margin tissues in patients with breast cancer

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Abstract

Backgrounds: Breast cancer is one of the three most common cancers worldwide. MicroRNA (miRNA) has been connected to kinds of cancer types like breast cancer. In this analytical article, we constructed an initial attempt to address the differential expression of the mRNA-miRNA interaction map between tumor and margin tissues samples.

Materials and Methods: The gene expression profiles for miRNA and mRNA were collected from Gene Expression Omnibus (GEO). Datasets related to genes (GSE61724, GSE86374, and GSE37751) and miRNAs (GSE40525, GSE42072, GSE45666, GSE143564) were separately downloaded and analyzed by "R" software with the usage of "LIMMA". By using Cytoscape, the miRNA- mRNA interaction and regulatory network were built. Enrichr and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis was applied to estimate the possible molecular mechanisms of DEGs. Dysregulated miRNAs were predicted by miRTarBase.

Results: Based on our result, 270 miRNAs and 325 mRNAs were differentially expressed. The enrichment results from analyzing DEmRNAs were shown to be associated with Methylation pathways.

Conclusion: Results show the prominent roles of miRNA- mRNA regulatory networks in breast cancer and revealed new prognostic and diagnostic approaches for better and more efficient treatment.

Keywords: Breast cancer, GEO, Microarray dataset, DEGs, DNMT

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In silico investigation of putative G-quadruplex-forming regions in spike sequence of SARS-CoV-2 Delta variant

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Abstract

Backgrounds: The ongoing COVID-19 outbreak is now becoming an emerging threat to human health worldwide. SARS-CoV-2 infection begins through the interaction between spike (S) proteins of virus with the host cellular receptor. Up to now, 11 variants of SARS-CoV-2 have been recognized, and these variants are anticipated to develop while new variants appear. Particular variant of SARS-CoV-2 is categorized via a class of the prevalent mutations in its genome, and the major parts of the described mutations have been reported in Spike protein. Recent studies of RNA viruses have revealed that G-quadruplex structures contribute in several important cellular processes such as recognition of a genome, recombination and HIV-1 RNA dimerization and packaging. In addition, they could play important role in HIV-1 transcriptional silencing. Furthermore, it has been revealed that G-quadruplex structures act as regulator in the translational and immune evasion of Epstein Barr Virus (EBV). Moreover, they might impact the human papillomaviruses (HPVs) replication and transcription. G-rich regions in the Zika viral genome were also recognized to form G-quadruplex structure. The aim of our study was to investigate if the spike gene of currently dominant SARS-CoV-2 Delta variant could form G-quadruplex structures.

Materials and Methods: The high quality and high coverage sequences of Delta (n = 1276) (as of Aguste, 2021) was downloaded from GISAID. The human SARS-CoV-2 spike protein sequence from Wuhan-Hu-1, China (NCBI accession code: YP_009724390.1)1 was used as reference sequence to examine the putative G-quadruplex forming sequences. SARS-CoV-2 spike genome of delta variant was analyzed using QGRS Mapper online software (http://bioinformatics.ramapo.edu/QGRS/analyze.php).

Results: We found ten G-quadruplex forming sequences with proper G-score. Only one of the G-cores in Delta variants was higher than Wuhan-Hu-1 reference sequence.

Conclusion: Taken together, our analysis of G-quadruplex- forming sequences in SARS-CoV-2 delta variant might provide insights into the design of anti-viral treatment by targeting the G-quadruplex structures.

Keywords: SARS-COV-2, Delta variant, G-quadruplex Structures, QGRS mapper

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Novel functionally validated L-asparaginases with anti-proliferating activity against leukemic cell line: A MetaGenomic survey in Caspian Sea

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Abstract

Backgrounds: For over 30 years, L-asparaginase has been widely used as an antineoplastic agent for treatment of acute lymphoblastic leukemia (ALL) and non-Hodgkin lymphoma. The critical role of L-asparaginases relies on its capability to selectively killing leukemic cells via depleting patient's serum of L-asparagine, an amino acid that tumor cells essentially depend on to guarantee their growth. In spite of current forms of enzymes commercially available, non-desirable features of L-asparaginases necessitates continuous explorations of new enzymes from new sources.
Materials and Methods: Herein, we screened almost 3 million predicted genes of its assembled metagenomes, resulting in annotation of 87 putative L-asparaginase genes. Three of these genes were selected, synthesized, cloned and their hydrolysis activity was evaluated. Also their activity against Jurkat cell line was assessed.
Results: We analyzed the hydrolytic parameters of the selected enzymes showing to be among the most desirable reported values. Two recombinant enzymes showed significant anti-proliferative activity against Jurkat leukemia cell line, while no cytotoxic effect on human erythrocytes or human umbilical vein endothelial cells was detected.
Conclusion: Similar salinity and ionic concentration of the Caspian water to the human serum highlights potential of secretory L-asparaginases recovered from these metagenomes as potential novel enzymes with new functions and potential applications to replace current enzymes in use.

Keywords: Metagenomics, L-asparaginases, Leukemia, Jurkat

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Effect of alterations in miR-483-3p expression on the expression of SMAD4 gene in breast cancer patients

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Abstract

Backgrounds: SMAD4 is a down-stream effector of transforming growth factor-beta (TGF-B) signaling pathway. Although the tumor suppressor role of this prognostic biomarker has been previously studied in many malignancies, its role as a prognostic biomarker in breast cancer has yet to be confirmed. The regulatory effect of microRNA-483-3p (miR-483-3p) as a tumor suppressor on SMAD4 has also been investigated, and a correlation has been reported in some malignancies such as the pancreatic cancer. This study aimed to assess the expression of miR-483-3p and its effect on the expression of *SMAD4* gene in breast cancer patients.

Materials and Methods: The expression of *SMAD4* gene was evaluated in 51 paired tumoral tissue/adjacent healthy tissue specimens by real-time polymerase chain reaction (PCR). *GAPDH* gene was used as the control (reference) gene. The correlation of SMAD4 expression with clinicopathological features was also evaluated. The expression of miR-483-3p was then evaluated in 16 SMAD4 negative tumoral specimens by real-time PCR, to assess its effect on the expression of SMAD4 by REST 2009 software. Data were analyzed by the Chi-square test.

Results: The results showed no significant correlation between the expression of miR-483-3p and SMAD4 ($P > 0.05$).

Conclusion: It appears that alterations in the expression of miR-483-3p have no significant effect on the expression of *SMAD4* gene in breast cancer patients.

Keywords: Breast neoplasms, SMAD4, Gene expression, miR-483-3p, Real-time Polymerase Chain Reaction

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Silibinin inhibits cell migration through downregulation of *RAC1* gene expression in highly metastatic breast cancer cell line

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Abstract

Backgrounds: Triple negative breast cancer is the most invasive breast cancer subtype and possesses poor prognosis and survival. Rho GTPase family, especially Rac1 participates in a number of signaling events in cells with crucial roles in malignancy, migration and invasion of tumor cells. Silibinin, a flavonoid antioxidant from milk thistle has attracted attention in the recent decades for chemoprevention and chemotherapy of tumor cells. In this study, the effect of Silibinin on the migration capacity of MDA-MB-231 cells, a highly metastatic human breast cancer cell line was investigated by evaluation of Rac1 expression.
Materials and Methods: MTT wound healing and transwell assays were performed to evaluate the effects of Silibinin on proliferation and migration of MDA-MB-231 cells. In addition, the influence of the Silibinin on the expression of Rac1 mRNAs was assessed by RT-PCR.
Results: Results indicated significant dose-dependent inhibitory effect of Silibinin on proliferation and migration of MDA-MB-231 cells. It significantly inhibited the expression of Rac1 mRNA.
Conclusion: In conclusion, the results demonstrated that Silibinin inhibits metastasis of the MDA-MB-231 breast cancer cell line. The anticancer effect of Silibinin may contribute to the inhibition of metastasis by decreasing the expression level of *Rac1* gene. Therefore, Silibinin can be used as an experimental therapeutic for the management of TNBC metastatic cancer, with the promise shown in terms of increasing cancer patient survival.

Keywords: Silibinin, Breast cancer, TNBC, Rac1, Metastasis

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Investigation of homologous chromosome recombination for immunotherapy in colon cancer

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Abstract

Backgrounds: Researchers are looking for immunotherapy methods that target genes associated with and treat the most common complications of colorectal cancer. Patients with colorectal cancer are not sensitive to immunosuppressive inhibitors due to microsatellite stability. We studied the recombination of homologous chromosomes for immunotherapy in colon cancer.
Materials and Methods: This study was conducted in 2021 by searching for keywords such as immunotherapy, colon cancer in reputable databases such as PubMed, google scholar. Finally, 8 articles were found and 3 articles were used.
Results: 17% of patients showed changes in HRR genes and then ATM 9%, RAD50 3%, ATR 3%, BRCA2 4%, BRIP1 3% showed the most mutations. Due to these mutations, HRR genes increase immune activity. This process also has a significant effect on the recombination of homologous chromosomes for immunotherapy in cancer. Although DNA double-strand breaks (DSBs) are substrates for homologous recombination (HR) repair, it is becoming apparent that DNA lesions produced at replication forks, for instance by many anticancer drugs, are more significant substrates for HR repair.
Conclusion: HRR gene mutations significantly increase immune activity in patients with intestinal cancer. According to the findings, it is better to set up a program that is not a risk factor for us.

Keywords: immunotherapy, Cancer, Colon cancer

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Pathogenicity analysis of E234A mutation in the *CITED2* gene in Ventricular septal defects (VSD)

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Abstract

Backgrounds: Ventricular septal defects (VSD) are congenital defects in the dividing wall between the two ventricles. The ventricular septum consists of an upper membranous region and under muscular region. The membranous anomalies are common and in most cases, surgery is needed, but small muscular defects often close themselves. These defects cause blood to leak from the left ventricle to the right ventricle and ultimately it leads to pulmonary hypertension and multiple complications.

Materials and Methods: In this study, we are looking for a dangerous mutation in a gene related to the important transcription factor, CITED2, in these defects. We found the missense and likely pathogenic mutation E234A at National Center for Biotechnology Information (NCBI) database. In this mutation, a hydrophilic amino acid, Glutamate, was exchanged into a hydrophobic amino acid, Alanine, at position 234. We analyzed this mutation at Sorting Intolerant from Tolerant (SIFT), Polymorphism Phenotyping (PolyPhen) and Protein Variation Effect Analyzer (PROVEAN) online bioinformatics databases.

Results: The result of analysis at PROVEAN database showed that this mutation is deleterious. Research on the SIFT database showed that substitution at position 234 from E to A is predicted to affect protein function with a score of 0.00. The result of analysis at PolyPhen showed that this mutation is predicted to be probably damaging with a score of 0.999.

Conclusion: According to the results of this study, this mutation most probably disrupts the function and stability of this protein and plays a role in causing these defects. However, more research is needed to prove conclusively that this mutation is pathogenic.

Keywords: VSD, CITED2, SIFT, PROVEAN, PolyPhen

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Pathogenic Analysis of one of the missense SNP in the *F9* Gene in Hemophilia B

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Abstract

Backgrounds: Hemophilia B is a single-gene disease and its inheritance is X-linked recessive. This illness is characterized by a deficiency of factor IX clotting activity. Clinical symptoms include prolonged bleeding after injuries or surgery, Spontaneous bleeding into muscles and joints, and so on. Hemophilia B is also known as "Christmas hemophilia". Worldwide, the prevalence of hemophilia B in live birth among boys is estimated at 1: 40,000 which is lesser than hemophilia A.

Materials and Methods: The *factor IX (F9)* gene locus is located at Xq27.1 (39kb) and contains 8 exons. More than 800 different mutations including point mutations, deletions and insertions have been reported on this gene. The aim of this study is the pathogenic analysis of one of the missense SNP in the *F9* gene. We study "rs137852231" (SNV) from NCBI SNP data bank. Then this SNV is considered by bioinformatics tools such as SIFT and PROVEAN web servers.

Results: Our analysis showed that the Q96P missense mutation affected protein structure and protein function. Scores of this mutation in SIFT (<0.05) and PROVEAN (≤-2.5) web servers are 0.00 and -5.110, respectively, which indicates that the mutation is deleterious. This mutation replaces a non-polar amino acid (Proline) with low flexibility instead of a polar amino acid (Glutamine). This replacement limits the peptide bond and changes the structure of the protein.

Conclusion: Based on the analysis and the results we obtained, we conclude that this mutation is pathogen. But this theory should be proved with experimental studies.

Keywords: Hemophilia B, Factor IX, X-Linked recessive, SNP, Missense mutation

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Mutations in the Delta 6 desaturase gene by UV and genetic analysis and comparison of GLA production in the mutant and wild strains of *Mucor rouxii*

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Abstract

Backgrounds: Mutation is one a way to obtaining the strains with high production capacity and higher efficiency of omega 3 and 6 essential fatty acids, use of raw materials in medium and the ability to grow in specific conditions like high temperature and aeration.
Materials and Methods: For mutation in Mucor rouxii, a fungus known to produce GLA (Gamma linolenic acid), and UV radiation was used. The fungus is cultured in PDA medium for one week to produce spores. Spores were isolated with normal saline and serial dilution was prepared. Finally, 106 Spore / ml dilution (dilution with PBS) was obtained. Spores were counted for this dilution with Toma Lam. Then 1 ml of the dilution was spread in media and exposed to UV rays. Then, for better screening of GLA-producing mutants, two methods were used, one growth at 15 ° C and the cerulenin antibiotic was used. In order to determine the sequence of Delta 6 desaturase gene in wild and mutant strains amplified by PCR method and sequenced. Comparisons between mutant and wild sequences were performed using CLC software and NCBI site.
Results: Examination of lipid changes in *Mucor rouxii* showed that in the presence of cerulenin antibiotic, there was a significant increase in lipid production and the increasing in GLA production by *Mucor rouxii* mutant was 15.8% compared to the wild strain. In a comparison of the mutant and reference genes, it was found that the bases had changed in different regions, but chromosomes in both the reverse and leading readings, showed that the *Mucor rouxii* gene differed in only one amino acid and only one base A Replaced C, and this heterozygous mutation altered GLA production.
Conclusion: According to the studies, it was found that the parts that have been altered in this protein are all related to extracellular sequences, and the sequences that pass through the membrane and inside the cell are quite similar to the reference protein.

Keywords: Omega 6, Mutation, *Mucor rouxii*, GLA

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Investigation of LincTNS1 expression in colorectal cancer

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Abstract

Backgrounds: Colorectal cancer is the 2nd leading cause of death because of cancer. Long noncoding RNAs (LncRNAs) involve in the tumor formation, angiogenesis, proliferation, migration, apoptosis and differentiation. Based on recent bioinformatics studies, lincTNS1 may be involved in the progression and metastasis of colorectal cancer. LincTNS1 is involved in regulating the expression of CAT and GSR genes which associate with cell antioxidant potential. As a result, the aim of this study was investigation of LincTNS1 expression in CRC tissue samples and evaluation of its potential as diagnostic biomarker in this cancer for first time.

Materials and Methods: The colorectal tumor samples and adjacent normal tissue samples were collected from thirty patients. After total RNA extraction from samples and cDNA synthesis, Real-time PCR was used to measure the LincTNS1 expression. Paired t-test was used for comparison of LincTNS1 expression in tumor and normal samples and receiver operating curve (ROC) was used to assess the diagnostic value of TNS1.

Results: The qPCR results showed that the expression of LincTNS1 was down-regulated 2/97 times in thirty paired colorectal cancer specimens ($p < 0.0322$). The AUC of ROC curve was 0.7056 and revealed that the expression level of LincTNS1 can detect up to 70.56 % of cases of colorectal cancer and can be used as a diagnostic biomarker.

Conclusion: Finally, the authors suggest that the considerably down-regulation of LincTNS1 in CRC tumor samples and its potential as biomarker highlight the need to further investigation of this LncRNA in larger population and cohort studies.

Keywords: LincTNS1, CRC, Cancer progression, Cancer metastasis, LncRNA

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Twist1 antisense oligo nucleotides and inhibition of invasion in advanced prostatic cancer cell line

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Abstract

Backgrounds: According to the statistics provided by the Global Cancer Observatory, prostate cancer is the second prevailing cancer in men worldwide. Androgen independent stage of the disease happens following bone metastasis. Therefore, it is important to find approaches for preventing of cancer invasion to other tissues. Twist1 is transcription factor initiates epithelial-mesenchymal transition process. So, it can be an appropriate target for down regulating leads to metastasis inhibition. In this research, we studied the effect of 2 antisense oligo nucleotides on invasion potential of PC3 cell line.

Materials and Methods: PC3 cell line was used as a model of advanced prostatic cancer cells. Cell invasion assay was done using CytoSelect™ 12-Well Cell Invasion Assay Kit (Cellbiolabs). For this purpose, 300 µl of FBS free RPMI medium containing 0.75*106 of PC3 cells was incubated for study. 500 µl of RPMI with 10 % FBS was used as chemoattractant agent. Two antisense oligonucleotides were designed readily separately used with concentration of 500 nmol as invasion inhibitor. Treatment time was 48 hours in cell culture incubator with 37o C and 5% CO2 atmosphere. Finally, invasive cells were stained and results were obtained by measuring OD560 in plate reader (BioTek).

Results: Antisense oligonucleotide 1(5' GTCCTGCATCATCTCTCGAG 3') was shown 33 % anti-invasive effect on PC3 cell lines. However, this effect was 29 % for antisense oligonucleotide 2 (5' CACGTCCTGCATCATCTCTC 3').

Conclusion: These results were showed that it is possible to decrease rate of metastasis in metastatic prostate cancer cell line with down regulating of *twist1* gene and it can increase survival chance even in patient with androgen independent grade IV prostate cancer.

Keywords: Prostate cancer, twist1, PC3, Metastasis, Invasion

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Investigation of associated between coronary artery disease risk and mir-146a (rs2910146) polymorphism in an Iranian population

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Abstract

Backgrounds: Coronary artery disease (CAD) is the leading cause of death in humans worldwide. CAD is considered to be caused by both environmental and genetic factors as well as the interaction of these two factors. Apart from modifiable risk factors such as diet and tobacco use, genetic factors have been estimated to account for 40–60% of the risk for CAD in epidemiology, family, and twin studies. Hence genetic risk factors predisposing people to CAD remain largely unknown. MicroRNAs (miRNAs) are a class of small, non-coding RNA molecules with 21–23 nucleotides in length, and negatively regulate gene expression at the post-transcriptional level through translational repression or mRNA degradation. There are more than a thousand miRNAs reported in a human genome. There is an increasing body of evidence that miRNAs play a critical role in the control of key biological processes including development, differentiation, growth, and metabolism as well as pathophysiology of neurodegenerative disease, cancer and cardiovascular disease. This study investigated the influence of the miR-146a GC rs2910164 in Iranian population with CAD.

Materials and Methods: One hundred and twenty angiografically confirmed CAD patients, and 118 healthy controls with no symptoms of CAD. Genomic DNA extraction from whole blood was performed for all of the participants. Genotyping of the polymorphism was done by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) method.

Results: Frequencies of CC, GC and GG genotypes were 0 %, 38.1%, 61.9% in the control group and 3.3%, 38.3% and 58.3% in CAD patients respectively. There was no significant difference in frequencies of the genotypes between case and control groups (P = 0. 0.1857).

Conclusion: The sample size was relatively small. A future study with larger sample size is needed.

Keywords: Coronary artery disease, Mir-146a, Polymorphism

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PEAR1 genetic variants in Essential Thrombocythemia: The prevalence and association with hematological parameters and ET mutations

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Abstract

Backgrounds: Essential thrombocythemia (ET) is a type of myeloproliferative neoplasm characterized by the expansion of the megakaryocytic/platelet line. Given the undeniable role of genetic variations in the pathogenesis of ET, as well as the proven effects of *PEAR1* SNPs on platelet function, the innovative purpose of this study is to investigate the prevalence of *PEAR1* variants (rs12041331 and rs12566888) and their relationship to hematological parameters and ET-related mutations.

Materials and Methods: We studied 105 ET patients and analyzed ET patients' mutational profiles, including *JAK2* V617F mutation (detected by Allele-specific PCR), *CALR*, and *MPL* mutations (both through PCR amplification). Two SNPs of the *PEAR1* gene were assessed through ARMS-PCR, and the Sanger method was used for the validation of ARMS-PCR amplification.

Results: The prevalence of rs12041331 and rs12566888 in ET patients were 43.9% and 38.5%, respectively, and rs12041331 was significantly associated with increased platelet counts (P-Value: 0.02). As expected, the incidence of thrombotic events in *JAK2* $^{+}$ patients was high and significantly associated with *JAK2* mutation (P-Value: 0.02). The prevalence of thrombotic events was also high in patients with the rs12041331 variant. Besides, a significant relationship was also found between the rs12041331 and *CALR* mutation (P-Value: 0.03).

Conclusion: In recent years, the footprint of the *PEAR1* variant's effect on platelet aggregation led to evaluating these variants in ET patients. Finally, the significant relationship between the rs12041331 variant and increased platelet count and *CALR* mutation announced that the idea of this study could be pursued and challenged in the future.

Keywords: Essential Thrombocythemia, Platelet endothelial aggregation receptor 1, Polymorphisms, Platelet, Janus kinase 2, ARMS-PCR, Prevalence

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Mutational screening through comprehensive bioinformatics analysis to detect C250T mutation in *TERT* promoter region among patients with brain tumor

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Abstract

Backgrounds: The principal mechanism of telomere maintenance, which plays a vital role in human tumorigenesis, is reactivation of *telomerase reverse transcriptase*. *TERT* promoter region (*TERT*p) mutations are common among solid tumors, particularly cancers originating from slow-replicating tissues, like brain tumors. Furthermore, two most common mutations in this region (C228T and C250T) are considered as potential prognostic and diagnostic biomarkers of brain tumors. Accordingly, detection of these mutations in cfDNA from a Liquid biopsy offers a less invasive tool in various steps of diagnosis and therapy.

Materials and Methods: In this study, 16 blood samples of brain tumor patients were collected. DNA extraction, polymerase chain reaction, gel electrophoresis and Sanger sequencing has been done. Identified point mutation has been analyzed using two online tools, Softberry and PROMO, in order to predict its effect on *TERT*p reactivation.

Results: C250T mutation were recognized in 8 samples including three glioblastoma multiforms, two pituitary gland tumors, one recurrent hemangioblastoma, one cerebellum tumor and an astrocytoma. Softberry indicated two de novo ETF binding sites. Similarly, PROMO showed two new ETF binding sites in promoter region.

Conclusion: This study indicated that C250T as a hotspot mutation in *TERT*p region, leads to de novo ETF binding sites which can reactivate the gene. Additionally, C250T where found in high grad and recurrent samples. Due to the prevalence of this mutation among brain tumor tissues, it can probably be considered as a biomarker for diagnosis and a landscape of tumor for patient follow ups.

Keywords: Brain tumor, Telomerase reactivation, *Telomerase reverse transcriptase*, *TERT*p, cfDNA

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Genomic and ancestral variation underlies the severity of COVID-19 clinical manifestation in individuals of European descent

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Abstract

Backgrounds: The coronavirus disease (COVID-19) caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is characterized by a wide spectrum of clinical phenotypes ranging in acuteness from asymptomatic, symptomatic with mild or moderate manifestation and severe involving pneumonia and respiratory distress.

Materials and Methods: We performed a genome-wide association study (GWAS) employing the genotyping data from AncestryDNA COVID-19 host genetic study that included COVID-19 positive patients and healthy individuals who had tested negative for SARS-CoV-2 infection at the time of recruitment. Further, we employed the asymptomatic individuals as controls instead of healthy individuals. GWAS was performed in PLINK v1.9 with and without age correction. The genomic ancestry of COVID-19 patients was determined using ADMIXTURE v1.3 and qpAdm algorithm implemented in AdmixTools v5.1.

Results: Our data revealed striking genomic differences between COVID-19 asymptomatic and severely symptomatic individuals. We identified 621 genetic variants that were significantly distinct (Multiple-testing corrected $P<0.001$) between asymptomatic and acutely symptomatic COVID-19 patients. These variants were found to be associated with pathways governing host immunity, such as innate and adaptive immune system, interferon signaling, interleukin signaling, and antigen processing by MHC, cytokine signaling and known COVID-19 comorbidities, such as obesity, cholesterol metabolism and smoking. Our ancestry analysis, employing *qpAdm* algorithm revealed that asymptomatic individuals possess discernibly higher proportions of Ancestral North Eurasian (ANE) and Eastern Hunter Gatherer (EHG) ancestry and lower fractions of Western Hunter Gatherer (WHG) ancestry, while severely symptomatic patients have higher fractions of WHG and lower ANE/EHG ancestral components, thereby delineating the likely ancestral differences between the two groups.

Conclusion: Overall, our studies suggest that asymptomatic individuals derived significantly larger proportions of their ancestry from ANEs/EHGs, which was introduced to Europe through Bell Beaker culture (Yamnaya related), a smaller proportion of indigenous WHG ancestry fractions, while severely symptomatic COVID-19 patients possess significantly larger fractions of WHG related ancestry.

Keywords: COVID-19, AncestryDNA, GWAS

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Bioinformatics analysis of hsa-miR-133a-3p target genes in Colorectal Cancer process

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Abstract

Background: Colorectal cancer (CRC) is one of most prevalent malignant gastrointestinal tumor types worldwide and is the leading cause of tumor-associated deaths. Hsa-miR-133a-3p, a member of the microRNA family, has been recently studied for its tumor suppressive role in various cancer types by targeting different related molecules. Hsa-miR-133a-3p has been identified as selective marker for human colon cancer by extensive screening of microRNA populations. However, the clinical significanc of hsa-miR-133a-3p and its regulatory function on the malignant behaviors in CRC have not been elucidated yet.

Materials and Methods: Bioinformatics analysis of this study have been done by using miRbase , miRDB , Targetscan , miRWalk , DIANA, mirSNP databases to get required data about microRNA basis, validated and predicted target genes and SNPs.

Results: According to hsa-miR-133-3p target genes, it has been revealed that TRAM2, UBA2, TAGLN2, SLC30A7, SLC6A1, ZC3H11A, PAX7, CNN2 and CAPN15 are considered as the most frequent genes in malignant process. Moreover, occurrence of rs7736199 in MAML1 and rs67604301 in LDLRAP1, two target genes, might have impact on the colon cancer progression, which in order to discover the exact role of these SNPs in colon cancer, the further analysis is needed.

Conclusion: Based on the scoring system of the bioinformatics databases and considering the best targeting scores, the foresaid genes are suggested as the potential genes, targeting the hsamiR-133-3p for future researches. Considering the significant role of the hsa-miR-133-3p microRNA on Colon cancer, the predicted genes and SNP can be used as the biomarkers for the early detection of colorectal cancer patients.

Keywords: Bioinformatics Database, Colorectal Cancer, hsa-miR-133-3p, SNP


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پالیندرم

کاوش ژنوم برای زندگی بهتر

ما پالیندرم هستیم

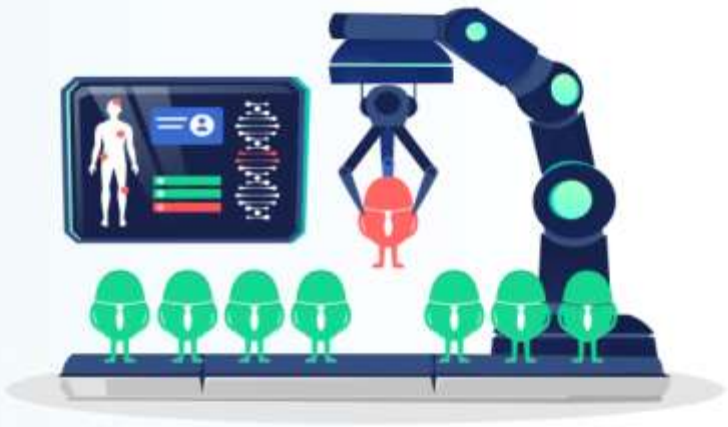
توالی‌یابی نسل جدید (Next Generation Sequencing یا NGS) در دهه گذشته توانسته دانش ژنتیک را دگرگون کند.

بهار ۱۳۹۷ هسته پالیندرم برای شرکت در مسابقه سراسری «تحلیل داده‌های توالی‌یابی نسل جدید » شکل گرفت. این مسابقه با همکاری معاونت علمی و فناوری ریاست جمهوری برگزار شد و سرانجام آذر ۱۳۹۷ گروه پالیندرم موفق به کسب **جایگاه نخست کشور** شد. این پیروزی، انگیزه آغاز فعالیت رسمی گروه پالیندرم شد.

اکنون پالیندرم با آزمایشگاه‌های ژنتیک پزشکی و دانشگاه‌های کشور همکاری می‌کند.

برنامه آنالیز اگزوم پالیندرم در پاییز ۱۳۹۹ موفق به کسب **گواهی دانش بنیان** شد.

PalinVar



الگوریتم ویژه پالیندرم با بهره‌گیری از شیوه‌نامه **ACMG** توانسته امکان پیشبینی بیماریزایی واریانت‌های اگزوم را به صورت خودکار فراهم کند.

الگوریتم PalinVar زمان لازم برای یافتن واریانت‌های بیماریزا را بسیار کوتاه می‌کند. این علاوه بر **کاهش نیاز به نیروی انسانی**، دقت آنالیز را بسیار افزایش می‌دهد.

PalinVar آنالیز خود را **مستقل از فنوتیپ** انجام می‌دهد. پس امکان تشخیص واریانت‌های بیماریزایی که فرد ناقل آن‌ها است (ولی بیماری را بروز نداده) را نیز فراهم کرده. این به ویژه در بررسی پرونده‌های ناقلین کاربردی است (در آزمایش اگزوم پیش از بارداری زوج).

غربالگری ناقلین

تقریباً همه ما انسان‌ها شماری واریانت بیماریزای نهفته در ژنوم خود داریم که ممکن است در نسل‌های پس از ما خود را آشکار کنند.

این می‌تواند سبب تولد نوزادانی با بیماری‌های ژنتیکی شود که گاهی مشابه آن بیماری **پیشتر در خانواده دیده نشده** است.

پالیندرم با بررسی اگزوم **زوج در آستانه بارداری** به آن‌ها کمک می‌کند تا زمینه ژنتیکی خود را بهتر بشناسند و از احتمال آشکار شدن بیماری‌های ژنتیکی در فرزندان آینده خود پیشگیری کنند.

GENE TECH PAJOUHAN

ژن تک پژوهان

شرکت ژن تک پژوهان با تکیه بر علم روز دنیا به همراه پرسنل مجرب و کارآزموده خود و با پیشبرد اصل رضایت مندی مشتری در راستای کمک به پیشبرد علم و فناوری های نوین در کشور قدم های مهمی را برداشته است.این شرکت با همکاری مراکز و متخصصان داخلی و خارجی در جهت توسعه کارآفرینی و توسعه اقتصادی در زمینه ژنتیک و بیو تکنولوژی کشور عمل کرده و با توجه به رشد و توسعه تحقیقات آکادمیک ، رویکرد جدیدی در امر انتقال تکنولوژی از بخش دانشگاهی به بخش صنعتی به وجود آورده است.

در این راستا این شرکت اقدام به ارائه خدمات در این زمینه نموده است و توانسته است شرایط مطلوبی را از نظر قیمت تمام شده و کیفیت محصولات و خدمات برای مشتریان خود فراهم آورد.

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metabion

MN MACHEREY-NAGEL

لذا خواهشمند است در صورت علاقه مندی با شماره تلفن های ۰۴۱-۳۳۳۵۱۴۱۸ و ۰۹۱۹۹۱۳۵۱۸۹ تماس حاصل فرمائید تا اطلاعات تکمیلی و کاتالوگ تجهیزات ، مواد و خدمات مورد نیاز به حضورتان ارسال گردد.

* ارسال به تمام نقاط کشور در کوتاه ترین زمان ممکن و حفظ زنجیره دمایی مناسب در زمان حمل و نگهداری
* ارائه خدمات سنتز و طراحی پرایمر و ژن و خدمات NGS و توالی یابی با بهترین کیفیت و جواب دهی در کوتاه ترین مدت و با قیمت مناسب
* اکثر موارد پرمصرف با تاریخ انقضاء طولانی و مناسب ترین قیمت بازار ، موجود بوده و در صورت عدم موجودی در کوتاه ترین زمان ممکن بدست مشتریان گرامی خواهد رسید.

ژن تک پژوهان

انواع کیت ها و مواد تحقیقاتی سلولی، مولکولی ، ژنتیک و بیوتکنولوژی
تجهیزات پیشرفته آزمایشگاهی ، بیمارستانی و تحقیقاتی و خدمات مولکولی

Takara - Bio basic - Abnova - Rocha - IBL - Gibco - Biosera - Quata Bioscience - SPL - Jet Biofil - Greiner ...

ANEUFAST QF-PCR

کیت های QF-PCR

life technologies

دستگاه PCR و qPCR
مواد و کیت های مورد نیاز بیولوژی مولکولی
Real Time PCR
Biochemical and PCR Material

ThermoFisher SCIENTIFIC

Fermentas

MN

انواع آنزیم های برشی و مواد و
کیت های سلولی و مولکولی

CAPP

eppendorf

انواع سمپلر، پیپت های تکثار کننده (اتمیز)
دیسپنسر دیجیتالی
پیپتور های برقی و دستی
سرنگ های دقیق شیمی
Macro and Micro Pipettes
Repeater Pipettes
Electronic and Manual Pipette Controllers
Digital Dispenser
Laboratory Syringes

SPL

پلیت کشت سلول
پلیت الایزا
هیرمه خنک نگهدارنده
رک کرایوتیوب
Laptop Cooler
Cryostore Boxes
Microwell Plates
Elisa Plates

Gibco

biosera Sigma

انواع محیط کشت سلول (مایع و پودری)
سرم ها، آمینه‌های آمینه، انواع آنتی بادی
و مواد ایمونولوژیک
Products for Cell Culture
Liquid and Powder Cell Culture Media
Immunology and Cytogenetic Material

BOSTER

Human Rat

انواع کیت های الایزا و آنتی بادی های
تشخیصی و تحقیقاتی فلوسایتومتری

AMPLIQON III

SMOBIO

انواع آنزیم ها و مسترمیکس های
PCR و qPCR
مارک های DNA , Protein

تبریز، خیابان آزادی ، جدیری جنوبی ، روبروی بوستان گلها ، جنب داروخانه
خراطی ، پلاک ۱۲۱ تلفکس: ۰۴۱-۳۳۳۵۱۴۱۸
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گروه علمی و تحقیقاتی کریسپر

گروه علمی و تحقیقاتی کریسپر به عنوان جمعی از دانشجویان و اساتید ارجمند، با هدف ایجاد فرصت های مطالعاتی و پژوهشی در حوزه های مختلف از جمله ژنتیک و سرطان در سال ۱۳۹۹ تشکیل گردید.
این مجموعه با بهره گیری از توانایی دانشجویان علاقمند و همکاری متخصصین حوزه های مربوطه توانسته است در عرض یک سال گذشته چندین مقاله و کتاب را به چاپ برساند و با مراکزی از جمله انستیتو پاستور، پژوهشگاه رویان، پژوهشگاه ملی مهندسی ژنتیک و زیست فناوری، ستاد توسعه علوم و فناوری های سلول های بنیادی و مرکز تحقیقات سلول و ژن درمانی کودکان افتخار همکاری را داشته است. در آینده ای نه چندان دور، گروه علمی و تحقیقاتی کریسپر به عنوان زیر مجموعه ای کوچک در کنار گروه های دیگر از یک شرکت دانش بنیان معرفی می گردد.

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