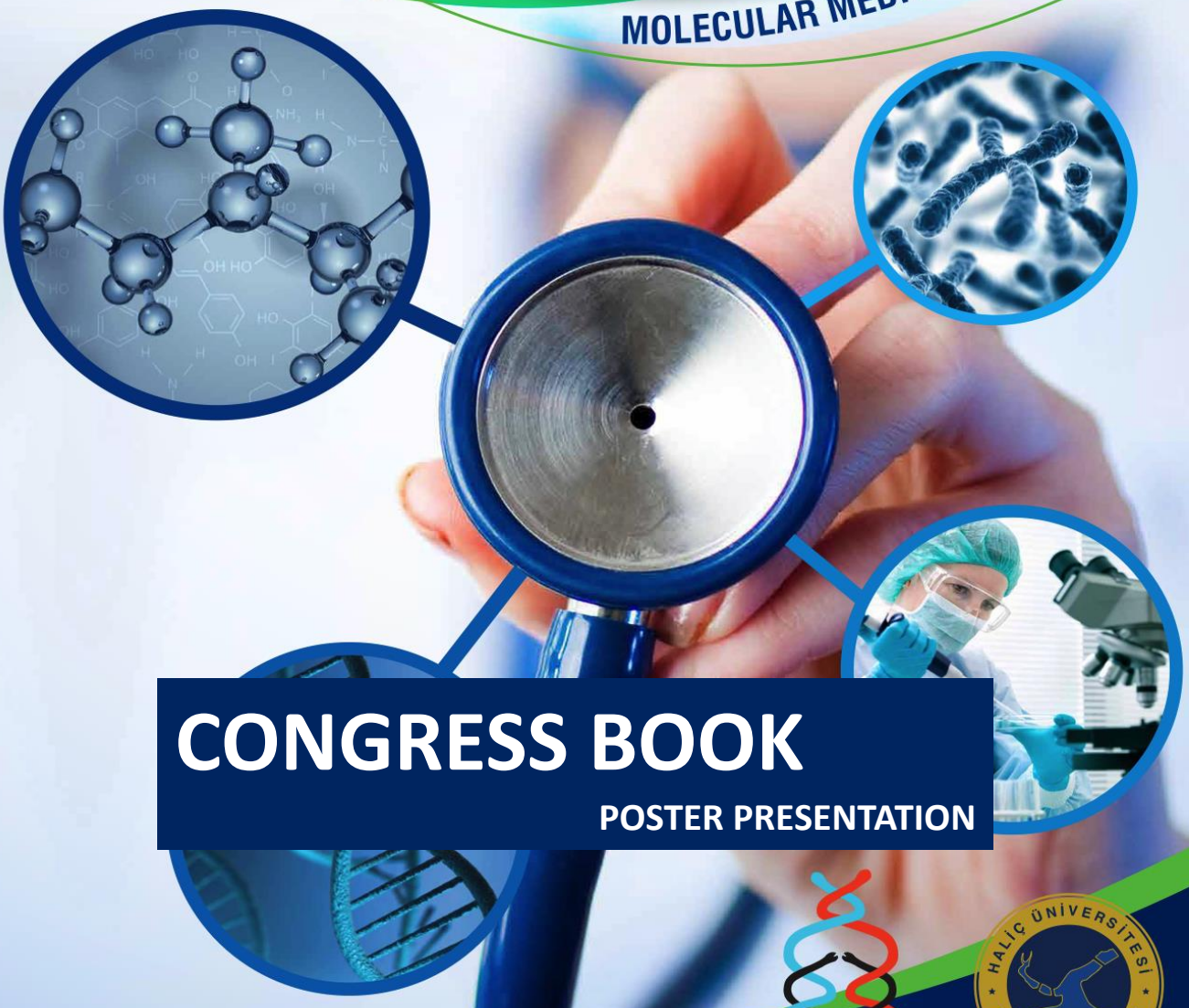
VII. INTERNATIONAL CONGRESS OF MOLECULAR MEDICINE

5-7 **September** 2019

Haliç University, Sütlüce Campus

Istanbul, Turkey

MOLECULAR MEDICINE IN LIFE SCIENCES



CONGRESS BOOK

POSTER PRESENTATION

Türk Moleküler Tıp Derneği 1999

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Dear Colleagues,

On behalf of the Organizing Committee I am delighted to invite you to the 7th International Congress of Molecular Medicine that will be held in Istanbul, Turkey on 5th – 7th of September 2019 under the auspices of the Turkish Society of Molecular Medicine.

Congress program will consist of outstanding lectures, including keynote talks, plenary sessions, applied workshop, oral & poster presentations & exhibition.

The congress biennial of molecular medicine is an important forum for researchers and clinicians from Turkey and all around the world to focus on the latest developments in molecular medicine.

Trends, technologies and clinical applications in areas including, “Sporty Molecules”, “Nutrition and Molecular Medicine”, “Inflammasome”, “Microbiota”, “Neurodegeneration”, “Metabolic Syndrome”, “Anti-Cancer Agents”, “Tumor Biology”, “Prospective Methods in Molecular Medicine “ , Molecular Aspects in Diabetes” , “Molecular Metabolism in Obesity” , “Data Mining” , “Bioinformatics” shall be discussed during the congress.

Taking the lead in science, modern values and social enlightenment throughout its history, Halic University was one of the private universities established in Istanbul Turkey. Dating back to ancient times even in the Mythology Halic called "golden horn" of Bosphorasea which is the cow shaped lower of Zeus. This school of science and education is also among the first ten universities in Istanbul. This University has a high prestige with more than 600 academicians and nearly 15.000 of students.

We are looking forwards to meet you in Istanbul on September 2019 for this outstanding congress and we hope you will enjoy scientific sessions, as well as Turkish hospitality and all the beauty of the Istanbul.

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ABSTRACTS OF POSTER PRESENTATIONS

PP1

LB42708, a Farnesyltransferase Inhibitor, Induces Apoptosis and Supresses Cell Growth without Altering p-Akt (Ser473) in $p53^{+/+}$ and $p53^{-/-}$ HCT-116 Cells

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Abstact

The main ethiology of colorectal cancer (CRC) is unknown, however most studies have shown that some genetic and enviromental factors play an important role on formation of CRCs. In this point of view, mutationally activated K-Ras, regulates genes transcription of cell proliferation and survival signals via Ras/MEK/ERK and Ras/PI3K/Akt pathways. LB42708, farnesyltransferase inhibitor, inhibits normal and alternative prenylation of K-Ras, leading to the inhibition of cell survival and proliferation via MAPK/ERK/p38 and PI3K/Akt pathways. In this study we aimed to investigate the apoptotic and anti-proliferative effects of LB42708, at different concentrations at a period of time on $p53^{+/+}$ and $p53^{-/-}$ HCT-116 CRC cell lines by MTT assay, AO/EtBr staining, BrdU, LDH release and DNA fragmentation assays. We also used quantitative RT-PCR and Western Blot analysis to evaluate the mRNA and protein levels involved in apoptotic and proliferative signaling pathways. Our results revealed that treatment with the increasing concentrations of LB42708 decreased the transcription levels of anti-apoptotic genes (BCL2, BCL2L1) and increased pro-apoptotic genes (BAX, BAK, BIM). Moreover, Cyclin D1 (CYCD1) and cMYC mRNA levels were decreased which involves in cell cycle and cell proliferation, respectively were decreased. Also on protein levels we showed that, treating with LB42708, cells tended to undergo apoptosis especially with the downregulation of Bcl-XL protein levels without altering Akt phosphorylation at Ser473 site. Our results along with *in vivo* models strengthen the idea LB42708 will be a potential antineoplastic agent against CRC.

Keywords: Apoptosis, colorectal cancer, farnesyltransferase inhibitor, LB42708

PP2

Therapeutic effectiveness of rectally administered fish oil in trinitrobenzenesulfonic acid-induced colitis

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Abstract

Background

Dietary Fish Oil (FO) is beneficial in experimental rodent models of colitis. FO have well-known anti-inflammatory and antioxidant effects; on the other hand, information related to intrarectal administration of FO is limited.

Aim

The present study was conducted to therapeutic effectiveness of rectally administered FO in rats with trinitrobenzenesulfonic acid (TNBS)-induced colitis.

Methods

Wistar albino rats were assigned to 3 groups as (1) Control (n=7), (2) Colitis (n=7), (3) Colitis+Fish Oil (Colitis+FO) (n=7). Intrarectally administered TNBS (50 mg/kg) induced colitis. 2 ml of fish oil was administered. At the end of the experiment, the rats' macroscopic and histopathologic lesions were rated and tumour necrosis factor (TNF)-α, Interleukin 6 (IL6), glutathione reductase (GR), glutathione peroxidase (GP), myeloperoxidase (MPO), malondialdehyde (MDA), Superoxide dismutase (SOD), Total nitrate and nitrite, and catalase (CAT) in serum and tissue were detected.

Results

As a result of macroscopic and microscopic examination, administrations of FO partly decreased the damage ($p<0.05$). It was observed that administrations of FO decreased the increase in serum and tissue TNF-α and IL-6 levels caused by colitis ($p<0.05$). It was observed that serum MPO, serum GR, tissue SOD, tissue nitrite/nitrate values of Colitis+F0 group were close to the control ($p>0.05$). Based on the histological results, inflammation damage in the tissue caused by colitis in the Colitis +FO group recovered partly.

Conclusions

The rectal administration of FO improved tissue damage, enhanced enzyme activities of antioxidants, and reduced inflammation. Intrarectal administration of FO may bring a new insight concerning the treatment of colitis.

Keywords: colitis, fish oil, oxidative stress.

PP3

What is the importance of TRPM2-8 channel?

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Abstract

In the organism, antioxidant and oxidant molecules are in an equilibrium state. Oxidative stress can cause damage of lipids, proteins, enzymes, carbohydrates, and DNA. Cell death, cancer, neurodegenerative, cardiovascular diseases, diabetes and autoimmune disorders may occur as a result of the damage of these enzymes and structural proteins.

Ca2 + is an intracellular secondary messenger responsible for many events such as fertilization, gene transcription, muscle contraction, hormone secretion, memory, learning, cell differentiation, development, necrosis and cell death that can be identified by apoptosis. It regulates with channels.

Transient Receptor Potential (TRP) channels were first discovered in vinegar fly, a species of drosophila. These channels are said to act as non-selective cation channels that play a vital role in many essential cellular functions. TRP channels are composed of seven subgroups as TRPC (canonical), TRPM (melastatin), TRPV (vanilloid), TRPA (anycrine rich protein), TRPP (polysistin), TRPML (mucolipin), TRPN (nompc).

In our last study; we search one of them which is TRPM. It consists of 8 members (TRPM 1 –8). The TRPM2 channel is referred to as a Ca 2+ permeable channel. As a result of the data obtained in the varicocele model, it was seen that TRPM channels were found to be significant role with vitamin D.

Especially in the brain there are numerous scientific articles about TRPM channels and their functions. For this reason, after this study and literature review, we plan to make further studies on the role of migraine disease.

PP4

Verification of automated approving system in terms of "atypic/abnormal" or "blast" lymphocyte

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Abstract

Aims

We aimed to investigate whether or not those proposed in the extended information-processing unit (IPU) flag correspond to clinical significance in peripheral smear for the outpatients over 18 years.

Methods

Blood counting was performed by means of XN or XE systems of Sysmex. Although all the other parameters were within the reference ranges, samples with flag information of “atypic / abnormal” or “blast” lymphocyte samples were included in our study. Cases with hematology and oncology follow-up were excluded from the study. Peripheral films (N=25) were prepared by SP-10 automated hematology slide preparation unit (Sysmex Corp.). The same experienced hematology consultant evaluated the films on the same day.

Results

For descriptive analysis of our patient/sample profiles, median (25th and 75 percentiles) values were as follows; 13.6 (12.8-15.1) g/dL for hemoglobin, 9.01 (6.0-10.3) ×10^9/L for WBC, 3.21 (2.27-4.05) ×10^9/L for lymphocyte, 0.66 (0.45-0.84) ×10^9/L for monocyte, 282 (228-311) ×10^9/L for platelet. In only one patient “atypical lymphocytes” were detected, %50 of all the lymphocytes were morphologically atypical.

Conclusions

In spite of providing high quality and precision, identifications of various automated analyzers may interfere with analysis; such as, overlap in the distribution of different cell types or interference from matrix components. Further improvement (specificity) of this flag system, which has gained importance with the approval support system, will increase the clinical benefit to stimulate the clinician or point the way through complete blood count outcome reports.

PP5

Investigating the effects of peroxisome proliferator activated receptor gamma variations Pro12Ala and C161T on breast cancer

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Abstract

Aims

Breast cancer is one of the most common types of cancer worldwide[1]. Peroxisome proliferating activated receptor gamma (PPAR gamma) is playing a very important role in this cancer type. These factors, which are ligand-bound transcription factors from the nuclear receptor superfamily, have previously been studied in cancer studies, but contradictory results have been found[2].

Methods

In this study, Pro12Ala and C161T variations of PPAR gamma were examined. For this purpose, DNA samples obtained from 95 breast cancer patients and 119 healthy individuals were subjected to Polymerase Chain Reaction(PCR), and Restriction Fragment Length Polymorphism(RFLP) methods and the obtained data were analyzed by SPSS program.

The present work was supported by the Research Fund of Istanbul University. **Project No. 24082**

Results

When Pro12Ala polymorphism was examined, ProPro genotype and Pro allele were found to be higher in patients ($p<0.001$). In the C161T polymorphism, minor T allele was more common in patients than in healthy subjects ($p<0.001$). In logistic regression analysis, it was observed that carrying ProPro genotype of Pro12Ala and T allele of C161T together increased the risk of breast cancer by 7.8 times ($p<0.001$).

Conclusions

In our study, PPAR gamma Pro12Ala ProPro genotype and C161T T allele were found to be associated with an increased risk of breast cancer. Also, it was observed that the risk of carrying both of the risky alleles was associated with increased risk in breast cancer. In conclusion, we can say that gene variations that alter PPAR gamma activity may affect breast cancer risk.

References:

1. American Institute for Cancer Research, World Cancer Research Fund, https://www.wcrf.org/dietandcancer/cancer-trends/breast-cancer-statistics, Accessed on: 13.07.2019
2. Tyagi, S., Gupta, P., Saini, A. S., Kaushal, C., & Sharma, S. (2011). The peroxisome proliferator-activated receptor: A family of nuclear receptors role in various diseases. Journal of advanced pharmaceutical technology & research, 2(4), 236–240. doi:10.4103/2231-4040.90879

PP6

Evaluation of CD70 expression related immune response in tumor microenvironment of colorectal cancer

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Abstract

Colorectal cancer (CRC) is the fourth leading cause of cancer related deaths. Recent studies have been focused on the immune checkpoint molecule CD70 as a potential new target in CRC.

CD70 is a costimulatory factor present on B and T-cells. Through its receptor, CD27, overexpression of CD70 can facilitate evasion of immune system.

Aims

We aim to explore expression profile of CD70, CD27, CD3, and FOXP3 molecules in tumor

microenvironment (TME) of CRC patients and to detect the recruitment of tumor infiltrating lymphocytes (TILs) present in TME. Also, we aim to investigate the predictive diagnosing value of soluble-CD27 for monitoring cancer.

Methods

The expression profile was analyzed by western blot wet transfer system. The total protein was isolated from tissue samples of 36 patients by TRIzol. Soluble-CD27 protein level in patients' serum was detected by ELISA.

Results

We detected low expression of CD70 (19,44%) in TME of CRC samples however, high abundance of CD27 (88.89%) was detected. Our results revealed that there is a high recruitment of CD3+ lymphocytes (83.33%) and FOXP3+ Tregs (44.44%) in TME.

Conclusions

Although, solid cancers are known to be negative for CD70 expression, we detected very few numbers of CD70 expression in TME of CRC patients. High number of CD27 and CD3 expressions shows the immune system recruitment in TME. Treg accumulation in TME was detected by FOXP3 expression which is shown to be relative expression pattern with CD70+ and CD27+ samples. Also, no correlation was found between high soluble-CD27 sera levels and CD70 expression.

PP7

Characterization of anti-glycan bispecific antibodies for cancer immunotherapy

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Abstract

Successful cancer immunotherapy is dependent on the generation of monoclonal antibodies (mAbs) with good specificity and potent killing. However, targeting only one antigen usually is insufficient. A generic methodology to convert existing antibodies into an IgG-like bispecific format would greatly facilitate the clinical development of bispecific antibodies. Bispecific antibodies combine specificities of two antibodies and simultaneously address different antigens or epitopes.

Aim

We aimed to detect the cell binding and killing ability of newly produced anti-glycan bispecific antibodies which are generated by using two different in-house mAbs for cancer immunotherapy and also checking tumor specificity for better clinical applications.

Methods

Characterization of bispecific antibodies was performed with cell surface binding assay and direct killing assay by Flow cytometry with cancer cell lines and organoids. Growth inhibition assay (WST8), antibody-dependent cellular cytotoxicity (ADCC) and complement dependent cytotoxicity (CDC) assays were carried out for cytotoxicity. Tissue binding of bispecific Abs were analyzed by immunohistochemistry.

Results

FACs results showed high level of cell surface binding of bispecific on tumor cells and organoids, and also showed very nice killing on ADCC and CDC. Furthermore, strong tumor tissue staining was shown by immunohistochemistry with also normal tissue staining.

Conclusions

Overall results showed that bispecific antibodies are functional and did not löse their binding affinity and ability to tumor cells and tissues which confirms that strategies to make bispecific Abs were successful. Good cytotoxic effect on ADCC and CDC states bispecific Abs still preserve their cell-mediated cytotoxicity which is good for better clinical applications.

PP8

The Effects of Peroxisome Proliferator-Activated Receptor Gamma C161T Gene Variation on Restenosis After Percutaneous Transluminal Coronary Angioplasty.

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Abstract

Aims

Increased restenosis risk after percutaneous transluminal coronary angioplasty (PTCA) or stenting are affected by genetic factors as well as clinical and angiographic characteristics. Although atherosclerotic structures which are effective in restenosis genetics and restenosis development are important, it is seen that gene variations of proteins regulating lipid metabolism have not been investigated sufficiently. We investigated PPAR-gamma C161T (rs3856806) variation effects on restenosis development and clinical parameters following PTCA.

Methods

PPAR-gamma C161T genotypes were studied in 132 coronary artery disease (CAD) (73 patients with restenosis, 59 patients without restenosis) patients and 124 controls by PCR-RFLP techniques. This study was supported by İstanbul University Scientific Research Projects Unit.Project Number:TYL-2017-26892

Results

The study revealed a high prevalence of type 2 diabetes (T2DM) and hyperlipidemia among patients with restenosis after PTCA. The rare T161 allele (TT+ CT genotypes) frequency was lower than CC genotype in restenosis group compared to CAD patients without restenosis (6.85% vs. 26.27%; x^2=18.139; OR=3.46; 95%CI:1.835-6.539). However, the T161 allele frequency was higher in restenosis patients with T2DM compared to non-diabetic patients. In CAD patients without restenosis according to controls, the T161 allele (174.07±97.66) was associated with higher triglyceride level compared to CC genotype (127.16±54.55). Multivariate regression analysis showed the T161 allele was associated with low restenosis risk and hyperlipidemia posed a risk.

Conclusions

Based on our findings, it can be suggested that PPAR-gamma C161T rare T161 allele has a protective effect on the restenosis risk, while may be a potential risk factor for T2DM.

Key Words: Peroxisome Proliferator-Activated Receptor Gamma, Restenosis, gene polymorphism, C161T.

PP9

The protective effects of viscum album and probiotics on CCl_4-induced acute liver injury

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Abstract

Aims

The aim of this study was to investigate the protective effects of mistletoe (Viscum album) and probiotics against acute liver injury induced by carbon tetrachloride (CCl_4).

Methods

Wistar male rats were randomly divided into four study groups as control, CCl_4, Viscum album+CCl_4 (VAC) and Viscum album+Probiotics+CCl_4 (VAPC). Acute liver injury was induced by intraperitoneal injection of 2 mg/kg CCl_4 at twenty-four hours prior to sacrifice. The methanolic extract of mistletoe was prepared in Pharmacognosy Laboratory at Anadolu University. Misletoe extract (300 mg/kg) and probiotics were given orogastrically daily to the related groups. At the end of the prosedure, liver tissue and blood samples were taken from all rats. Some enzyme activities (ALT,AST,ALP,LDH), lipid profile (total cholesterol,HDL-c,LDL-c,triglycerides), and total protein, albumin, total/direct bilirubin levels were measured in serum samples using commercial assay kits. Catalase activity, MDA and GSH levels in tissue samples were measured by manual methods. Liver tissue sections were stained by Hematoxylin-Eosin technique in order to evaluate histopathological changes.

Results

Biochemical analyses showed that CCl_4 administration caused to significant increases in concentrations/activities of the measured parameters compared to control group. These values were decreased significantly in VAC and VAPC groups. Histological examinations showed that CCl_4 group rats had degenerated hepatocytes, inflammation and vascular congestion in liver parenchyma, and that the damage was less in VAC group rats. As to VAPC group, histological appearance was close to control, excluding a few vascular congestions on portal area.

Conclusions

Biochemical and histological findings revealed that mistletoe extract and probiotics showed a protective effect against CCl_4-induced acute liver injury. The results from this study suggest that supplementation of intestinal flora with the use of probiotics may enhance the efficacy of orally given therapeutic extracts.

Key Words: Acute liver injury, carbon tetrachloride, probiotics, viscum album.

PP10

Novel and Known Mutations of HNF4A and GCK Genes in Patients Prediagnosed with MODY: A Case-control Study from Turkey

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Abstract

Aims

Maturity-onset diabetes of the young (MODY) is a monogenic diabetes form which is characterized by autosomal dominant inheritance, To date, numerous mutations in 14 different genes have been identified and these mutations may affect the clinical profile of MODY. There are few studies investigating the mutations of MODY genes in our population. Therefore we analyzed hepatocyte nuclear factor-4 alpha (HNF4A) and glukokinase (GCK) genes to discover the mutations which are related to MODY-1 and MODY-2 in a Turkish population.

Methods

Exons and exon-intron boundaries of HNF4A and GCK genes were sequenced with next generation sequencing methods in 79 healthy control and 75 patients prediagnosed with MODY. This study was supported by the Research Fund of Istanbul University (Project No. 44381).

Results

We identified twelve known and predicted as pathogenic/bening/likely bening *HNF4A* and *GCK* gene mutations (*HNF4A*-***rs137853335***, ***rs137853336***, ***rs137853337***, ***rs137853338, rs745975***, ***rs61737145***, ***rs1800961 and*** *GCK*-***rs104894008***, ***rs104894009***, ***rs193922289***, ***rs2908274,*** Chr7:44186138 G>A) and two novel mutations (*HNF4A*-chr20-43043093 G>A and *GCK*-chr7-44186292 G>A) in our study population. Moreover, we identified two intronic (*HNF4A*-***rs140102932*** and ***rs200071662***), two 3'UTR (*HNF4A*-***rs11574743*** and ***rs965250768***) and one 5'UTR (*GCK*-***rs367774728***) variants.

Conclusions

The mutations *HNF4A*-chr20,43043093 G>A and *GCK*-chr7,44186292 G>A were first observed in this study. Interestingly, some of the known *HNF4A* and *GCK* mutations which were found in our study group identified in other populations, while others (HNF4A-***rs61737145, rs140102932***, ***rs200071662, rs11574743***, ***rs965250768*** and GCK-***rs367774728***) were not observed at all. Our results confirm that MODY has a heterogeneous genetic background in the Turkish population in Istanbul.

Keywords: MODY, HNF4A, Glucokinase, Next Generation Sequencing

PP11

Effect of *rev-erb alpha* rs72836608 on Serum High Density Lipoprotein Cholesterol Level in Patients with Type 2 Diabetes

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Abstract

Aims

Nuclear receptor Rev-erb alpha is a transcription factor that regulates the function of genes in glucose

and lipid metabolism and also links circadian rhythm and metabolism. The aim of this study is to evaluate *Rev-erb alpha* rs72836608 variation on serum high density lipoprotein cholesterol (HDL-C) level in patients with type 2 diabetes (T2DM).

Methods

Rev-erb alpha gene was sequenced in genomic DNA samples of 42 patients with T2DM and 66 healthy subjects by Next Generation Sequencing (NGS). The correlation of rs72836608 intronic variation with clinical and biochemical parameters was analyzed with SPSS (version 20.0) statistical program. This study was supported by the Research Fund of Istanbul University (Project No.54879).

Results

Frequencies of *Rev-erb alpha* rs72836608 CC, AA and CA genotypes among the patients with T2DM were 0.452, 0.095 and 0.452, respectively; among the control subjects, they were 0.5, 0.091 and 0.409, respectively. The *Rev-erb alpha* rs72836608 C>A genotypes and alleles were not found significantly different between study groups and they were consistent to Hardy-Weinberg Equilibrium. Serum HDL-C levels were statistically lower in patients with T2DM carrying *Rev-erb alpha* rs72836608 minor A allele (AA+CA genotypes) (36.97±2.87 mg/dL) than in those with CC genotype (45.64±2.2 mg/dL).

Conclusions

This study is the first to sequence *Rev-erb alpha* gene and determine the effects of its variations on clinical phenotype and biochemical parameters as risk factors in patients with T2DM. It was observed that *Rev-erb alpha* intronic variation rs72836608 may have a promoting effect on diabetic dyslipidemia by lowering HDL-C levels.

Keywords: *Rev-erb alpha*, polymorphism, Next Generation Sequencing, HDL, type 2 diabetes mellitus

PP12

Evaluation of BMP-2, ZEB2 and Integrin α5-β1, Expressions After Recombinant BMP-7 Application in OVCAR-3 Adenocarcinoma Ovarian Cancer Cell Line

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Abstract

Aim

Ovarian cancer is important with late diagnosis and metastasis. Bone morphogenetic proteins (BMP), transcription factors and integrins are effective in the epithelial mesenchymal transition process. The aim of this study is to determine the changes in BMP-2, ZEB2 and integrin α5, β1 expressions after recombinant BMP-7 (rBMP-7) application in OVCAR-3 ovarian cancer adenocarcinoma cell line.

Methods

The expression of BMP-2, BMP-7, ZEB2, ITG α5 and ITG β1 were determined by immunofluorescence, western blot and qPCR methods before and after administration of rBMP-7 in OVCAR-3 cell line. Lateral movement was determined by wound healing test.

Results

Increased expression of BMP-7, ZEB2, integrin β1 and decreased expression of BMP-2 was detected by WB method after rBMP-7 administration. Immunofluorescence labeling and qPCR results supported the counter regulation in the expression of

BMP-2 and BMP-7. The scratched areas were closed slower in rBMP-7 applied cells in wound healing test.

Conclusions

Our findings are consistent with the literature and showed that BMP-2 expression was stronger and BMP-7 expression was weak in cancer cells. With rBMP-7 treatment, decrease in expression of BMP-2 and accelerated lateral movement of cells display the counter regulation between BMP proteins. This result suggests that increase in the level of BMP-7 expression may play a role in protective mechanisms by decreasing expression of BMP-2.

This study was supported by Hacettepe University Scientific Research Unit (TSA-2017-13046).

Key words: Ovarian cancer, BMP-7, BMP-2, ZEB2, integrin α 5, integrin β1

PP13

Synergistic Efficacy of Sorafenib and Sodium Dichloroacetate Cotreatment for Human Neuroblastoma Cell Line, SH-SY5Y

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Abstract

Aims

Main purpose of this study is to evaluate the synergistic efficacy of sorafenib and sodium dichloroacetate combination on neuroblastoma cell line, SH-SY5Y by means of Warburg effect. Sorafenib (SOR) is a multikinase inhibitor known for anti-angiogenic and anti-tumorigenic properties, particularly hepatocellular carcinoma. Recent studies demonstrate that it triggers apoptosis resulting in diminished cell proliferation for human neuroblastoma cell lines. On the other hand, sodium dichloroacetate (DCA) is a pyruvate mimetic employed to inhibit pyruvate dehydrogenase kinase and subsequently to induce oxidative phosphorylation. DCA treatment in SH-SY5Y leads to enhanced autophagy and consequently reduced cell viability.

Methods

Human neuroblastoma cell line acquired from departmental cell bank was treated with SOR (1-30 µM) and DCA (25-100 mM) for 18 hours. Cell proliferation assay (MTS) were performed and data used for synergism calculations by using CompuSyn software. In addition, the changes in cellular acetylome and expression levels of respiratory chain complexes were examined with immunoblotting analysis against acetylated-Lysine antibody and MitoProfile® total OXPHOS rodent antibody cocktail.

Results

MTS and CompuSyn data indicated 15 uM for SOR and 50 mM for DCA were synergistic doses. Co-treatment of selected doses demonstrated cell death up to 33.2% with combination index value lower than 1. In addition, we have revealed changes in overall acetylation profile and expression levels of oxphos subunits.

Conclusions

Presented data state that the combination of sorafenib with sodium dichloroacetate synergistically affects neuroblastoma cells, SH-SY5Y resulting in reduced survival rate through changes in Warburg effect.

PP14

Functional +874T/A polymorphism of interferon-gamma gene is associated with serum cholesterol levels

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Abstract

Aims

While the inflammatory effects of interferon-gamma (IFN-gamma) are well known, the role of this cytokine in cholesterol metabolism is unclear. IFN-γ regulates the expression of several genes that are key players in cholesterol metabolism. The +874 T/A polymorphism (rs61923114) of the IFN-gamma gene is located in the translation start site at position +874. It was shown that the T and A alleles of this polymorphism are associated with high and low IFN-gamma expression, respectively. Therefore, we investigated whether interferon-gamma functional +874 T/A polymorphism is associated with serum lipid levels and the occurrence of coronary heart disease (CHD) in a Turkish population.

Methods

The IFN-gamma +874 T/A genotypes were determined of 199 patients with CHD and 99 controls by ARMS-PCR technique. Serum lipid levels were measured by enzimatically.

Results

The IFN-gamma +874 T/A genotypes and alleles were not found significantly different between study groups ($p>0.05$). Serum total-cholesterol levels (TC) and white blood cell (WBC), lymphocyte and platelet counts were significantly higher in controls with the +874-T allele when compared with the AA homozygote ($p<0.05$, $p=0.04$, $p=0.006$ and $p=0.024$, respectively). However, this association was not found in CHD patients. We think that the effect of +874-T allele on TC level and blood cells' counts may be masked due to the patient group is under statin therapy.

Conclusions

Our study indicated that the +874 T/A polymorphism of the IFN-gamma gene may have an important effect on serum cholesterol levels and WBC and lymphocyte values and may be a potential risk for CHD.

PP15

Phenoxodiol Sensitizes Metastatic Colorectal Cancer Cells to 5-Fluorouracil- and Oxaliplatin-Induced Apoptosis through Mitochondrial Intrinsic Pathway

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Abstract

Colorectal cancer (CRC) is one of the most common types of cancer seen in the world in both sexes. Chemotherapy is frequently used as the main regimen in most advanced CRCs. In this study, we aimed to investigate possible apoptotic, anti-proliferative and cytotoxic effects of Pxd, a synthetic derivative of genistein, preconditioning with 5-Fluorouracil (5-Fu) in combination with Oxaliplatin

(Oxa) at specific doses and durations in CRC cell lines [HCT-116 $p53^{+/+}$ and mutant HCT-116 $p53^{-/-}$]. MTT and LDH assays were performed to determine the effect of Pxd and 5-Fu with Oxa on cell viability and cytotoxicity. The percentage of apoptotic and necrotic cells were determined by fluorescence microscopy analysis. Besides, active Caspase 3 levels by ELISA and relative mRNA levels of Caspase 3 (CASP3), CASP8 and CASP9 genes were determined by quantitative Real-time PCR method (qPCR). The viability of CRC cells decreased significantly after treatment with 5-Fu and Oxa followed by Pxd treatments, compared to 5-Fu with Oxa alone. When compared to 5-Fu with Oxa alone treatment, Pxd pretreatment overwhelmingly increased apoptosis level in CRC cells. Moreover, qPCR analyses showed that CASP3, CASP8 and CASP9 mRNA levels increased after treatment with 5-Fu and Oxa followed by Pxd treatments, compared to 5-Fu with Oxa alone. Our findings are needed to confirmed by other preclinical *in vitro* and *in vivo* models and clinal trials. According to our results, we suggested that Pxd may be a potential candidate agent in advanced CRC.

Keywords: Apoptosis, colorectal cancer, 5-Fluorouracil, oxaliplatin, phenoxodiol

PP16

Roles of renin-angiotensin system gene variants in atherosclerotic peripheral arterial obstructive disease

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Abstract

Aims

Peripheral artery disease (PAD) is characterized as the partial or complete occlusion of lower extremity arteries. PAD is mostly caused by atherosclerosis. Renin-angiotensin system (RAS) and related genes, encoding various enzymes and receptors, have crucial roles in vessel function since they play a part in arterial pressure and vascular remodeling. Angiotensin II has been shown to affect pro-inflammatory, proliferative and vasoconstriction processes in vascular system. The aim of this study is to investigate angiotensinogen (*AGT*) rs699 (M268T), angiotensin-converting enzyme (*ACE*) I/D (rs1799752), angiotensin II receptor type 1 (*AGTR1*) rs5186 (A1166C) and angiotensin II receptor type 2 (*AGTR2*) rs35474657 gene variants in the clinical development of PAD and its subtypes.

Methods

Real-time polymerase chain reaction (RT-PCR) were used to detect *AGT* rs699, *AGTR1* rs5186, *ACE* I/D (rs1799752), and *AGTR2* rs35474657 variants in 63 PAD patients (33 femoro-popliteal, 30 aorta-iliac) and 70 healthy controls.

Results

No significant relation was observed in *AGT* rs699, *AGTR1* rs5186, *ACE* I/D (rs1799752), *AGTR2* rs35474657 variants between PAD patients and controls. However, *AGT* rs699 TT genotype carriers demonstrated significantly higher fasting glucose levels in PAD group. Additionally, rs699 CC genotype carriers exhibited increased HDL-cholesterol levels in PAD patients. Moreover, *AGTR1* rs5186 CC genotype was associated with elevated LDL-cholesterol and triglycerides levels in PAD patients.

Conclusion

This report is the first showing an association between RAS-related gene variants and their relation with the biochemical characteristics of PAD and suggests that *AGT* rs699 and *AGTR1* rs5186 variants may have significant roles in the cardiovascular phenotypes of PAD patients.

Key words: Peripheral artery disease, *ACE* I/D rs1799752, *AGT* rs699, *AGTR1* A1166C rs5186, *AGTR2* rs35474657

Note to the scientific committee: Part of this study was supported by Scientific Research Projects Coordination Unit of Istanbul University-Cerrahpasa (Project number; 34151).

PP17

Synthesis of novel thiosemicarbazone complexes with 5-nitrosalicylaldehyde and their cytotoxic effects in breast cancer cells

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Abstract

Aim

Thiosemicarbazones are an important subject of medicinal drugs. In this study, mixed-ligand thiosemicarbazone complexes were synthesized and the cytotoxic activities were investigated in vitro breast cancer cells.

Methods

Nickel(II) complexes, (**I**) and (**II**), were synthesized by reaction of 2-hydroxy-5-nitrobenzaldehyde-N-methyl-thiosemicarbazone(L1) or 2-hydroxy-5-nitrobenzaldehyde-S-methyl-thiosemicarbazone(L2) ligands and N,N-diethylethylenediamine, respectively. The structures were characterized by spectroscopic methods and single crystal X-ray diffraction for complex I. Cytotoxic activities of compounds were investigated against breast cancer cell lines (MDA-MB-231, MCF-7) and 3T3 fibroblast cells as control cells, in the concentration range of 1-10 µg/mL by MTT assay.

Results

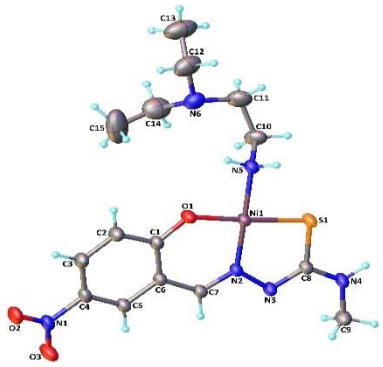
In MDA-MB-231 cells that is hormone negative, no significant change was determined by the concentration of 10 µg/mL of the ligands, whereas cytotoxic effects of slightly more than 50% were observed by **I** and **II**.

In MCF-7 cell line that is an receptor estrogen and progesterone positive breast cancer type, a 40% decrease in viability was determined by the concentration of 10 µg/mL of the ligand of **I**, whereas the cells were increased significantly by the ligand of **II**. In contrast, no significant difference in cytotoxicity was observed by the complexes. In addition to all, it was not determined any change in viability ratios of 3T3 cells.

Conclusion

As a result, both the **I** and **II** showed selective cytotoxic effects for MDA-MB-231 cells. We can suggest that these newly synthesized specific complexes may be highly effective in cancer treatment because it has no toxic effect on healthy

cells, contrary to that showed cytotoxic effect on hormone negative breast cancer cells.



The structure of complex **(I)** that determined by single crystal X-ray diffraction method.

PP18

Investigation of Pro12Ala polymorphism in the peroxisome proliferator-activated receptor-gamma gene in cancer cell lines

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Abstract

Aims

The Peroxisome proliferator-activated receptor-gamma (PPARγ) is a member of the nuclear receptor family of transcription factors. Several studies have shown that Pro12Ala polymorphism in PPARγ gene is associated with different types of cancer. However, the molecular mechanism underlying these associations has not been elucidated. Therefore; in this study, we aimed to investigate the relationship between Pro12Ala polymorphism and cancer, in cancer cell lines naturally carrying Pro12Ala polymorphism. In a recent study, Pro12Ala polymorphism was shown to affect PPARγ mRNA expression in the context of obesity. Thus, we aimed to elucidate whether Pro12Ala polymorphism has an effect on PPARγ mRNA expression in cancer cell lines.

Methods

In our study, PPARγ gene was screened for Pro12Ala polymorphism in a number of cancer and normal cell lines, via using RFLP and Sanger Sequencing, independently. The effect of the Pro12Ala polymorphism on PPARγ mRNA expression was investigated via using Real Time Polymerase Chain Reaction.

Results

Heterozygote Pro12Ala polymorphism was detected only in AGS and Caki-1 cancer cell lines amongst screened cell lines. PPARγ mRNA expression in cell lines with Pro12Ala polymorphism was found to be lower than PPARγ mRNA expression in cell lines without Pro12Ala polymorphism such as MCF10A, SK-BR-3, MDA-MB-453, MDA-MB-468.

Conclusions

Our results suggest that the Pro12Ala polymorphism may modulate the mRNA expression level of PPARγ in cancer cells. The exact molecular mechanism of the effect of Pro12Ala polymorphism should further be investigated.

PP19

In vitro and *in silico* investigation of antioxidative and HMG-CoA reductase inhibitory effects of various coumarin derivatives

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Abstract

Cardiovascular diseases are one of the primary causes of deaths worldwide and development of atherosclerosis is closely related to hypercholesterolemia. Since reducing the low-density lipoprotein cholesterol level is critical for treating these diseases, inhibition of 3-hydroxy-3-methyl-glutaryl coenzyme A reductase, which is essentially responsible for cholesterol biosynthesis, stands out as a key solution to lower plasma cholesterol levels. In this study, we synthesized several dihydroxycoumarins and investigated their antioxidant and *in vitro* HMGR inhibitory effects. Furthermore, we carried out *in silico* studies and examined quantum chemical properties of the coumarin derivatives. We also ran molecular docking experiments and analyzed the binding strength of each coumarin derivative. Our results revealed that compound IV displayed the highest HMGR inhibitory activity (IC_{50} = 42.0 µM) *in vitro.* CUPRAC and FRAP assays demonstrated that coumarin derivatives have potent antioxidant activities. According to the results obtained from quantum mechanical calculations, a close relationship between HOMO energy levels of coumarins and their inhibitory activities was found.

Keywords: Antioxidant, lipid lowering, radical scavenging, coumarin, HMG-CoA reductase

PP20

Enhanced Cytotoxicity of Mangiferin and Paclitaxel Combination by Increasing Apoptosis and Autophagy in MCF-7 Breast Cancer Cell Line

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Abstract

Aims

Paclitaxel (PTX) is a chemotherapeutic drug routinely used in the treatment of breast cancer, However, the nonspecific cytotoxicity, insensitivity and limited therapeutic efficacy of PTX can restrict the treatment. Therefore, recently, several studies have shown that the combination of chemotherapeutic and phytotherapeutic agents have the high therapeutic potential in cancer treatment. Mangiferin (MNG) is a natural substance that has been reported may have an important role in several cancer types. The aim of this study was to investigate the effects of MNG and PTX and their combinations on cell proliferation, apoptosis, autophagy and survival on MCF-7 cancer cell line.

Methods

The effect of MNG (6.25-300 µM) and PTX (0.25-15.9 µM) alone and their combination on MCF-7 cells were examined by ATP cytotoxicity test. To determine the effect of PTX (3,98 µM) and MNG (100 µM) combination on apoptosis, autophagy, and survival proteins, related protein markers were determined by western blot.

Results

According to the ATP assay, the cytotoxic effect increased synergistically in a dose-dependent manner in the combination group. The inhibition of p-mTOR and the increase of LC3B along with the increase of FAS and BAX with cleaved caspase-7 and cleavage of PARP1 was shown that apoptosis occurred through autophagy. Furthermore, combination treatment induced phosphorylation of c-Jun and supression of

JNK proved that JNK/c-jun pathway plays a pivotal role in autophagy.

Conclusions

According to results, MNG in combination with PTX selectively increased apoptosis in the presence of autophagy. Mangiferin and chemotherapy combinatorial treatment could be a promising potential for the development of new strategies in the treatment of cancer.

Keywords: Mangiferin, Breast Cancer, Paclitaxel, Apoptosis, Autophagy.

PP21

Evaluation of nutritional and inflammatory findings in patients with acute myocardial infarction

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Abstract

Aims

The aim of this study was to investigate the possible effects of indices such as Controlling Nutritional Status (CONUT) and Prognostic Nutrition Index (PNI) and other laboratory parameters in acute myocardial infarction (AMI) at the first admission to the emergency department.

Methods

Blood counts, serum cholesterol, albumin and CRP levels were investigated in 46 control individuals (23 males, 23 females) and 74 patients diagnosed AMI (51 males, 23 females). Patients with known sepsis, pulmonary embolism, stroke and subarachnoid hemorrhage, renal failure, chronic cardiac/aortic disorders, surgical intervention (trauma), severe anemia were all excluded.

Results

There was no statistical difference between the two groups in CONUT, PNI, CRP/PNI ($p>0.05$). Proportions of subjects with CONUT ≥3 were 4/46 (8.7%) in the controls and 9/74 (12.2%) in the patients. The correlation between CRP and PNI was not statistically meaningful in controls ($r= -0.24$; $p=0.11$), but it was significant in patients ($r= -0.417$, $p<0.0001$),

Conclusions

Our findings are in favor of the relationship between nutritional status and inflammation in patients diagnosed AMI. In contrast to the PNI scoring, using serum cholesterol levels in the CONUT scoring is remarkable; high cholesterol level lowers scoring. Besides, this patient group may be under drug treatment due to hypercholesterolemia. PNI may be evaluated in risk determination of AMI in further studies with more patients' participation and long-term follow-up.

PP22

Competetive lateral flow assay for bpa detection in water samples

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Abstract

Bisphenol-A (BPA) is a monomer of polycarbonate plastics and epoxy resins used as raw materials in food and beverage packaging materials. BPA which passes into food through our packaging materials and takes into our body affects the endocrine system even in low doses. Approximately 0.2-0.3 µg / mL BPA

passes into the water from polycarbonate based plastic water bottles or carboys. In this study, an immunosensor based competitive lateral flow test was developed to determine the amount of BPA in water samples. To prepare the conjugation pad from the components of the lateral flow test, BPA antibody and colloidal gold was conjugated. Then BPA antibody-BPA conjugate was prepared to be placed on the test line of the competitive lateral flow test strip. For the lateral flow test, the other components of the test strip are prepared and assembled on the backing card. The preliminary trials of the lateral flow test were carried out by preparing water samples containing different concentrations of BPA. As a result, it was determined that the concentration of red color in the test line decreased with the increase in BPA concentration in water. In this study, it was shown that the competetive lateral flow test strips we developed were working in the targeted way and different water samples were collected and it was planned to complete the validation of the test strips for use in BPA measurement.

This study was supported by TÜBİTAK with the project numbered 117M032.

Keywords: Bisphenol-A, Competitive lateral flow test, immunosensor

PP23

Modified nitrocellulose membrane as a Lateral flow immunoassay material.

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Abstract

The aim of our study was to enhance the signal in Lateral Flow Immunoassay (LFAI) by using Polycaprolactone (PCL)/ Silk fibroin (SF) based nanofiber instead of nitrocellulose (NC) membrane.

LFIAs, belong to a kind of simple devices that are designed based on the point-of-care testing strategy, to perform an easy detection of a specific analyte in body fluid or other sample.

Bisphenol-a (BPA) is used as a monomer for the production of polycarbonate plastics, which are applied as protective linings in e.g. cans and other products.

PCL and SF mixed in 1:1 ratio and dissolved in DMF and DCM mixture. The PCL/SF based nanofiber electrospun on NC membrane. This novel membrane was tested on LFIAs. LFIA components were combined on a backing card. BPA in water was detected by using the prepared LFIA strip. The signal intensity that was obtained with either NC or PCL/SF based nanofiber was compared.

PCL/SF based nanofiber showed higher signal intensity when compared to NC membrane. Owing to it's unique biochemical properties and great compatibility hybridizing of PCL and SF created a biodegredable and biocompatible membrane that can be succesfully used as a membrane material in LFIAs.

Biomaterials made from natural sources such as silk are preferred over those made from synthetic materials. The modified NC surface that is prepared in this study can be used as a material for protein immobilization.

This study was supported by TUBITAK with the project number 117M032.

PP24

Altered apoptosis-related gene expressions in bisphenol A and diethylhexyl phthalate exposed zebrafish embryos

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Abstract

Aims

Endocrine disrupting chemicals (EDC) have been associated with many diseases such as obesity, diabetes, cancer. Bisphenol A (BPA) plays an active role in the production of materials such as polycarbonate plastic and polyester. The water-permeable chemicals in polyethylene terephthalate (PET) bottles include the plasticizer Di-ethylhexylphthalate (DEHP). DEHP and BPA are considered as EDCs and exposure to these chemicals may adversely affect the development, especially in first years of life. This study aims to investigate the effects of DEHP and BPA on zebrafish embryos focusing on the expressions of apoptosis relates genes.

Method

Range-finding experiments were conducted to estimate the lethal concentration to cause 50% mortality in the zebrafish embryos. Embryos were exposed to BPA and DEHP to doses as 1µg/L BPA and 2,5 µg/L DEHP in well plates containing 20 embryos, having four replicates for each group. RT-PCR was used to determine expressions of apoptosis related genes at 72 hours post fertilization (hpf) and beta-actin was used as the house keeping gene.

Results

The expressions of bax and casp8 significantly increased whereas casp3, ifng1 and fas decreased both in BPA and DEHP exposed groups. Tp53 expression increased in BPA but decreased in DEHP groups significantly.

Conlusion

Increased apoptosis and altered gene expressions support potential danger of BPA and DEHP contaminated products. Biomolecules involved in the apoptosis signaling mechanisms play roles in many serious diseases, particularly cancer. Our study has shown that expression of biomolecules in apoptosis may change upon EDC exposure in developing zebrafish embryo.

PP25

Investıgatıon of the possıble effect of foxp3 c/a gene varıants ın laryngeal cancer

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Abstract

Aim

Foxp3 is an immunoregulatory protein with high expression in T-reg cells. In the case of increased Foxp3 transcription gene expression, T lymphocytes are inactivated and the immune system is silenced. It is thought that the expression level of Foxp3 molecule in laryngeal cancer, which is a marker of high

potential to give information about the development of various cancers, affects very important immune mechanisms. In this study, we aimed to investigate the genetic variants of Foxp3 protein that may play a role in immune mechanisms in patients with laryngeal cancer.

Materials-Methods

The study was conducted on 97 patients and 141 healthy controls diagnosed as laryngeal cancer in Haydarpaşa Numune Training and Research Hospital. In order to determine the different gene variants of Foxp3 C/A(rs:3761548) molecule in the blood samples of the laryngeal cancer and healthy controls, DNA isolation was performed and then polymerase chain reaction-restriction fragment lenght polymorphism (PCR-RFLP) was applied. Statistical analysis of the study was determined by SPSS 13 program.

Results

There were an increased frequency of CC genotype and C allele in laryngeal cancer patients than those with controls (p=0,029;p=0.002).

Conclusion

We have observed that Foxp3 C/A(rs:3761548) polymorphism is associated with the risk of laryngeal cancer in this study. Our findings regarding the association of Foxp3 C/A(rs:3761548) polymorphism and clincopathological characteristics should be considered in the further studies with larger sample sizes to assess the impact of Foxp3 C/A(rs:3761548) gene on disease.

Keywords: Foxp3 C/A(rs:3761548) polymorphism, laryngeal cancer.

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PP26

Investıgatıon of the possible effect of CD27 gene polymorpiısm in gastric cancer

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Abstract

Aims

CD27 stimulatory checkpoint molecules are members of the tumor necrosis factor (TNF) receptor superfamily. This receptor is required for generation and long-term maintenance of T cell immunity. It is also a memory marker of B cells. This study was conducted to understand the possible effects of genetic variation of CD27, which plays a key role in immune system activation, on gastric cancer (GC).

Materials-Methods

CD27 A/T (rs:2267966) gene polymorphism was investigated in 170 subjects (67 subjects with GC and 103 healthy individuals as controls) by using polymerase chain reaction-restriction fragment lenght polymorphism (PCR-RFLP).

Results

According to our data, it has been found an increased frequency of AA genotype in gastric cancer patients but this difference was not statistically significant (p>0,005).

There is no AT genotype carriers in patients who have no node metastasis in this study. But heterozygous AT genotype frequency in patients who have node metastasis, was found as (% 42,4) and this value was statisticaly significance (OR:1,652, CI:1,203- 2,267, p= 0,005). In other words; AT genotype carriage was statistically significant in patients with positive node metastasis (N +) than those with negative node metastasis (N-).

Moreover; the patients who have angiolymphatic invasion have increased frequency of T allele (% 83,3) than those with negative angiolymphatic invasion (% 36,1). This value was statisticaly significance (p=0,035 OR:2,311 %95CI:1,416-3,770).

Conclusion

According to our research, CD 27 A/T polymorphism is associated with the progression but not on the risk of gastric cancer in this study. Our findings regarding the association of CD 27 A/T polymorphism and clincopathological characteristics should be considered in the further studies with larger sample sizes to assess the impact of CD 27 gene on disease.

Keywords: CD 27 A/T, polymorphism, gastric cancer.

The present work was supported by TUBITAK -2209-A programme

PP27

The Importance of CTLA-4, CD28 Genetic Variants in the Risk of Non-Small Cell Lung Cancer

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Abstract

Cytotoxic T-Lymphocyte Associated Protein 4 (CTLA-4) is an important immune check-point used as a drug target in the field of immuno-oncology. CTLA-4 competes with CD28 and binds to B7.1 and B7.2 which are costimulatory molecules expressed on antigen-presenting cells. 80 patients with Non-Small Cell Lung Cancer (NSCLC) and 39 healthy volunteers were enrolledin this study. In this context, molecular assessment of CTLA4 (rs231775) and CD28 (rs3116496) variants were determined with polymerase chain reaction restriction fragment length polymorphism techniques. We found no significant difference between the patient and control for CTLA-4 49A / G genotypes and allele frequencies. On the other hand, according to our results, it is thought to be CTLA-4, 49 A / G heterozygous AG variant may be associated with disease progression. We also observed that there is a significant difference in the distribution of CD28 genotypes between NSCLC patients and controls (p=0.009). CD28 CT genotype was higher in patients with NSCLC cancer than in controls [odds ratio (OR)=3.023; 95% confidence interval (CI)=1.274-7.168, *p*=0.004]. Our study data are guiding the studies on the evaluation of CTLA4 and CD28 genotypes status in terms of risk marker or therapeutic value of NSCLC. Considering the limited size of the study, we believe that the analysis of observations in larger sample groups will be

important in the development of future studies on NSCLC.

The present work was supported by the Research Fund of Istanbul University. Project No. 25437 and 24517

PP28

Alterations of Basal Membrane of Granulosa Cells in PCOS

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Abstract

Aim

The role of basement membrane evaluated in PCOS pathogenesis that may suggest quality of interaction between granulosa and theca cells.

Methods

PCOS model was achieved to Sprague-Dawley rats. Study groups are; control group which received 1% w/v carboxymethyl cellulose and PCOS group which received 1mg/kg letrozole for 3weeks, PCOS model conformation made by serum LH/FSH with ELISA. Basement membrane thicknesses were measured between granulosa-neighbouring theca cells for 10follicles in 5regions. Statistically significance P<0.05 was evaluated by Shapiro-Wilk.

Results

All follicles were evaluated in both groups. PCOS group has many cystic follicles at cortex. Inflammatory cells were not seen in ovary of control group in adversely to PCOS group. On the wall of cystic follicles, there are less granulosa cell layers than controls(Fig1). Measurements were obtained from 65micrographs at 300dpi. The median of total values were control 1,102μm and PCOS 2.160μm. The difference between groups were statistically significant (p<0.001) in Table1.

Conclusions

The basal membrane is responsible for size and charge selectivity to molecules and hormones that provide cross-talk between cell and extracellular matrix by paracrine signals. Thickness of basement membranes suggest its anionic property that enables FSH and other cytokines passaging to granulosa cells, it affects access of cytokines-hormones to granulosa cell charge like Schwart-Jampel syndrome. In our study we examined the increased thickness of basement membrane, within PCOS group. Thickness coursed inefficacy of transition of hormones and other cytokines on granulosa cells might suggest impairment of proliferation and follicular development upon their direct or indirect interactivity in PCOS.

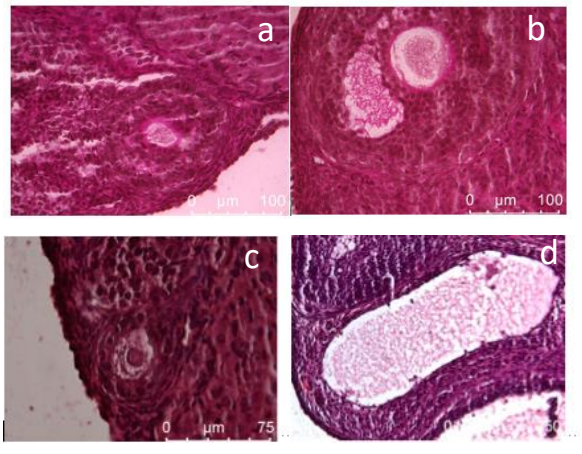

Figure 1. A: Control group PAS, B: PCOS group PAS, C: Control group H&E, D: PCOS group H&E.

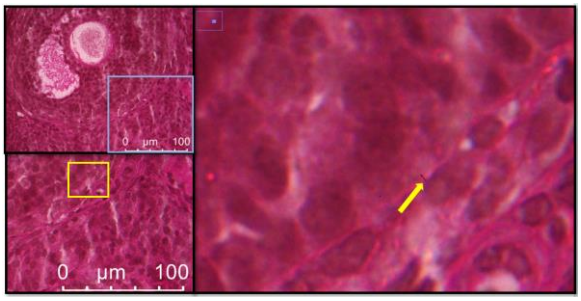

Figure 2. Blue and yellow squires indicate the area of the tissue zoomed in, in order to measure the thickness of the basement membrane. The yellow arrow indicates the measured scale line on basement membrane.

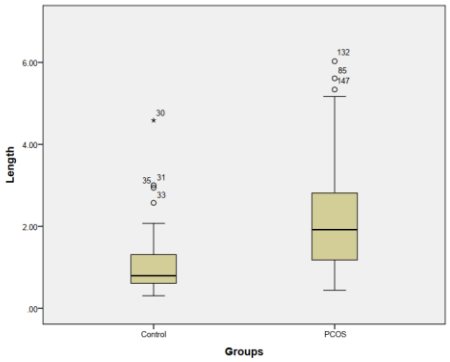

Figure 3. Graphic shows the difference between the thickness of the basement membranes

Table 1. Statistically analysis

Independent Samples T-Test		
	W	**p**
lenght (µm)	908.5	< .001
Note. Mann-Whitney U test.		

Test of Normality (Shapiro-Wilk)			
		W	**p**
lenght (µm)	control	0.754	< .001
lenght (µm)	pcos	0.914	< .001
Note. Significant results suggest a deviation from normality.			

Group Descriptives					
	Group	**N**	**Mean**	**SD**	**SE**
lenght (µm)	control	47	1.102	0.816	0.119
	pcos	102	2.160	1.213	0.120

PP29

Determination of new candidate genes by methylation array method among sub-groups of oral premalignant lesions

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Abstract

Aim

Oral premalignant lesions (OPML), related with malignant transformation (MT), are one of the etiological factors of oral cancers. Therefore, it is important to understand the underlying molecular mechanisms of neoplastic progression in order to define the biomarkers for early diagnosis, screening, identifying the risk of MT and the potential therapeutic targets. Gene silencing stemmed from abnormal methylation is a promising epigenetic mechanism to identify new methylation biomarkers. In our study (TUBITAK-SBAG-114S497), we aimed to the hypermethylated genes by determining methylation status of tumor and matched-normal tissues of sub-groups of oral premalignant lesions [oral leukoplakia (OL), oral lichen planus (LP) and oral lichenoid dysplasia (OLD)].

Methods

Tumor and matched-normal tissues were collected from 4 OL, 4 LP and 4 OLD patients. The samples were analyzed histopatologically and after DNA isolation and BC-DNA modification, the methylated gene

profile was examined using "Illumina Human Methylation 450 chips". Bioinformatics analysis was performed in R environment using Probe Lasso approach implemented in ChAMP Bioconductor package.

Results

In our findings, 9 genes for LP, 4 genes for OL, 320 genes for OLD was identified as hypermethylated with a significance level p<0.05 and change of methylation threshold (|Δß >0.2), whereas 2 genes were found as hypermethylated when tumor tissues of all OPML groups were compared with their adjacent normal tissues.

Conclusion

We considered these candidate genes may be potential biomarkers playing role in the identification of OPMLs. Further validation of candidate hypermethylated genes will be performed in the larger subgroups of OPML patients.

PP30

The association between decreased expression of *Thioredoxin Interacting Protein (TXNIP)* gene and recurrence in oral squamous cell carcinoma patients.

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Abstract

Aim

Oral squamous cell carcinoma (OSCC) has a high morbidity and mortality rate due to the stage that it can be clinically observed and is usually diagnosed in the advanced stage of the disease. There are no reliable biomarkers to distinguish patients who are at risk of early diagnosis. Demokan et al. showed the decreased expression (p=0.032261) of *TXNIP* gene in OSCC patients' tumor tissues via gene expression array method in our project (TUBITAK-SBAG-114S497). The *TXNIP* gene product acts as a transcriptional suppressor; its overexpression induces arrest of the G0/G1 cell cycle. In our study (I.U.BAP-TTU-2018-31834), we aimed to investigate the differentially expressed levels of *TXNIP* gene in Turkish OSCC patients.

Methods

The expression status of *TXNIP* was analyzed in tumor and matched-normal tissue samples of 35 OSCC patients using LightCycler 480 by the quantitative real-time polymerase chain reaction method.

Results

TXNIP and the reference gene expression status were analyzed by calculating the threshold cycle numbers (Ct) as fold changes using the $2^{-\Delta\Delta Ct}$ method. We selected the ratio of >=2 as the threshold for the differentially expressed *TXNIP*. The decreased expression levels of *TXNIP* were observed in 57.4% (20/35) of tumor samples compared with matched normal tissue, whereas the expression levels were increased in 31.4% (11/35) of patients. Statistically significant difference was found between the decreased expression levels of *TXNIP* and recurrence of disease (p=0.018).

Conclusion

We concluded that there is a statistically significant relationship between suppressed expression of *TXNIP* gene and recurrence of OSCC.

PP31

The Role of Salivary Carbonic Anhydrase VI for Caries Risk Evaluation in Children with Pyelonephritis

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Abstract

Aim

Caries risk evaluation is identified as one of the most significant issues of management of oral diseases in all the periods of childhood. Pyelonephritis is one of the most widely distributed infectious disorders among children. There is definite interrelation between the common health status and oral-dental health. The contemporary tendency of wide spectrum implementation of non-operative and atraumatic restorative techniques of treatment of caries lesions entirely corresponds to the conception of utilization of saliva as a non-invasive, but informative medium for control of the dynamics of caries process.

Methods

For the purpose of our study we applied the ICDAS method of clinical investigation of caries, colorimetric method of determination of salivary pH level and statistical method of correlation by Pearson.

Results

We established a slight negative correlation between the salivary enzyme CA-6 and irreversible carious lesions (-0,091), as well as between CA-6 and the common health disorder of pyelonephritis (-0,007). We confirmed slight, with tendency to moderate positive correlation between the number of irreversible carious lesions and the disease of pyelonephritis (0,209). There is ascertained a slight positive correlation between CA-6 and salivary pH (0,053). Although suffering also from recurrent respiratory tract infections, both of the patients with the highest values of salivary CA-6 are characterized with relatively low level of reversible and irreversible carious lesions, compared to the maximal value of 8, respectively 14 in the whole group of the study.

Conclusions

We assess the potentials of the salivary marker of carbonic anhydrase VI as a reliable criterion for proper prognosis, diagnosis and adequate therapy of tooth decay in children with pyelonephritis.

Key words: salivary carbonic anhydrase VI, caries, children, pyelonephritis

PP32

Investigation of MiR-21, MiR-32 and MiR-181a/b in terms of Treatment Response in Multiple Myeloma.

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Abstract
Introduction/Aim

Multiple myeloma (MM) is a B-cell neoplasm characterized by the proliferation of clonal malignant plasma cells in the bone marrow. The incidence rate is higher in leukemia and hematologic system comes second after lymphoma among malignant tumors and

constitutes about 15% of all haematological cancers. Despite the identification of new drugs such as thalidomide, bortezomib, and lenalidomide, which result in a higher overall response rate and longer life span in MM treatment, MM is still an untreatable disease.

MicroRNAs (miRNAs) play a role in critical biological processes such as cell differentiation, apoptosis and cell proliferation in cancer. Recent studies have identified miRNA profiles in human myeloma cell lines and primer patient specimens, and these miRNA expression patterns have been associated with specific genetic anomalies and the patient's surveillance. The aim of this thesis work was to examine that difference in expression levels of the 4 miRNAs (miR-21, miR-32, miR-181a and miR-181b) associated with response to treatment.

Material and methods

The level of expression of (miR-21, miR-32, miR-181a and miR-181b genes) in cells of Multiple Myeloma patients, RNA samples that obtained from whole blood samples of 38 MM patients (pre-treatment and post-treatment) and healthy control groups were investigated the expression pattern of miRNAs using Real-Time PCR technique.

Results

The comparison of MM group with healthy controls revealed upregulation of 4 miRNAs levels before starting of chemotherapy treatment, and after treatment there were decreased in these levels as response in treatment, but some patients showed non-response effect to treatment. In chemotherapy response group, the length of time free from MM disease was associated with decreased miR-32 Expression levels as a result of treatment response.

Conclusion

miR-21, miR-32, miR-181a and miR-181b regulate cell differentiation, proliferation, apoptosis and participate in vascular invasion and metastasis of tumor cells.

We believe that the inhibition of miR-21, miR-32, miR-181a and miR-181b in future experiments with anticancer drugs, and the investigation of whether drug activity develops if these microRNAs are inhibited can also contribute to both the patient's benefit and the literature.

PP33

Expression of the multiple drug resistance associated genes: MRP1, LRP and BCRP among leukemia patients in Gaza strip (Palestine).

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2Department of Biology, Faculty of science, Islamic University, Palestine

Abstract

Introduction/Aim

Haematological neoplasms are usually sensitive to chemotherapy, but with relatively high rate of relapse. Cell resistance to drugs is a major determinant of response to chemotherapy and its detection may be of clinical relevance. The role of expression of transmembrane carriers such as multidrug resistance related Protein 1 (MRP1), breast cancer resistance protein (BCRP) and lung resistance protein (LRP) genes in neoplastic cell survival and risk of relapse for leukemia patients was previously documented. Therefore, the aim of this study was to

estimate the level of expression of MRP1, BCRP, and LRP genes in blood cells of leukemia patients in Gaza strip by quantitative real-time RT-PCR technique, and to investigate any correlation between the expression of these genes and other previous and current clinical findings of the patient.

Material and methods

The level of expression of MRP1, LRP, and BCRP genes in cells of leukemia patients were quantitated by quantitative Real Time- PCR technique and normalized by the expression level of an endogenous control gene porphobilinogen deaminase (PBGD).

Results

MRP1 and LRP but not BCRP mean level of gene expression was significantly higher in leukemia group than normal control group.

LRP gene expression was significantly higher in AML and CML patients than in control group (AML: P=0.021 and CML: P=0.001). LRP gene expression in ALL patients were significantly lower than CML patients (P=0.024); and in CML patients higher than CLL patients (P=0.046). MRP1 and LRP mean levels of expression in remission was less than with no remission patients and this decrease of expression was statistically significant (MRP1: P=0.003 & LRP: P=0.050).

Conclusion

The outcome of the current study indicates that higher levels of MRP1, LRP and BCRP expression are correlated with chemotherapeutic treatment failure of leukemia patients. Therefore we suggest these factors to be included in the design and application of chemotherapy protocols in Gaza Strip.

PP34

Assessment of Antioxidant, and Protective Effect of Salvia Cadmica in Fibroblast Cells From *t*-BHP İnduced Oxidative Damage

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Abstract

Background

Salvia species have been used for centuries worldwide, reported to exhibit antioxidant, cardioprotective, hepatoprotective and antitumor activities. Biological activities of Salvia are generally attributed to its substance of chemical composition. The aim of this study was to assess the in vitro antioxidant properties and also the protecting effect of Salvia cadmica ethanolic extract (ESCE) in fibroblast cells from tertiary-butyl-hydroperoxide (t-BHP) induced oxidative damage.

Material and methods

Total phenolic content and radical scavenging capacity of ESCE, and also the protective effect of ESCE on t-BHP-induced oxidative damage in fibroblast cells; MDA, SOD, CAT, GPx antioxidant enzyme levels and DNA damage were determined using spectrophotometric methods. The effects of ESCE and t-BHP on cell viability were determined using XTT.

Results

The TPC and DPPH values of ESCE were 18.25 ± 0.64 mg gallic acid per g powder, and 80± 0.51 IC50 (µg/mL), respectively. Considering the cytotoxicity analysis, after a recovery time of 4 h, appropriate damage agent t-BHP concentration was 300 µM. After

4 h of recovery in 300 µM t-BHP-damaged fibroblast cells, it was observed that different concentrations of ESCE reduced the amount of MDA and 8-oxo-guanidine formed compared to only t-BHP group.

Conclusion

It was observed that CAT, SOD, GPx activities decreased. It was concluded that this could be done through radical scavenging effect. ESCE may be considered as a potential antioxidant resource and/or a pharmaceutical agent.

Keyword: Antioxidant activity, Cytotoxicity, Salvia Cadmica