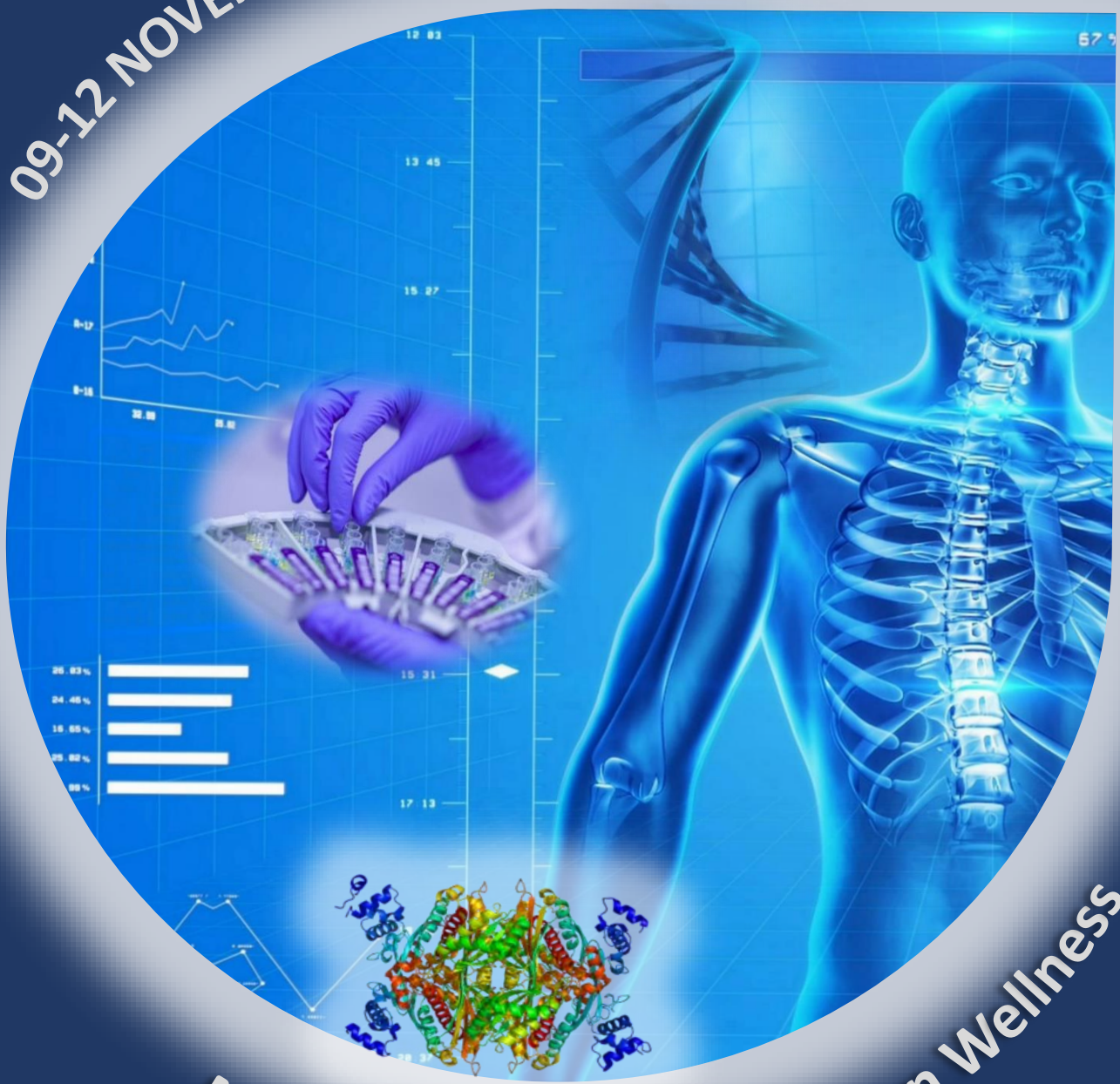
VIII. INTERNATIONAL CONGRESS OF MOLECULAR MEDICINE

09-12 NOVEMBER 2021



Molecular Aspects of Human Wellness

CONGRESS ABSTRACT BOOK

VIII. INTERNATIONAL CONGRESS OF MOLECULAR MEDICINE

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Molecular Aspects of Human Wellness

Dear Colleagues,

On behalf of the Organizing Committee I am delighted to invite you to the 8th International Congress of Molecular Medicine that will be held in Istanbul, Turkey on 9th – 12th of November 2021 under the auspices of the Turkish Society of Molecular Medicine and Istanbul Yeni Yüzyil University, Faculty of Health Sciences.

Congress program will consist of outstanding lectures, including keynote talks, plenary sessions, 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, “Tumor Biology”, “Anti-Cancer Agents”, “Sportive Performance and Genetic”, “Nutrition and Epigenetic Aspects”, “Metabolic Syndrome”, “Prospective Methods in Molecular Medicine“, Molecular Aspects in Diabetes” , “Molecular Metabolic Syndrome” shall be discussed during the congress.

Istanbul Yeni Yüzyil University aims to bring the scientists needed by the society into the country and to become a higher education institution and centre of excellence connected to Atatürk's principles and reforms, aiming to educate knowledgeable, contemporary, equipped and experienced young people who are useful to the society.

Taking into account the developments in the world, this university considers itself responsible for the upbringing of the workforce trained at associate, undergraduate, graduate and doctoral level to exceed the level of civilization academically and technologically and to contribute to researches and studies. To this end, Istanbul Yeni Yüzyil University provides universal education in different disciplines in cooperation with stakeholders such as government institutions, private sector and civil society institutions and organizations with its expert and experienced academic staff.

We are looking forwards to meet you in Istanbul on November 2021 for this outstanding congress and we hope you will enjoy scientific sessions, as well as Turkish hospitality and all the beauty of the Istanbul.

Prof. Dr. Ümit Zeybek

Chair of the Turkish Society of Molecular Medicine,
Istanbul University, Department of Molecular Medicine,
Aziz Sancar Institute of Experimental Medicine,
Istanbul, Turkey

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Molecular Aspects of Human Wellness

Main Theme

- Molecular Aspects of Human Wellness

Main Scientific Topics

- Tumor Biology
- Anti-Cancer Agents
- Sportive Performance and Genetic
- Nutrition and Epigenetic Aspects
- Metabolic Syndrome
- Prospective Methods in Molecular Medicine
- Molecular Aspects in Diabetes
- Molecular Metabolic Syndrome

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OP1

Anti-Leukemic Effect of Wharton Jelly Derived Mesenchymal Stem Cells in Vitro

Mediha Süleymanoğlu[1], Ayşe Erol[1], Figen Abatay Sel[1], İsa Aykut Özdemir[2], Fatma Savran Oğuz[1], Dürdane Serap Kuruca[3], Zerrin Aktaş [4], Zeynep Karakaş[5], Mustafa Oral Öncül[6]

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Besides that mesenchymal stem cells (MSCs) have the capacity for self-renewal and multipotency, their possible anti-cancer effects making them a primary candidate for cell-based therapy. The purpose of this study was to evaluate in vitro anti leukemic effect of Wharton Jelly derived MSC (WJ-MSC) on the K562 and HL-60 cells.

In this study, WJ-MSCs were isolated from an umbilical cord. According to standard culture conditions, the cells incubated and characterized by flow cytometry. For experiments, WJ-MSC and leukemic cells were incubated in the direct co-culture at a ratio of 1:5 (leukemia cells:WJ-MSC). We analyzed the apoptotic effect of WJ-MSCs on K562 and HL-60 cells with AnnexinV/PI assay by flow cytometry.

After the direct co-culture of WJ-MSCs on leukemic cell lines, we observed anti-leukemic effect by inducing apoptosis. We had 2 groups of determination apoptosis with and without WJ-MSCs. In untreated and treated experimental groups for K562, we found increasing of apoptosis respectively (from 3,7% to 11,5%). For HL-60 cells, when compared between two groups apoptosis percentages were 15% (untreated) and 56% (treated). The increasing ratio of apoptotic cells was (approximately 3 folds) similar both for HL-60 and K562 cells.

MSCs are known to inhibit tumor growth of hematopoitic and non-hematopoietic origin in vitro. Treatment with WJ-MSC led to potentproliferation inhibition of HL-60 and K562 cells with inducing apoptosis. Our results provide new insight into how WJ-MSCs inhibit tumor growth in vitro. In the future, WJ-MSCs may be an option for their clinical use for the inhibition of cancer cells.

Keywords: WJ-MSC, Co-culture, Anti-leukemic effect

OP2

The Apoptotic Effect of Human Umbilical Cord Blood Derived Mesenchymal Stem Cells on Colorectal Cancer Cell Lines

Figen Abatay Sel[1,2], Mediha Süleymanoğlu[1], Ayşe Erol[1], Gökhan Demirayak[3], Çiğdem Kekik Çınar[1], Dürdane Serap Kuruca[4], Fatma Savran Oğuz[1]

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Colorectal cancer (CRC) is the third common cancer worldwide. Stem cell-based therapies are becoming new therapeutic focus for cancer. Mesenchymal stem cell (MSC) has been generated interest for the treatment option for cancer due to its apoptotic effect. In this study, evaluating the apoptotic effects of cord blood derived-MSC (CB-MSC) on HT-29 and HCT- 116 cell lines were aimed.

MSCs were obtained from human umbilical cord blood, characterized by flow cytometry (FC). CRC cells and CB-MSCs were incubated in different ratios (1:5, 1:10) in transwell co-culture for 72 hours. Cell viability was evaluated by Trypan blue. The apoptosis rates of colorectal cells were also analyzed by FC using Annexin V-FITC/PI. The apoptosis increases as a result of co-culture of HT-29 and HCT-116 cancer cells with CB- MSCs at a ratio of 1:5 were 1,08 and 1,17, and at a ratio of 1:10 were 1,24 and 1,81, respectively. When compared the apoptotic effects of CB-MSC on CRC cell lines, we found

that MSCs induced on HCT-116 more apoptotic effect. Although the effect of MSC on tumor microenvironment is controversial, we observed that CB-MSC induced the apoptotic effect on HT-29 and HCT-116. In this preliminary study, we anticipate that further works would be helpful for a better understanding of MSC with

the development of cell therapy which might lead to widespread use of MSCs in efficacious CRC and other solid tumor treatment. This study was granted by Istanbul University Scientific Research Commission (ID:37059) and CoHE 100/2000 PhD Scholarship Program.

Keywords: Human umbilical cord blood derived MSC, Colorectal cancer, Apotosis

OP3

Examination of CXCL12 Expression Regulation and Association with Multiple Myeloma and Other Diseases

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Chemokines are peptides that act as chemoattractant cytokines involved in cell activation, differentiation, migration and adhesion. CXCL12 is a homeostatic chemokine protein encoded by the CXCL12 gene on chromosome 10 in humans and is derived by stromal cells, bone endothelium, multiple myeloma (MM) cell lines, and primary myeloma cells. CXCL12 also has chemotactic properties for mesenchymal stem cells. In addition, CXCL12 has been shown to regulate CD20 expression on B cells via signaling. CXCL12 also plays an important role in angiogenesis by stimulating endothelial progenitor cells (EPC) from the bone marrow through a CXCR4-dependent mechanism. It also plays a role in functional states such as embryogenesis, osteoclastogenesis, development of the immune system, development of infection, tissue homeostasis, tumor growth, metastasis. MM is a plasma cell malignancy characterized by infiltration and growth of malignant plasma cells in the bone marrow (BM). MM is the most common type of cancer in plasma cells. The relationship between CXCR4 and CXCL12 is crucial for targeting MM cells to the protective BM niche. We examined the regulation of expression of CXCL12 (eQTL effects and microRNAs (niRNAs); co-regulated gene sets), and disease associations of CXCL12 sequence variants, eQTLs/meQTLs for CXCL12 together with related miRNA variants to learn about its pathophysiological roles. The BioGrid Database identified 31 genes interaction with CXCL12, including 8 additional CXCL genes in the vicinity of CXCL12. The most significant co-expression pattern was noted in the bone marrow followed by other organs (brain, kidney, heart, lung, kidney and skin). The gene set enrichment analysis of the co-expressed gene set on the GSEA/MSigDB tool suggested enrichment of genes involved allergic disease, arthritis, autoimmune disease of musculoskeletal system, bone inflammation disease (FDR<5E-06). We selected the miRNAs targeting CXCL12, and determined their other target genes using Target Scan. 593 miRNAs were identified, and the targets of each miRNA were subjected to the same GSEA analysis. The results nearly significant as the co-expressed gene set suggesting that miRNAs play a major role in the regulation of CXCL12 expression. Examination of disease associations of SNPs from each miRNA gene region in GWAS databases yielded results for B-lymphoblastic leukemia/lymphoma at P<7E-40. SNPs within CXCL12 did not show any GWAS associations, but SNPs acting as eQTL/meQTL in blood for CXCL12 showed GWAS associations with respiratory system disease, intestinal disease, combined immunodeficiency, multiple sclerosis, hepatit (P<8E-06). miRNAs showed stronger genetic associations with inflammatory, immune disorders and MM. We conclude that the role played by CXCL12 is stronger in autoimmunity, inflammation and possibly in MM.

Keywords: CXCL12, CXCR4, Multiple Myeloma, Expression, Pathways, SNP

OP4

The Use Of Dual İnhibitors Targeting LSD1/HDAC6 as a New Method for Treating MLL-AF9 Leukemias

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Leukemia is a blood and bone marrow condition characterized by a lack of differentiation during hematopoiesis, which results in uncontrolled cell proliferation. Mixed lineage leukemia (MLL) is a type of acute leukemia with a poor prognosis, where chromatin modifying enzymes are aberrantly expressed due to

hyperactive MLL fusions. Therefore, MLL leukemias are mostly based on epigenetic irregulations rather than genomic instability, due to chromosomal translocations. The targeting of key epigenetic regulators, such as Lysine-specific demethylase (LSD1) and Histone deacetylase (HDAC), has been proposed as a new therapy option. The overexpression of these enzymes causes the activation of numerous genes in MLL-AF9 leukemias, which impede differentiation and promote uncontrolled cell proliferation.

A chemical switch including the addition of HDAC binding pocket to the clinical candidate LSD1 inhibitor GSK2879552, produced the multitargeting analogue for LSD1 and HDAC6. In our study, we used in vitro enzyme activity tests to show that the compounds inhibit target enzymes, then we used a cellular thermal shift assay to show target engagement enzymes in the cell (CETSA). The dual targeting agent inhibited a panel of four acute myeloid leukemia (AML) cell lines at a higher potency than GSK2879552. Dual engagement with LSD1 and HDAC6 was further supported by increases in substrate levels and downstream genes using RT-qPCR. Dual inhibitor sensitized AML cells to treatment with doxorubicin, inducing cell death with a sublethal concentration of the drug.

Considering the limitation on generation and usage of dual targeting inhibitors, this study may provide future applications for leukemia therapy and clinical application.

Keywords: Epigenetics, Leukemia, LSD1-HDAC, Anti-cancer drug, Dual inhibitors

OP5

Developing Quantitative Experimental Model Systems to Study Drug Resistance

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It is widely known that secondary resistance inevitably leads to treatment failure. Existing experimental model systems to study drug resistance have several limitations such as lack of quantitative evaluation of the process, clinically infeasible drug concentrations, and a low number of cells used in the existing experimental models fail to capture the true dynamics of cancer growth and relapse observed in the clinic. Therefore, quantifying the clonal evolution using novel experimental model systems can hold a great promise in designing evolutionarily informed therapies, and thus, in predicting drug response. In this talk, I present a recently published work1 that contributed to the understanding of collateral drug sensitivity with its direct link to clonal evolution to overcome the drug resistance in non-small cell lung cancer cell line model system. More specifically, high-complexity cellular barcoding allowed the identification of the resistance that was ultimately driven by the presence and emergence of multiple pre-existing and de novo resistant clones, respectively. Overall, the work I will present highlights evolutionary trade-offs and it provides an opportunity to exploit the tumour's vulnerability.

Keywords: Cellular barcoding, drug resistance, cancer evolution

OP6

The Effect of Whey Proteins on Methotrexate-Induced Liver and Kidney Damage

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Methotrexate (MTX) is a cytotoxic chemotherapy agent and an immunosuppressant that is widely used in the treatment of tumours, rheumatoid arthritis, and psoriasis. Whey proteins have antioxidant, antitumor, antihypertensive, antiviral, hypolipidemic and antibacterial properties. This study aims to determine the effect of whey protein on MTX induced liver and kidney damage in rats. For this purpose, rats were divided into four groups as control, control+whey, MTX, MTX+whey. A single dose of 20 mg/kg MTX was administered intraperitoneally to the MTX group. Control+whey and MTX+whey groups were given 2 g/kg whey protein concentrate by gavage every day for ten days. At the end of day 10, blood and tissue samples were taken for the biochemical analyzes.

Serum TNF-α and IL-6 values decreased, and IF-γ values did not significantly change in the MTX group. With the

administration of whey protein to the rats treated with MTX, TNF-α and IL-6 values significantly increased compared to the MTX group, while IF-γ values did not change. An increase in lipid peroxidation and a decrease in glutathione levels were detected in the liver and kidney of the MTX given rats. Giving whey protein to the MTX treated rats decreased lipid peroxidation and increased glutathione levels in the liver and kidney tissues. In conclusion, while a decrease was detected in the blood cytokine levels of the MTX treated rats, oxidative damage was also detected in the liver and kidney tissues. Whey protein administration ameliorated the oxidative damage induced by MTX due to its antioxidant properties.

Keywords: Milk serum proteins, whey, methotrexate, liver, kidney, oxidative stress

OP7

The Influence of Lactobacillus Cell-Free Supernatants on Growth and Biofilm Formation of Different Pathogenic Bacteria

Fatma Kalaycı Yüksek

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Aims. It is well known that antibiotic resistance is a global health concern. Thus, alternative and supportive options gained importance. Probiotic bacteria have roles in preventive/supportive medicine. Lactobacilli are commonly used probiotic microorganisms. Therefore, the influence of lactobacillus cell-free supernatants (CFSs) on growth and biofilm formation of different pathogenic bacteria was investigated.

Methods. The inhibitory effects of various Lactobacillus species' (L. acidophilus-La, L. plantarum-Lp, L. fermentum-Lf and L. rhamnosus-Lr) on Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Enterococcus faecalis and Staphylococcus aureus were investigated. Growths were determined at 4, 6 and 24 hours. Growth and biofilm were examined using the spectrophotometric method and microtiter plate assay, respectively. Growth and biofilm alterations were calculated by using one-way and two-way ANOVA followed by Dunnett's multiple comparison tests, respectively.

Results. The growth of E.coli was found to be decreased in the presence of only Lf at six hours and all CFSs reduced the growth of E.coli at 24 hours. Similarly, all CFSs decreased the growth of P.aeruginosa, K.pneumoniae, E.faecalis and S.aureus at 6 and 24 hours. Furthermore, biofilm formation of gram-positive bacteria reduced statistically significantly ($p \leq 0.006$) in the presence of all CFSs. Moreover, CFSs of L.rhamnosus had the most inhibitory effect on biofilm formation.

Conclusions. The inhibitory roles of CFSs on growth of bacteria were variable depending on exposure time and strain tested. On the other hand, biofilm inhibition levels were variable. These findings suggested that lactobacilli as probiotics have inhibitory effects on different kinds of pathogens.

Keywords: Cell-free supernatants, lactobacilli, growth, biofilm

OP8

Can Epigenetic Targeting of Lysosomal Exocytosis/Biogenesis Overcome Cisplatin Resistance in Cancers?

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Resistance to chemotherapy due to a decrease in drug efficacy is one of the main challenges of cancer therapy. Lysosomes are recognized as essential factors in cell signaling, sequestration, and expulsion of many components, including toxic metals and chemotherapeutic agents. Besides, the epigenetic regulation of lysosomal biogenesis and exocytosis has just begun to be investigated. Our research focuses on the emerging idea that drug sequestration in the lysosomes followed by lysosomal exocytosis or change in lysosomal biogenesis contributes to cisplatin resistance in cancer. This idea is unexplored in the context of epidrugs and is currently under investigation in our laboratory. Our study aims to elucidate the epigenetic factors that regulate these processes, and we hypothesize that the epidrugs that decrease lysosomal functions are potential candidates for cisplatin synergy.

In our study, an epidrug library containing several readers, writers, and erasers are screened for their effect

on exocytosis (β-Hex Assay), biogenesis (Lysotracker), and combinatorial action with cisplatin (SRB-viability assay). Interestingly, while there is a connection between exocytosis and biogenesis, epidrugs' action on these tightly linked cellular processes does not always follow the same fate. Our preliminary data show that most epidrugs increase lysosomal flux and/or biogenesis. PRMT1 inhibition decreased the flux upon stimulation of exocytosis, and indeed its combination enhanced the potency of cisplatin. Additionally, we identified HDAC1/3 and PRMT5 inhibitors as hits that stimulated cisplatin efficacy. We are currently investigating whether other chemotherapeutics, known to undergo lysosomal sequestration, will synergize with the same epidrugs. By establishing their mechanisms, we wish to set future targets for intervention in cancer.

Keywords: Cisplatin Resistance, Epigenetic Regulation, Lysosomal Exocytosis, Lysosomal Biogenesis

OP9

Does Caprylic Acid İmprove the Expression of Mitochondrial Proteins Altered by Rotenone Exposure in Zebrafish?

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Rotenone is an insecticide that has an inhibitory effect on the mitochondria complex 1 and it is used to establish Parkinson's Disease (PD) models in experimental animal. Caprylic acid (C8) is a medium chain saturated fatty acid (MCFA) and is the main fatty acid component of medium chain triglycerides in ketogenic diets. In this study, it was aimed to investigate the effects of caprylic acid on rotenone toxicity to obtain information about the effects of ketogenic diets on neurodegenerative diseases by using MS-based proteomic approaches. Initially, adult zebrafish exposed to rotenone were treated with two different doses of caprylic acid. Total proteins from whole body samples were digested using the FASP (filter assisted sample preparation) method. Proteomic analyzes were performed using Q-Exactive Plus tandem mass spectrometry (MS) coupled with nano LC systems. MS analysis results allowed the identification of over 5000 proteins. A significant portion of the proteins whose expression changes due to rotenone responded to caprylic acid treatment. In addition, bioinformatic analyzes revealed that these proteins are associated with electron transport, respiratory chain and oxidative stress. Preliminary results showed that disrupted protein profile associated with energy and redox system in rotenone exposed zebrafish was significantly improved with caprylic acid. In our further study, we plan to confirm the significant protein expression differences using targeted proteomic methods such as PRM.

Keywords: Parkinson's Disease, rotenone, caprylic acid, proteomics

OP10

Preliminary Study: Measurement of Iron in Breast Tissue Samples by Inductively-Coupled Plasma/Mass Spectrometry.

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Breast cancer has the highest incidence and mortality rates among women, regardless of improvements in diagnosis and therapies. Thus, a better understanding of the cellular and molecular processes underlying in breast cancer development and progression is required for a change in this situation.

Iron (Fe) is an essential element for cell growth and division. Studies have shown that progression, aggressiveness and recurrence of breast cancer were associated with the deregulation of iron's metabolism. It is considered that higher intercellular concentrations of Fe have a role in chronic failure of the redox balance which can modulate specific signaling networks and affects cancer malignancy. The use of inductively-coupled plasma/mass spectrometry (ICP-MS) to measure metal ion content in biological tissues offers a highly sensitive means to study metal-dependent physiological processes.

Thus, in this study we developed an ICP-MS based in-house method of Fe analysis for breast tissue samples. Following a wet digestion method, evaluation of the total

Fe content of the samples has been conducted using ICP-MS (Agilent 7700) with enhanced helium mode. Fe contents were determined in 5 tissue sets (tumor and adjacent tissue) collected from 5 women diagnosed with invasive ductal breast cancer. In addition two cancer free breast tissues, obtained from breast reduction surgery, were used for normalization. Our method showed a low rate of measurement error (<3%). A significant (p= 0.045) ~2 fold difference of Fe concentrations were observed in tumors (20.67 ± 3.37 ppb/mg) as compared to adjacent tissues (10.64 ±3.54 ppb/mg). Further studies must be conducted with higher number of samples to investigate the association of Fe levels with histological type of tumor, its size, grading and receptor status. Our ICP based method can be reliably performed at the established conditions for tissue specimens, and have also potential to be used in clinical practice.

Keywords: Breast cancer, Iron, ICP-MS

0P11

Investigation of PD-1/PD-L1 Critical Genes Variant and Protein Analysis in Non- Small Cell Lung Cancer

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Background: Cancer is a complex disease and it is generally accepted that it begins as a result of changes in the structure of more than one gene, with the presence of various molecular, genetic and epigenetic abnormalities. In local immun response, the interaction between T cells and immun checkpoints molecules are very important for managing the signaling cascades that stimulates efficient antitumor immune response The aim of this study was to examine the polymorphisms and protein analysis of PD-1 / PDL-1 immun checkpoint molecules in terms of susceptibility to NSCLC disease and possible relationship with clinical parameters.

Methods: PD-1 (rs2227981) and PD-L1 (rs2890658) gene variants were genotyped by using PCR and RFLP in 80 non small cell lung cancer patients and 79 healthy individuals. Soluble PD-1 levels in serum was detected with ELISA and Western blot was used for analysis of PD-L1 protein expression. The mean values of differences in clinical parameters between the two groups of NSCLC cases and healthy individuals were evaluated. Results: PD-L1 A/C AA genotype was higher in patients than in controls and the difference was found significant (p=0.043). PD-1 C/T CC genotype was higher in the presence of angiolymphatic invasion than CC genotype in the absence of angiolymphatic invasion (p=0.028). The frequencies of PD-1 CT genotype was higher in patients without angiolymphatic invasion compared to patients with angiolymphatic invasion(p=0.047). The CC genotype was found to be associated with the presence of perineural invasion (p=0.026). Serum PD-1 levels was statistically signifcantly found to be higher in patients who have CC genotype than those with control group (p=0.008). When the PD-1 and PD-L1 genotypes were examined together, CTAC combined genotype carrying in the control group was found to be higher than those of the NSCLC patients (p=0.016). Expression of PD-L1 was found higher in tumor tissue (p<0,0001). Conclusion: The results of the study contribute to clinical research in terms of elucidating the PD-1 and PD-L1 polymorphisms seemed to be associated with their expressions. Those relations may help to create new treatment strategies in NSCLC patients.

Keywords: Non-small cell lung cancer, genotyping, PD-1, PD-L1, PD-L1 expression

OP12

Investigating the Effect of Polyphenolic Compounds on Gene Expression of Migration Related Genes Jam-A, LFA-1 And VLA-4 in Hormon Positive and Negative Breast Cancer Cell Lines

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Aim: Proteins managing the cell migration play role in the occurrence of cancer metastasis. Integrins and cell junctions have crucial importance in cancer proliferation and metastasis. Polyphenolic compounds have cytotoxic and apoptocic effects on cancer cells. The aim of the study is to investigate the effects of the polyphenolic compounds on the cell migration and gene expression of

VLA-4 (very late antigen-4, α4β1, ITGA4, CD49d/CD29) and LFA-1 (Lymphocyte function-associated antigen-1, αL/β2, ITGAL, CD11a/CD18) integrins and Jam-A (junctional adhesion molecule-A, F11R), a kind of tight junction, that interact with each other in the tumor metastasis in ER+ MCF-7, Triple-negative MDA-MB-231 and fibrocystic breast epithelial MCF-10A cell lines.

Methods: Real-Time PCR (RT-PCR) was applied for gene expression studies. Scratch assay was used in order to evaluate cell migrations.

Results: Polyphenolic cocktail with 20% dose was found to cause a reduction in Jam-A gene expression in MCF-7 ve MCF-10A ($p<0,001$), an increase in LFA-1 gene expression in MDA-MB-231 and MCF-10A ($p<0,001$), a reduction in VLA-4 gene expression in MDA-MB-231 and MCF-10A ($p<0,0001$) cells at 48th hour of cell culture. Moreover, it was determined that polyphenolic cocktail decreased the cell migration in each and every cell in the study. It was observed that cell migration was totally arrested in MDA-MB-231 cells which were treated with 35% polyphenolic cocktail. Anti-migratory effect of the polyphenolic cocktail was occurred with lower doses (10%) in MCF-7 cells.

Conclusion: Our results indicate that polyphenolic compounds have anti-metastatic effects in addition to their cytotoxic and apoptotic effects on breast cancer and might be considered as a part of cancer treatment.

Keywords: Polyphenolic compounds, breast cancer, metastasis, Jam-A, LFA-1, VLA-4

OP13

The Effects of PCSK9 and Apolipoprotein E Functional Gene Variations on Hypercholesterolemia and Clinical Phenotype in Restenosis Patients After Percutaneous Coronary Angioplasty

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Aim: In-stent-restenosis is a case restricting the benefits of percutaneous-transluminal coronary angioplasty (PTCA). PCSK9 controls LDLR levels, and variations in PCSK9, ApoE and ApoER genes may affect the development of restenosis. The aim of this study was to assess the effects of genetic variants on restenosis risk after PTCA.

Methods: The study groups include 109 CAD-patients with restenosis (S-CAD) and 82 CAD-patients without restenosis (open-stent,OS-CAD). SNPs were analyzed by RT- PCR. PCSK9 levels were detected via ELISA method.

Results: The distributions of ApoE Epsilon, APOER (rs5174), PCSK9 rs2182833 and rs11206510 polymorphisms were found similar between study groups while the frequency of the PCSK9 E670G G allele in S-CAD group was found significantly higher than OS-CAD patients ($p= 0.015$). No difference was found between study groups in terms of the serum levels of PCSK9. LDL-C was found lower and HDL-C was found higher in OS-CAD group comparing with S-CAD group ($p=0.042$, $p=0.008$, respectively). Frequencies of Type 2 DM and hyperlipidemia were also found higher in S-CAD group than OS-CAD group ($p=0.007$, $p=0.001$, respectively) while EF% was found lower in S-CAD group than OS-CAD group ($p=0.007$).

Conclusions: Our findings indicate that although ApoE Epsilon, APOER (rs5174), PCSK9 rs2182833, rs11206510 and E670G polymorphisms has no effect on serum PCSK9 levels, PCSK9-rs505151G-allele and hyperlipidemia may be risk factors in the development of restenosis.

Keywords: PCSK9, ApoE, ApoER, mutation, restenosis, hypercholesterolemia

OP14

Investigation of Hepatic and Intestinal Responses to Rotenone and Acetic Acid in Zebrafish

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Rotenone is a neurotoxin belonging to the rotenoid family isolated from tropical plants. It functions as herbicide and pesticide in agriculture. Due to its high lipophilicity, it easily crosses the blood-brain barrier and inhibits the activity of mitochondrial complex I. It causes the formation of reactive oxygen species and disruption of mitochondrial functions. It is used to create a Parkinson's Disease (PD) model in experimental animals. Pain is considered one of the most important non-motor symptoms in PD. The main function of pain is to be a warning signal that protects the organism from harm or minimizes injury. The second main function of pain occurs after injury. Internal mechanisms exacerbate pain intensity, location, and duration. Pain radiates from the damaged area to the undamaged areas and continues during healing. Chemical, thermal and mechanical harmful stimuli are used when creating pain models in animals. While heat and cold exposure are used as thermal harmful stimuli, various electrical mechanisms are used as mechanical stimuli. Acetic acid is one of the chemical agents used to create pain in animals. In our study, lipid peroxidation, nitric oxide, superoxide dismutase and glutathione-S transferase analyzes were performed spectrophotometrically in the liver and intestinal tissues of zebrafish that were treated with acetic acid, rotenone and acetic acid together with rotenone. Our results showed that liver and intestinal tissues respond differently in terms of oxidant-antioxidant status when acetic acid is administered in case of rotenone toxicity.

Keywords: Rotenone, asetic acid, liver, intestines, oxidant-antioxidant status

OP15

Efficacy of The Gemcitabine-Loaded Chitosan Nanoparticles on the Pancreatic Cancer

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Chitosan nanoparticles (NPs) are gaining more attention recently since their properties include improving drug efficacy, good blood flow characteristic, enhanced bioavailability, and biodegradability. We used chitosan to synthesize gemcitabine-loaded nanoparticles to overcome adverse effects and poor survival outcomes of gemcitabine therapy used for patients with pancreatic cancer. Blank and gemcitabine-loaded biodegradable chitosan nanoparticles were prepared with a method that combines ultra-sonication and ionotropic gelation. CFPAC-1 cells were treated with increased concentrations of gemcitabine, empty NPs, and gemcitabine-loaded NPs respectively. Cells were collected after treatments and cell proliferation, oxidative stress metabolism, and nutrient metabolism of CFPAC-1 cells were investigated to evaluate biocompatibility and efficacy of gemcitabine-loaded NPs on the pancreatic cancer cells. Our data showed that gemcitabine-loaded NPS leads to decreased cell proliferation and impair enzymatic activity involved in the oxidative stress metabolism compared to gemcitabine alone. Our study highlighted biocompatibility and increased anti-tumor activity of gemcitabine-loaded chitosan nanoparticles on the CFPAC-1 cells in vitro.

Keywords: Gemcitabine, chitosan, nanoparticle, oxidative stress, polymer toxicity, pancreatic cancer

OP16

How Does BRPF Proteins Revert Taxane Resistance in Prostate Cancer? A Molecular Approach…

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Objective: Epigenetic regulation of cancer cells affects cancer development, progression and drug resistance. While localized prostate cancer can be treated with androgen suppression and surgery, many patients develop castration-resistant prostate cancer (CRPCa), which is more aggressive and/or metastatic. CRPCa patients are treated with chemotherapeutic taxanes (Docetaxel and Cabazitaxel), however they develop resistance to these drugs over time. It is important to determine epigenetic mechanisms in drug resistance in order to develop therapies. Epigenetic drug library and CRISPR screens with taxane resistant CRPCa cells (Du145

and 22Rv1) has shown that BRPF inhibition reverses taxane resistance. Our aim is to elucidate molecular pathways of BRPF (epigenetic reader proteins containing bromodomain group) inhibition in reversing taxane resistance in these cells.

Materials-Methods: Suppression of BRPF1 and BRPF2 expression was achieved with siRNA and CRISPR/Cas9. Following BRPF inhibition, cell viability and colony formation capacity were monitored via SRB analysis and colonogenic assay, respectively. Transcriptomic differences were examined by RNAseq, direct target genes were analyzed by ChiPseq method.

Results: BRPF inhibition with small molecules resensitized taxane-resistant CRPCa cells to taxane. While BRPF2 knock-out of taxane-resistant CRPCa cells reversed taxane resistance, parental cells were not further sensitized to taxanes as predicted. The sequencing results were investigated by bioinformatic analysis, and the differentially expressed genes will be discussed within the scope of the presentation.

Conclusion: Our aim was to investigate the molecular pathways of BRPF inhibition in reversing taxane resistance. Our findings show that BRPF inhibiton is a promising anticancer strategy in CRPCa.

Key messages: BRPF family proteins emerge as important epigenetic regulators to resensitize taxane-resistant cancer cells to taxane. These findings seem promising for clinical application of the combination of BRPF inhibitors with taxanes.

Keywords: BRPF, castration-resistant prostate cancer, drug resistance, epigenetics, taxane

OP17

NEK2 Regulates Centrosome Clustering in Cancer Cells with Extra Centrosomes

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Objective: Unlike normal cells, cancer cells frequently exhibit extra centrosomes, which tend to form multipolar spindles (MPS), triggering cell death. Nevertheless, cancer cells divide successfully by clustering their extra centrosomes into two poles. Nek2 kinase is a key molecule regulating mitotic processes, including centrosome cycle. In this project, we tested whether Nek2 has a role in centrosome clustering in addition to its role in splitting centrioles, and which of the Nek2 targets might be responsible. This way, we wish to find novel strategies that may selectively kill cancer cells exhibiting supernumerary centrosomes.

Materials-Methods: Unclustering effect of Nek2 was studied in cells with endogenously supernumerary centrosomes (N1E115), or via induction of extra centrosomes via microtubule inhibitors and PLK4 overexpression (U2OS, MDA-MB-231). Nek2 was overexpressed under a Dox inducible promoter or silenced using siRNA or knockout using gRNAs. Centrosomes were labelled using ɣ-Tubulin. Known Nek2 targets with relevant function were assessed for their involvement in centrosomal unclustering (C-NAP1, Rootletin, Gas2L1, Trf1) using KO or siRNA. Live cell imaging was utilized to determine the duration of metaphase.

Results: Overexpression of Nek2 induced unclustering of extra centrosomes and lead to MPS, while reduction of Nek2 reclustered the poles, leading bipolar divisions in the cell lines studied. Known Nek2 targets tested have shown that they don't involve in the centrosome clustering mechanism which Nek2 regulates. Nek2 organizes centrosome clustering independent of a known pathway orchestrated by Kifc1 (HSET). Moreover, overexpression of Nek2 abridges the duration of metaphase, which could interfere centrosome clustering events requiring time during metaphase. We are currently studying to elucidate the mechanism of Nek2 regulating centrosome clustering in cancer cells.

Conclusion: In our studies, we assigned a novel function for Nek2 in centrosome clustering. Understanding the mechanism will provide new translational approaches for cancer-specific treatment.

Keywords: Nek2, centrosome clustering, cancer

OP18

Laboratory and in Silico Analysis of the Pathogenic Variant of Interleukin-17 (rs763780) in Patients Diagnosed with Covid-19

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In the pathogenesis of COVID-19, there is an effective inflammatory response that triggers many cytokine groups, including interleukins. The aim of this study is to investigate whether the pathogenic variant of the IL-17F gene (7488 A/G = rs763780) has both a clinical and genetic relationship in patients diagnosed with COVID-19. A total of 278 COVID-19 patients and 100 healthy controls were included in the study. The PCR test results of 200 of 278 patients were positive and the PCR test results of 78 patients were negative and the diagnosis was made with CT findings. DNA isolation was performed after the blood samples of the patient groups and healthy controls were collected. PCR-RFLP technique was used for genotype analysis of rs763780 and statistical analyzes were performed in IBM SPSS version 21.0 program. Gencard, HaploReg4, rVarBase and SNP & GO programs were used to predict the pathogenetic effect of IL-17F. There was no statistically significant difference in allele and genotype frequencies between the patients and the control group, and no significant difference was found in terms of clinical parameters ($p > 0.05$). In conclusion, this study is the first to investigate the association of the pathogenic variant rs763780 with COVID-19 in the Turkish population. These results indicate that the rs763780 variant is not associated with COVID-19 susceptibility in the Turkish population. Further studies, both at the whole gene level and in larger groups and different ethnicities, are needed to determine the impact of this variant on the risk of developing COVID-19.

Keywords: COVID-19, IL-17F, polymorphism

OP19

Investigation of The Effect of Betulinic Acid on EMT Pathway in Renal Cancer Cells

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Renal cancer accounts for 2-3% of adult cancers worldwide and is the most fatal cancer type among urological cancers. In addition to being a type of cancer resistant to chemotherapy and radiotherapy, its metastasis level is also high. The process, called epithelial-mesenchymal transition (EMT), contributes to cell differentiation, development, and is also considered a key step in initiating metastatic process of cancer cells to distant organs. Betulinic acid is a pentacyclic triterpenoid of lupane-type naturally occurring in various plants. Various studies have demonstrated that betulinic acid has a strong anti-cancer activity as well as anti-viral, anti-inflammatory, and anti-bacterial activities.

The effects of betulinic acid on EMT pathway was examined with WST-1, Real-Time PCR, and migration/invasion assay methods on renal cancer cell lines; CAKI-2 clear cell renal carcinoma and ACHN metastatic renal adenocarcinoma.

According to our results, SDC-2 gene expression, which is a mesenchymal marker, was statistically decreased in both CAKI-2 cell groups. In the ACHN cell group, SNAIL1 gene expression was statistically increased. Migration assay findings showed a decrease of 28% in ACHN25 group and 46% in the ACHN50 group. In the invasion findings a decrease of 12% in ACHN25 group and 15% in the ACHN50 group was determined.

These results showed that betulinic acid can be effective on EMT in different ways in both cell lines. Particularly, determining the effect of betulinic acid on EMT pathway may constitute an important approach for treatment options in renal cancer with high metastasis level.

Keywords: Betulinic acid, renal cancer, EMT

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OP20

The Investigation of Brain and Intestine Nitric Oxide Level and Protein Profile in Methotrexate and Whey Protein Concentrate Treatment

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Methotrexate induces inflammation of the intestinal mucosa and changes the protein metabolism in the intestine, regardless of reduced food intake. The brain has a direct influence on the intestines. A disturbed intestine can send signals to the brain just like a disturbed brain can send signals to the intestine. Therefore in the present study, the effect of whey proteins on the methotrexate induced intestinal and brain damage was investigated. Sprague Dawley rats weighing 200-300 grams were used. Methotrexate was administered as a single dose of 20 mg/kg intraperitoneally, and 2 mg/kg of whey protein was administered by oral gavage for ten days. The SDS-polyacrylamide gel electrophoresis of brain and intestine tissues were carried out, and nitric oxide level was determined. While methotrexate treatment caused some changes in the protein profiles of intestinal and brain tissues, the application of whey proteins ameliorated these changes. Nitric oxide levels did not change in the brain tissue of rats treated with methotrexate, while an increase in intestinal nitric oxide levels was detected. Giving whey protein to rats treated with methotrexate increased nitric oxide levels in both intestine and brain tissue. In conclusion, the present study suggests that administration of methotrexate disrupts the protein profile of brain and intestine tissues. Potentiation of the effects of whey proteins by consecutive (ten days) administration might be one of the main reasons to ameliorate the intestine and brain protein profile and nitric oxide level in methotrexate-induced damage.

Keywords: nitric oxide, brain, intestine, methotrexate, whey protein

OP21

Protective effect of Moringa oleifera on oxidant damage caused by valproic acid in the parotid gland of rats

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Valproic acid (VPA) is a broad spectrum anti-epileptic drug that is effective in migraine, bipolar disorder, anxiety and other psychiatric disorders. In addition to many known clinical side effects of VPA, it is stated that it causes sialadenosis and dry mouth, and it is also claimed that VPA treatment prevents the growth of salivary gland tumors.

Moringa oleifera Lam. (M. oleifera) is also known as “miracle tree” among people because of its healing of various ailments and chronic diseases. Extracts from M. oleifera exhibit multiple nutraceutical or pharmacological functions including anti-inflammatory, anti-oxidant, anti-cancer, hepatoprotective, neuroprotective, hypoglycemic, and blood lipid-reducing functions.

In this study, the possible protective effect of M.oleifera alcoholic extract on the parotid gland, which is one of the major salivary glands, was investigated in VPA-treated rats. Parotid gland lipid peroxidation values were significantly increased in the VPA group compared to the control group. Lipid peroxidation values were significantly decreased with the administration of M. oleifera extract.

Keywords: Valproic acid, M. oleifera extract, parotid gland, lipid peroxidation

OP22

Investigation of the Relationship between Gene Polymorphisms of the FABP2(Rs1799883) Gene and Its Alleles in terms of Glucose and HbA1C Parameters in Diabetic Obese and Non-Diabetic Obese Patients

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Some genes are thought to be associated with diabetes, which is one of the most common chronic diseases in the world. In this research, we aimed to examine the gene polymorphisms of the FABP2 gene, which is one of the genes thought to influence both diabetes and obesity, in terms of Glucose and HbA1C parameters in diabetic obese, non-diabetic non-obese patients and control groups.

This research was conducted in three groups. Groups: The diabetic obese patient group consisted of 82 people, the non-diabetic non-obese patient group consisted of 82 people, and the control group consisted of 70 healthy people. Glucose and HbA1C parameter values and blood samples were taken from the individuals in the groups in the last three months, and after DNA isolation from the blood samples, Real-Time PCR Reaction (qPCR), Tetra-primary Amplification Refractory Mutation system PCR techniques were used. Demographic information of our groups was evaluated with SPSS.

As a result of the research, Comparisons of the FABP2 gene and its alleles were made with all groups in terms of glucose and HbA1C parameters. In the results, glucose and HbA1C parameter values of the FABP2 gene and its alleles were highly significant, while statistically significant in all groups.

As a result, the gene, and alleles of FABP2; It has been determined that this gene and its alleles are associated with both diabetes and obesity, based on the high significance obtained.

Keywords: FABP2 Gene and Alleles, Diabetes and Obesity, Polymorphism, Glucose, HbA1C

OP23

Bisphenol A Exposure Affects Locomotor Activity, Acetylcholinesterase and Redox System Parameters in Zebrafish Embryos

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Endocrine disrupting chemicals (EDC) are either synthetic or natural compounds in the environment that can interfere with endocrine functions. Exposure to EDCs during development is a major concern, and the health consequences may be permanent or long-lasting (1). Bisphenol A is known to be an EDC and prenatal BPA exposure has been related to differences in children's brain microstructure, leading to differences in children's behavioral symptoms. Moreover high BPA exposure during pregnancy is related to increased behavioral problems throughout childhood (2). In our study we aimed to evaluate the effects of BPA exposure in zebrafish embriyos focusing on locomotor activities and biochemical parameters. Zebrafish embryos were exposed to 1µg/L, 5 µg/L and 10 µg/L BPA until 72 hpf. At the end of exposure period locomotor activities were determined and acetylcholinesterase (AChE), glutathione S-transferase (GST) and superoxide dismutase activities were determined using spectrophotometric methods. Concentration dependent changes were determined in the AChE, GST and SOD activites in accordance with the altered locomotor activities. Our preliminary findings point out the importance of concentration in the neurotoxic effects of BPA in zebrafish embryos.

Keywords: Bisphenol A, neurotoxicity, zebrafish embryos

OP24

Effects of Testosterone on Hepatic Redox System and Locomotor Activity

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Testosterone is a hormone produced primarily in the testicles and that helps maintain men's bone density, fat distribution, muscle mass and strength, facial and body hair, red blood cell production, and sperm production. Low testosterone level may be due to aging or due to hypogonadism. Testosterone therapy is used to help to reverse the effects of hypogonadism. It is also used to suppress female secondary sex characteristics and masculinize transgender men.

On the other hand, it is unclear whether testosterone therapy has some side effects. For instance, some studies have shown that exogenous testosterone may increase the risk of cardiovascular disease in transgender men (1-3). In our study we aimed to evaluate the short term effects of intaperitoneal testosterone injection in adult zebrafish. Accordingly locomotor activity, oxidant-antioxidant status and acetylcholinesterase (AChE) activity were determined in hepatopancreatic tissues of testosterone injected zebrafish. Our initial results indicate the potential importance of the alterations of the hepatic oxidant-antioxidant status in the side effects of testosterone.

Keywords: Testosterone, oxidant-antioxidant status, locomotor activity

OP25

Antitumor Activities of a 7-hydroxy-coumarin Derivative in Some Human Tumor Cell Lines.

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Coumarin is a natural compound (phytochemical) found in many plants such as tonka bean, lavender, vanilla grass. Coumarin and its derivatives are the best known aromatic lactone compounds and are widely used in a lot of different application areas such as laser dyes, nonlinear optical materials, fluorescent whiteners. Coumarins and its derivatives are attract great attention because of biological properties such as antibacterial, antifungal, antitumor, antiinflammatory This study aimed to evaluate the in vitro cytotoxicity of a coumarin compound (2-chloro-3-hydroxy-7,8,9,10-tetrahydro-6H-benzo[c]chromen-6-one). A 7-hydroxycoumarin derivative (50, 100, 150, and 200 µM) has been synthesized and evaluated for their in vitro cytotoxicity against three human cancer cell lines (MCF-7, Ishikawa, A549 cells) and normal osteoblast cell line (HOB) by LDH method. The 7-hydroxycoumarin derivative showed IC50 range from 286.9 to 764.3 µM. The result of the study showed that the 7-hydroxycoumarin derivative significantly increased cell cytotoxicity on cancer cells and also it was observed that there was no cytotoxic effect in normal osteoblast HOB cells. The 2-chloro-3-hydroxy-7,8,9,10-tetrahydro-6H-benzo[c]chromen-6-one exerts cytotoxic effects in breast carcinoma cell line (MCF-7), endometrial adenocarcinoma cell line (Ishikawa) and human lung adenocarcinoma cell line (A549), and can be considered for further mechanistic evaluations in human cancer cells. These results candidate 2-chloro-3-hydroxy-7,8,9,10-tetrahydro-6H-benzo[c]chromen-6-one for further studies to evaluate its biosafety and anti-cancer effects.

Keywords: Coumarin, antitumor, 7-hydroxycoumarin, MCF-7, Ishikawa, A549 cells, HOB cells

OP26

The Effects of Ankaferd Blood Stopper and Celox on the Tissue Healing of Rat Tooth Extraction Sockets

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Ankaferd Blood Stopper is a medicinal extract of five different plants, which has been used for the control of external hemorrhage and bleeding during dental surgery. The mechanism of action for Ankaferd blood stopper is the formation of protein network that establishes focal points for erythrocyte aggregation (1, 2). Celox is made of chitosan (poly-N-acetyl glucosamine) that is a biodegradable, nontoxic, and complex carbohydrate derivative of chitin. The positively charged Celox reacts with the negatively charged red blood cells on direct contact with blood. This interaction causes clotting without exothermic reaction and without damaging the surrounding tissue (3, 4). The aim of this study is to evaluate the effects of local hemostatic agents (Ankaferd blood stopper and Celox) on wound healing at rat tooth extraction sockets. In our study, right and left lower first molars were extracted from 16 Sprague-Dawley male rats and a total of 32 extraction regions were created. These regions were divided into three groups (control, Ankaferd and Celox hemostatic agent groups). Control group (n=8 extraction sockets) was left without any drug application. Ankaferd (n=12) and Celox (n=12) groups had undergone topical application of the corresponding hemostatic agents. On the 2nd and 21st days after surgical procedure, rats were sacrificed and mandibles were removed for histological evaluation. For light microscopy, samples were fixed in 10% neutral buffered formaldehyde and routinely processed for paraffin embedding. Approximately 5-µm thick sections were stained with Hematoxylin and Eosin (HE) and Gomori's One Step Trichrome. On the 2nd day of experiment, new bone formation and epithelial regeneration were not yet present in all groups. On the 21st day, new bone formation in control and Ankaferd groups were prominent while it was moderate in Celox group. Epithelial regeneration in control and Celox group were moderate while it was mild in Ankaferd group. In this study, two hemostatic agents were found to be effective in the healing of extraction sockets and well tolerated as neither of them caused foreign body reaction.

Keywords: Ankaferd blood stopper, Celox, tooth extraction sockets, rat, histology

OP27

Association between rs213045 and rs2038089 Genetic Variants of Endothelin Converting Enzyme-1b and Risk of Coronary Artery Ectasia

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Aim: Coronary artery ectasia(CAE) is described as the enlargement of a coronary artery segment to 1.5 times or more compared to the adjacent normal coronary artery. Polymorphisms in the endothelin(ET) gene family have been shown associated with the development of atherosclerosis. Membrane-bound endothelin converting enzyme-1(ECE-1) is involved in the maturation process of ET-1. The aim of the study is to investigate the effects of rs213045 and rs2038089 polymorphisms in ECE-1 gene which have been previously shown to be associated with the atherosclerosis and hypertension in the atherosclerotic CAE patients.

Methods: Ninety-six CAE and 175 patients with normal coronary arteries were included into the study. ECE-1 gene variations rs213045 and rs2038089 were determined by real-time PCR. SPSS 21.0 was used for statistical analysis.

Results: Frequency of ECE-1 rs213045(C338A) normal GG genotype was found higher in CAE patients than controls (60.4% vs 35.4%,p>0.001). The rs2038089A>G polymorphism, ancestral A allel was found higher in CAE patients than controls (90.6% vs 78.9%,p=0.022). The distributions of gender, Tip2 diabetes and hypertension were found similar among the study groups while the frequency of hyperlipidemia was found higher in CAE patients comparing with controls (59.4% vs 36.6%,p>0.001). Serum alanine aminotransferase(ALT) and creatinine levels were found higher in CAE patients comparing with the controls (24.16±15.76 vs 20.61±7.14,p=0.04; 0.91±0.26 vs 0.84±0.20,p=0.026, respectively). The multivariate regression analysis confirmed that the ECE-1 rs213045 GG genotype (p<0.001), rs2038089 A allele (p<0.017), and hyperlipidemia (p=0.001) are risk factors for CAE.

Conclusion: This study suggests that ECE-1 rs213045 G>T and rs2038089A>G might be associated with development of CAE. Further studies conducted in larger study groups and in different ethnic populations will be clarified exact role of ECE-1 polymorphisms in CAE.

Keywords: endothelin, ECE-1b, polymorphism, Coronary artery ectasia

OP28

Acetylcholine Esterase Inhibition's Effects on Muscle Tissue Energy Metabolism in Rats with Sepsis

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Aim: Sepsis is defined as a life-threatening syndrome associated with physiopathological abnormalities caused by a dysregulated host response to infections. Myopathic changes, muscle damage, energy metabolism irregularities are the early symptoms observed in sepsis. In the inflammatory process, it has been reported that the release of acetylcholine esterase (AChE) increases with the release of a mediator such as cytokine. This increase is manifested by a weakening in neuromuscular modulation and occurring fatigue and weakness in the muscle following infection. Imbalance between high-energy compounds is also one of the factors that impair energy metabolism in muscle tissue with sepsis. In this study, we aimed to investigate, the effects of AChE inhibition by Bicuculline on muscle energy metabolism in sepsis induced rats.

Methods: Adult male Wistar albino rats were divided into four groups; control, LPS (10 mg/kg i.p.), Bicuculline (1.5 mg/kg s.c.), LPS+Bicuculline. Experimentally sepsis was induced with applying of LPS. After 24 hours from first injection, rats were decapitated and muscle tissue was taken and homogenated for analyzing creatine, creatine phosphate, adenosine monophosphate (AMP), adenosine diphosphate (ADP), adenosine triphosphate (ATP) levels with using high performance liquid chromatography (HPLC). One-way analysis of variance and Tukey test were used for statistical analysis. $p<0.05$ was statistically significant.

Results: In sepsis group induced with LPS, and Bicuculline group; AMP, ATP and creatine levels were decreased and ADP levels were increased compared to other experimental groups. In LPS+Bicuculline group, AMP and ADP levels were decreased and creatine phosphate levels were increased.

Conclusion: As a result, we observed that sepsis disrupts the energy balance, also Bicuculline administration alone consumes energy by overstimulating the muscles, and can be a balancing effect when applied to rats with sepsis.

Keywords: Lipopolysaccharide, sepsis, bicuculline, acetylcholinesterase, muscle

OP29

Investigation of the Molecular Mechanism of Endothelial Dysfunction and ADP-Induced Platelet Aggregation in Alzheimer's Disease.

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Objective: It is recommended that vascular risk factors play an curicial role in the pathophysiology of Alzheimer's Disease (AD) and platelets are efficient in this process. In this study, we planned to investigate the plasma levels of Glycoprotein 1b(GP1b) proteins and von Willebrad Factor (VWF) in AD patients and healthy individuals to determine platelet aggregation and the relationship of platelets with endothelium. In order to investigate the regulation of GP-1b activation which is one of the proteins that associate between the platelet and endothelium, at the molecular level, we detected mir26a-5p, which we think may be effective in this pathway, and the von Willebrand Factor at the molecular level, by detecting mir24-3p levels with qRT-PCR, and determining their relationship with the disease, intended to be determined.

Materials-Methods: 23 patients and 35 controls were included in the study. Plasma GP1b and vWF levels were determined by ELISA. Platelet functions were studied with a lumiagregometer device by giving ADP stimulus. miR26a-5p and miR24-3p levels were determined by qRT-PCR.

Results: In our study, platelet aggregation % amplitude value ($p=0.028$) and GP1b levels ($p=0.107$) were found to be higher in the patient group than controls.

MMSE(p=0.001) and hsa-mir26-5p (p=0.043) were found to be lower in the patient group than controls.

Conclusion: High platelet aggregation % amplitude value in the patient group indicates an increase in platelet functions. Low levels of hsa-mir26-5p expression may be associated with increased GP1b levels in the Alzheimer's Disease.

Keywords: Alzheimer's Disease, ADP, Platelet Aggregation, GP1b, miR26-5p

OP30

Investigation of CD27, CD28 and Gal-3 Serum Levels in Terms of Risk and Progression for Colorectal Cancer

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Background: Immune checkpoints can be regulated in favor of tumor cells in the escape from the immune system. Investigating the mechanisms of these molecules may be critical to the discovery of new markers to differentiate subsets of patients susceptible to immune therapy and to predict therapeutic outcomes. In our study, the levels of CD27, CD28 and galectin 3 (GAL-3) molecules, which are among the immune control points, were investigated and their possible relationships with parameters effective in colorectal cancer (CRC) risk and progression were investigated.

Material and Methods: Blood samples were obtained from 77 patients with different stages of colorectal cancer and 79 age and gender-matched control subjects. Plasma soluble (s) CD27, CD28 and GAL-3 concentrations were measured with quantitative sandwich enzyme-linked immunoassay.

Results: The levels of sCD28(p<0,0001), sGAL-3(p<0,0001) and sCD27(p<0,05) were significantly higher in all patients with CRC compared to control. In addition, a negative correlation was found between sCD28 and sCD27 levels (r2 = 0,917 p<0,010) and a positive correlation was found between GAL-3 and CD28 levels (r2= 0,452 p<0.0001) in patients. Accordingly, the Area Under the Curve (AUC) for GAL-3 was 0,996, for sCD27 was 0.850 and for sCD28 it was 0.885. The cut-off value was determined as 97.428 ng / ml with a sensitivity of 85% for sCD27, as 2.259 with a sensitivity of 85% for sCD28 and as 0.93 with a sensitivity of 96% for sGAL-3.

Conclusion: In our study, we think that increased sCD27, sCD28 and sGAL-3 levels may be important factors to identify patients for CRC risk.

Keywords: Colorectal Cancer, sCD27, sCD28, sGAL-3

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OP31

The Rrelationship between Physical Activity Level AND Obesity in High School Students

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Obesity is among the most common and costly chronic disorders worldwide. Multiple factors like genetic, epigenetic, physiological, behavioral, sociocultural and environmental factors can lead to development of obesity. The aim of this study is to determine whether there is any relation between physical activity and obesity levels of high school students, and if so, the direction and dimension of this relationship. The sample of the research included a total of 304 high school students, 150 male and 154 female students, enrolled in Eskişehir during the 2016-2017 academic year. The data of the study were collected through "Physical Activity and Obesity Survey Questionnaire".

As a result; it was revealed that 65.50% of high school students participated in sports activities. In general, students perform sports three times a week for an average of 62 minutes and assess the difficulty of the activity as "a little difficult". Students' average weight is 61.60 kg. and height is 1,70 m (60 kg and 1.70 m for men; 51 kg and 1.60 m for women). The mean BMI value is 21.37. The obesity rate is 3.62% (%6 for men; %1,3 for women). In addition, as the number of sports, the number of times and the degree of difficulty increased, the BMI, that is, the obesity, decreased at a weak level. According to gender; the participation rate in physical activity, exercise frequency and the degree of difficulty of sports made (favoring men) and the weight, height and BMI (in favor of women) significantly differ.

Keywords: Physical Activity, Obesity, High School Students.

OP32

Valproic acid and Propyl Paraben Exposure Affects Redox System in Zebrafish Embryos

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Parabens are widely used as preservatives in personal care products, foodstuffs and medicines because of their antifungal and antibacterial effects. There are significant contradictions in the literature on paraben toxicity (1). Propyl parabens are one of the most widely used parabens today. Studies on the toxicity of parabens have mostly focused on the reproductive system (2). Studies on the effects of paraben exposure during the embryonic period are very few. Valproic acid is an agent used in the treatment of diseases such as epilepsy, neuropathic pain, tremor and migraine. Its mechanism of action occurs by increasing the effects of gamma amino butyric acid via voltage-sensitive sodium channels. Valproic acid toxicity has been demonstrated in zebrafish embryos and there is evidence that it adversely affects their development (3,4). In our study, the effects of propyl paraben and valproic acid exposures on the redox system in zebrafish embryos were investigated. Zebrafish embryos were exposed to propopyl paraben and valproic acid for up to 72 hours after fertilization and lipid peroxidation, nitric oxide levels, glutathione S-transferase and superoxide dismutase activities were investigated. Our results showed for the first time in the literature that valproic acid and propyl paraben cause disruption in the oxidant-antioxidant balance in zebrafish embryos. There are very few studies in the literature on the toxic effects of propylparaben which is known as a potential endocrine disruptor. Our studies on the possible mechanisms of the toxic effects of propylparaben are continuing.

Keywords: Propylparaben, valproic acid, redox system, zebrafish embryos

OP33

The Cellular Response of The Oxygen Sensitive Soleus Muscle to Acute and Chronic Hypoxia via HIF1α, HSP90, and nNOS

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Nitric oxide is known as one of those synthesized molecules in response to hypoxic stress and neurol nitric oxide synthase (nNOS) is effective in the soleus muscle. In addition, hypoxia inducible transcription factor 1 alpha (HIF1α) has a primary responsibility during the process of cellular adaptation to hypoxia. The stabilization of HIF1α is provided by Heat Shock Protein 90 (HSP90) and nNOS. Therefore, mRNA levels of HIF1α, HSP90, and nNOS were assumed to increase during an acute and chronic hypoxia. The aim of the study is to determine mRNA expressions levels of HIF1α, HSP90 and nNOS in the oxygen-sensitive soleus muscle in response to acute and chronic hypoxia compared to controls. Adult male Wister Albino rats were randomly divided into control, acute (48 hours) and chronic (2 weeks) hypoxic groups. After acclimatization, the experimental groups were exposed to 6000m altitude. At the end of treatments, all rats were sacrificed, and the soleus were extracted. mRNAs were determined by Q-PCR. mRNA levels of HIF1α, HSP90, and nNOS were higher in acute and chronic hypoxic groups than their respective controls ($p<0.05$ for each). While mRNA expressions of HIF1α and, HSP90 were higher in acute than chronic hypoxic group, mRNA expression of

nNOS was higher in chronic than acute hypoxic group ($p<0.05$ for each). HIF1α and HSP90 seem to have a role during acute hypoxia, while nNOS might have a role during chronic hypoxia as a cellular response.

Keywords: Acute and Chronic Hypoxia, The Soleus Muscle, HIF1α, HSP90, nNOS

OP34

Prospective Investigation of The Oxidative DNA Damage and Lipid Peroxidation Levels in Patients With Rheumatoid Arthritis

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Rheumatoid arthritis (RA) is an autoimmune, chronic, and inflammatory disease. Reactive oxygen species, which occurs endogenous or exogenously, can cause oxidative damage in macromolecules. This study aims to investigate the changes in DNA nucleoside damage and lipid peroxidation levels in patients with RA after six months of treatment, and comparison of healthy controls and patients with RA. We also aim to examine the relationship between the patients' clinical findings and oxidative macromolecule damage levels.

In the patient (n=69) and healthy control (n=31) groups, 8-hydroxy-deoxyguanosine (8-OH-dG), and R-S forms of 8,5'-cyclo-2'-deoxyadenosine, which are the main indicators of oxidative DNA damage; and 8-isoprostane (8-iso-PGF2α) levels as a lipid peroxidation indicator had examined. LC-MS/MS was used to determine nucleoside damage; ELISA was used to determine the level of lipid peroxidation.

8-OH-dG, R-cdA, and 8-isoprostane levels of the patients were found higher than controls. After six months of treatment, a significant decrease was observed in the 8-OH-dG, R-cdA, and S-cdA levels of the patients; on the contrary, the level of 8-isoprostane was found higher after treatment than before. No correlation had found between clinical parameters and oxidative damage levels except ESR and S-cdA measured at diagnosis.

This is the first study that compares three different DNA damage parameters and lipid peroxidation product levels simultaneously before and after the treatment, besides the comparison of healthy controls and patients with RA. We believe that these findings will shed light on the differential diagnosis of RA, its clinical course, and the evaluation of the response to treatment.

Keywords: ELISA, Oxidative Damage, Rheumatoid Arthritis, Tandem Mass Spectrometry

OP35

Investigation of the Relationship between the Oxidative Stress-Induced Heart and Aortic Damage and Tissue Factor Activity.

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Clotting and inflammation are closely related processes. Excessive clotting can trigger inflammation, while the formation of inflammatory cytokines can aid clotting. The initiation of one of these two processes can lead to the activation or reinforcement of the other. The triggered condition can lead to tissue damage or even to multiple organ failures. The tissue factor (FIII, CD 142) plays a central role in the cycle of both phenomena. Tissue factor is a coagulation protein that can be affected by oxidative stress-based damages in the tissues. In this study, anti-inflammatory effect and oxidant damage was induced by methotrexate (20 mg/kg, i.p). Then, the effect of antioxidant whey proteins (2 g/kg, oral gavage, ten days), on the heart and aorta tissue factor activities in methotrexate-induced oxidative damage was investigated. Heart and aorta tissue factor and superoxide dismutase activities, glutathione and lipid peroxidation levels were also measured. Methotrexate administration decreased tissue factor activity of the aorta and did not change heart tissue factor activity. Although methotrexate caused oxidative damage in both tissues, tissue factor activity was found to be decreased only in the aortic tissue. While whey protein concentrate administration caused an antioxidant effect in heart and

aorta tissue, whey protein concentrate only increased the aortic tissue factor activity and did not change the heart tissue factor activity in methotrexate-induced rats. In conclusion, it has been determined that the change of heart and aortic tissue factor activity with oxidative damage may vary depending on the characteristics of these tissues.

Keywords: Whey proteins, methotrexate, heart, aorta, tissue factor activity.

OP36

Investigation of the Effects of Bisdemethoxycurcumin on Candidate Genes and miRNA associated with Resistance Mechanism in Ovarian Cancer Cells

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Objectives: The aim of this study was to investigate the effects of bisdemethoxycurcumin (BDMC), one of the active compounds of curcuma longa, on cell proliferation and apoptosis in human ovarian cancer and cisplatin-resistant ovarian cancer cell lines after single and combined administration with cisplatin, and to determine the resistance mechanism and related miRNA gene expression changes.

Materials and Methods: To examine the effect of BDMC on cell proliferation, WST-1 analysis was performed in both cell lines a wide dose and time range. Apoptosis experiments were performed by flow cytometry of BDMC and BDMC groups combined with cisplatin. In addition, the expression study of candidate gene (GSTP-1) and microRNA (miR-133b) related to glutathione metabolism, which is one of the resistance mechanisms, in cisplatin-resistant ovarian cancer cell line was performed by Real Time PCR.

Results: As a result of WST-1 analysis, BDMC inhibited cell proliferation in both cell lines. BDMC and cisplatin groups combined with BDMC have been shown to induce early apoptosis when administered to both cell lines. In addition, co-administration of BDMC with cisplatin in the resistant ovarian cancer cell line caused a decrease in the expression level of GSTP-1 and miR-133b genes and contributed to the elucidation of the resistance mechanism.

Conclusions: Despite the rapidly increasing number of new treatment options with the advancement of technology in recent years, there has not been a significant decrease in mortality due to ovarian cancer and has led to the emergence of alternative approaches that include natural active ingredients to clarify the role of glutathione metabolism and miRNA in the mechanism of cisplatin resistance.

Keywords: Ovarian Cancer, Drug Resistance, Bisdemetoxycurcumin

OP37

The Urine Could Affect the Growth of an *E. Coli* Strain Even Compared to Host-Like Minimal Medium

Defne Gümüş

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Aims. It is well known that host conditions have the ability to modulate virulence, antibiotic susceptibility and growth of bacteria. Once infection occurs, all host conditions mean the environment of bacteria. The interactions of bacteria and host are provided by inter-kingdom communication which is known as quorum sensing (QS). Previous studies have reported that some host biological fluids may affect various bacterial traits. In the present study, urine was selected to evaluate host conditions and it was aimed to investigate the effects of human urine on growth of an *Escherichia coli* (a standart stran *E. coli* SPC105 which is also known to possess multiple antibiotic resistance (*mar operon*).

Methods. Overnight culture of *E. coli* was prepared in Standard American Petroleum Institute (SAPI) medium which was preferred because it is known as host-like serum supplemented culture media. Urine sample which was taken from a healthy male individual used as the culture medium. SAPI supplemented with 30% (v/v) adult bovine serum was used as the *in-vivo* host condition (control). *E. coli* was incubated at 37°C and growth alterations were detected by measuring the changes in the absorbance at 600 nm in four, six and 24 hours. To detect the growth alterations, two-way ANOVA Bonferroni post – test was used.

Results. The growth of *E.coli* SPC 105 was found to be significantly increased ($p < 0.0001$) in the presence of

urine when compared to SAPI medium in four and six hours incubation; on the other hand, when incubation was prolonged to 24 hours the growth was significantly decreased (p< 0.0001).

Conclusions. It is possible to suggest that optimization is important to show the alterations of microorganisms' biological properties in in-vivo conditions. It is once more proven that, diferent body fluids (such as urine) could act as an inducer on microbes' different behaviors and becomes an important regulator during infectious processes.

Keywords: Urine, *E. coli*, SAPI, growth

OP38

Investigation of ATG3 Expression in Mice Fed a High-Fat Diet and Exercised

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Aims: Obesity is defined as abnormal or excessive fat accumulation. The World Health Organization classifies obesity according to body mass index. Adipose tissue along with its important role in energy storage is an important endocrine organ. Obesity may be causing a low-grade chronic inflammatory in adipose tissue and this low-grade chronic inflammation in the adipose tissue spreads to systemic inflammation in the body. Moreover, its cause activated mitochondrial dysfunction and mitophagy pathway. Therefore, the examination of mitophagy- related genes as ATG3 in mice fed high-fat diet and obese mice with exercised. Method: Thirty female C57BL/6J mice were gathered in Institute of Experimental Medicine, Istanbul University (Istanbul, Turkey), aged approximately 5 to 6 weeks. The study carry out control group, obese group and obese with exercised. The obese mice and exercise group received a 60% kcal high-fat diet. Exercised starting 6 th week of study until sacrificed. The control group received %10 kcal high-fat diet. And all mice remained on the same diet until sacrificed. ATG3 gene expression levels were determined by using Real-Time PCR system in liver and adipose tissue.

Result: Compared to the obese group, the ATG3 gene expression level was found lower than exercised group (p<0.001), and the ATG3 gene expression level was found in adipose higher tissue than in liver tissue (p<0.001).

Conclusion: We found significant associations exist between increase gene expression levelsof ATG3 in obese and exercised group. Therefore, we could say that the gene expressionincreases in response to mitochondrial dysfunction in the obese and exercised group.

Keywords: Obesity, Mitophagy, ATG3, Real Time PCR

Acknowledgements: The present work was supported by the Research Fund of Istanbul University. Doctoral of Science Project No: 38008

OP39

Invesigation of the Effect of TRAIL in Obese Patiets

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Obesity is a condition in which there is abnormally increased body fat, which results from increased energy intake because of energy expenditure. One of the defining characteristics of obesity is the chronic-low-grade inflammation and the changes in the amount of secretion of adipokines-adiponectin and Tumor Necrosis Factor(TNF)-alpha.

The members of the TNF family play roles in the pathogenesis of obesity-related diseases. TRAIL(Apo2L/TNFSF10/CD25), which is a member of the TNF-ligand family, is expressed on the cell-surface of many cells as a Type-II transmembrane protein. There is significant evidence that TRAIL plays protective roles against obesity in mice-models and in in-vitro systems. In our study, we evaluated the results of TRAIL expression

levels in obese patients and aimed to determine the role of the results in the development of obesity.

This study of 80 obese and 80 healthy individuals were included. The expression level of the TRAIL gene was determined by using RT-PCR method in the scope of the study. Compared to obese individuals, the expression level of TRAIL gene was found significantly higher in control patients (p<0.001). We found that TRAIL may have protective roles on obesity in Turkish population. According to these results, the TRAIL gene is a scientific data for new studies to be conducted on obesity.

Keyword: TRAIL, gene expression, obesity

OP40

The Relationship between CK-MM and IL-6 Genes and Athletic Performance Levels in Professional Young Basketball Players

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Introduction and Purpose: In the present study, the relationship between the physical and athletic performance levels of professional young basketball players and CK-MM and IL-6 gene variations were examined.

Method: The study (n=17) was carried out with the voluntary participation of professional young basketball players playing in the U15 league. The athletic performance values of the athletes have measured a total of 2 times at the beginning of the season and in the middle of the season, and the test measurement data were compared with the CK-MM and IL-6 genotype variations of the athletes. Obtained data were analyzed at p<0.05 significance level.

Findings: The BMI (Body Mass Index) of the athletes with the CK-MM GG genotype participating in the study was lower than the athletes with the AA genotype, p= <0.021, and the body mass index of the athletes with the IL-6 GG genotype was lower than the athletes with the CC genotype. p<0.048. Athletes with IL-6 GG genotype showed higher jump performance than athletes with CC genotype in the vertical jump tests at the beginning of the season, p<0.010. Likewise, athletes with IL-6 GG genotype showed higher jump performance in mid-season vertical jump values than athletes with GC and CC genotypes, p<0.001.

Result: A significant relationship was found between the BMI levels of professional young basketball players and the CK-MM CG and IL-6 GG genotypes. A significant relationship was also found between IL-6 GG genotypes at the beginning and mid-season vertical jump values.

Keywords: Young basketball players, Athletic Performance, CK-MM, IL-6.

OP41

The Effects of Electrocal Stomulatoon and Dynamic Muscle Exercises on Upper Extremity Muscles

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In this research it was aimed to examine the effects of electrical stimulation and dynamic muscle exercises on the upper extremity muscles. The research group consists of 12 persons who have a training background of 6 months and are selected on a voluntary basis. The participants filled in the personal information and measurement form and the fatigue severity scale. Arm circumference measurement, biceps and triceps skin-fold and 1RM curl tests were made. The participants were divided into two groups of 6 people each. First group had resistance exercises. Second group had resistance exercises with EMS. The participants continued the same way of exercising 3 times a week for 6 weeks. After 6 weeks, the tests and measurements were repeated. Data analysis were made by SPSS version, 25.0 programme. Research results show that there are significant differences between the tests and measurements made before and after the training period for both grups (p<0,05). Besides, there were no findings for a significant difference between the last measurements and tests of the two groups (p<0,05).

Keywords: EMS, Resistance Exercises, Hypertrophy, Strength

OP42

Discrepancies of Human-Rat Age Correlation in Animal Models of Human Diseases

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Rats are the most ideal experimental animal models for pre-clinical and clinical trials because of having smaller body size, easer maintenance, presenting similar metabolomic and genomic characteristics with humans. Also, it is much easier and more ethical to sight rats' life periods in laboratory husbandry conditions due to their higher reproductive capacities and adaptive abilities. Having shorter life expectancy, developing rapidly in childhood periods, and becoming sexual maturity earlier, which is equal to approximately 2.5 human years, makes harder to establish an accurate age correlation between humans and rats. Interestingly, in different life frames like prepubescence, adolescence etc. rats aging rates varies differently.

Age-adjustment expertise is necessary to be taken into consideration if the research purpose is related to time correlation with the human life scale and disease stage due to mentioned reasons. When mimicking human diseases in rat models, it is crucial to determine proper durations of established pathology, adjust accurate administration periods of pharmacologic approach, and decide tissue sampling time.

In order to assess adjusted human-rat age algorithm for pre-clinical and clinical trials, it is necessary to conduct more studies for comparable outcome measures and future strategies.

Keywords: aging, human, rat, correlation, animal models, human diseases

OP43

The Relationship Between Respiratory Tract and Throat Involvement in Covid-19 patients

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DEFINITION: Corona virüs family can cause wide spectrum of symptomps like common flu to Middle East Respiratory Syndrome, (MERS) and Severe Acute Respiratory Syndrome, SARS). Corona virüs common subtypes that infected people are HCoV-229E, HCoV-OC43, HCoV-NL63 and HKU1-CoV. They usually occurs a flue symptomps like fever, Shortness of breath or difficulty breathing · Fatigue · Muscle or body aches · Headache, cough, runny nose, throath pain. In 2003 SARS-CoV is founded as a new virüs and MERS CoV causes so many deaths in the saudi arabia region in 2012. In 2019 WHO China Office anounced unkonwn orginated pneumonia cases in Hubei region Wuhan City an 30 of january WHO anounced international health emergencies and named virüs Covid 19 because of its similarty to SARS.

CLINIC: Common symptomps in covid 19 is fever, fatigue, muscle or body aches, headache cough and breath diffuculties, Covid virus usually spread by air with the drops of infected patients material. First enterance way of body is usally upper resporatry track; nose, mouth and throath. Virus first colonisation occurs in upper resporatry tract and the highly contagineus at this time because it is easly spread by air. Infection can be limited only in upper resporatry and couldn't contaminate to lungs and bronshial arc. This patients also get small amount of viruses and it stopped it self on the upper resporaty system. Unclear all this theories and new ones we need genetic analysis both virus types and the patients to determine imminologic respond as well. In our study we found that most common symptoms in women were fever (24.1%), cough (20%), body pain (15.2%), sore throat (13.1%) and headache (11.7%). Fever (28.3%), cough (20.2%), body pain (17.3%), respiratory distress (15%) and sore throat (11.6%). Are common symptoms in men.

CONCLUSION: In our study we determine that the patients who suffer from throat pain has less tendency to get severe symptomps in their lungs like pnemonia. Also it need to approved by future studies the rason fort hat may be the strong ummıne respond for covid 19 on the patient. According to datas obtained It was understood that 22.1% of the women and 20.2% of the men were sick during the control. It is noteworthy that there is a significant difference and negative correlation between fever, headache, sore throat, fatigue, diarrhea, patient's

job status, cough, risk factor, respiratory distress, taste disorder, tremor, and body pain, which are most correlated with other symptoms.

Covid pandemia is life threathing illness and corona virus has high capability of mutaions Also vaccinations programs are overheld all over the World personal respond is highly important for all patients not symptomps also ummınologic respond is determine patients clinical aspects.

Keywords: Covid-19, public health, pandemia

OP44

Interraction of APOA2/APOA5 Gene Variatiants by Using qPCR and DNA Sequencing in Obese Patients

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Aim: Obesity can be defined as a disorder in the system of regulating body weight, characterized by excessive accumulation of body fat. As obesity increases, the risk of obesity-related hypertension, diabetes, cardiovascular diseases and cancer. Obesityis a multifactorial disease due to genetic reasons in rates between 20-80 %. It has been seen in studies that genetics has a decisive importance in obesity. We aimed to evaluate APOA2 and APOA5 gene variations, which are considered risky from obesity susceptibility genes, by using DNA sequencing and qPCR analysis methods.

Methods: Peripheral blood and buccal mucosa swab were taken from 200 patients who applied with the complaint of obesity. The patients were determined according to the body mass index (BMI) of the patients. Non-obese, overweight, obese, and morbidly obese. After DNA isolation, variatiants in related genes was investigated by using DNA sequencing and qPCR analysis methods. The results were evaluated statistically.

Result: As a result of the analysis of the correlation between the mutation profiles and BMI values of the participants, a statistically significant relationship was found between the BMI and the mutation profile ($p<0.05$). ApoA2 and ApoA5 gene variants were found to give corelative results in obese and morbidly obese individuals in both analysis methods.

Conclusions: APOA2 and APOA5 gene variants, which carry potential risk of obesity, were determined by two analysis methods to be important in Obesity. As a result, variants in the APOA2 and APOA5 genes are associated with the development of obesity and metabolic processes of obesity.

Keywords: APOA2, APOA5, DNA sequencing and qPCR, Obesity

OP45

Comparison of Between CETP and ANKK1 Gene Variatiants by Using qPCR and DNA Sequencing in Obese Patients

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Aim: Obesity can be defined as a disorder in the system that regulates body weight. As obesity increases, the risk of obesity-related hypertension, diabetes, cardiovascular diseases, stroke, infertility and cancer. It has been seen in studies that genetics has a decisive importance in obesity. We aimed, to investigate CETP and ANKK1 gene variations, which are considered risky from obesity susceptibility genes, by using DNA sequencing and qPCR analysis methods.

Methods: Peripheral blood and buccal mucosa swab were taken from 200 patients who applied with the complaint of obesity. The patients were determined according to the body mass index (BMI) of the patients. Non-obese, overweight, obese, and morbidly obese. After DNA isolation, variatiants in related genes was investigated by using DNA sequencing and qPCR analysis methods. The results were evaluated in line with statistical analysis.

Result: As a result of the analysis of the correlation between the mutation profiles and BMI values of the participants, a statistically significant relationship was found between the BMI and the mutation profile ($p<0.05$). CETP and ANKK1 gene variants were found to give corelative results in obese and morbidly obese individuals in both analysis methods.

Conclusions: CETP and ANKK gene variants, which carry potential risk of obesity, were determined by two analysis methods to be important in Obesity. As a result, variants in the CETP and ANKK1 genes are associated with the development of obesity and metabolic processes of obesity. In addition, it is aimed to establish a panel with other similar obesity susceptibility genes.

Keywords: Obesity, CETP, ANKK1, DNA sequencing and qPCR

OP46

Who We Are? Mycrobiata Genomic Affects

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General information: Mycrobiata is alla mycroorganisms that live with us. Mycrobiom is all genetic materials in mycrobiata. Human mycrobiata constitues of mostly bacteria, viruses, fungal and eucaryotic mycroorganisms that exists mostly in gastrointestinal tracts, skin and genitourinary trackt.

MYCROBIOTA is so important in human life even normal healthy person 70kg weith has 1-2 kg bacteries which of exsist 90% in intestines. This means 100 trillion bacteria and ten times more than human cells in the body and genomic consumption is 100 times more than human genom. It is shown that humans has 50 % common mycrobiota named cor mycrobiota (cMBT) rest of other effected by diet, genetics, environment, etc. Human mycrobiota is stable and it si shown in studies it has little changes in one year. As Mycrobiota Corruption Reasons could be listed: Low Breast Milk intake (I.Factor), Medications, Antibiotics, Steroid, Antienflamatuar, C/S section, Diet, Carbonhidrates over taken diet, Rafinered foods, Fast feding, Less water intake, Toxines : Heavy metal, vacciness, hormones, Less exercise.. Skin has 6-7 layers Cornea has 5 layers of epithelium but intestinal mucoza has only one layer ephitelium with tight junctions. Because it is designed for permeability becuse otherwise it will be unpermable. Intestinal mucosa has almost the same number of neurons lke brain itself, thats why it called second brain. Zonuline and ouklidine proteins which exisits in blood –brain barrier also exists in intestinal system barrier. If intestinal bacterial consumption broken patogenic opprtunites bacteries begin to breeds very fast. Patogenic microorganisms and their toxines makes diseases (disbiyozis) . Disesases make intestine Wall leak and open a great holes on the Wall (leaky gut syndrom).

Conclusion: MYCROBIYOM can be determine one the most important organ we have by ourself that produce vitamins, essential food supply, energy, vitamins, immune system cells differantiation, genetic consumption of the body. Somebody call it new organ super organ.

Keywords: Mycrobiata, Mycrobiyom, Human Health

OP47

Evaluation of Mutation Profiles of PLIN and POMC Genes in Different BMI Groups

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Aims: Obesity due to environmental and genetic causes at rates varying between 20-80% is multifactorial. Many mutations have been identified that will enable screening of genetic and obesity risk in individuals. In the present study, we analyzed PLIN ve POMC gens.

Methods: In the study oligos targeting 2 different SNPs were designed and used in qPCR reactions. 200 whole blood samples. Samples were grouped as 50 patients Non-obese (BMI<25)-Overweight (25≤BMI<30)-Obese (30≤BMI<35)-Morbid obese (35≤BMI).

Results: As a result of, the mutation profiles and BMI values of the participants, a statistically significant relationship was found between the BMI and the mutation profile (r=0.628, p=0.00; statistical significance p<0.05).

Conclusions: Examination of genetics in individuals and comparison with BMI is important for the detection of polymorphisms that can provide a comprehensive definition of obesity risk. If the study is expanded by including metabolic syndrome grups and increasing the number of cases, the significance of the results may be increased. BMI can be classified into more detailed information.

Keywords: Obesity, PLIN, POMC, mutation, qPCR

OP48

Investigation of Frequency Distributions of FADS1 and NPY Genes in Patients with Colon Cancer

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Colorectal cancer (CRC), classified as the third most prevalent cancer worldwide, after lung and breast/prostate cancer, is also the second leading cause of cancer-associated death. It is estimated that ~50% of CRC patients die from metastase with treatment of this complication still posing significant difficulties. Liver metastasis (LM) cascade is known in the literatüre but its mechanisms are still unclear. LM in CRC, as a usually asymptomatic condition, is often recognized in late stages. In recent studies, a connection is suggested between nervous system dysfunctions and a range of Neurotransmitters (Nts), Neuropeptides (NPs), Neurotrophins (Ntt) and their receptors (Rs) in development of CRC. Neuropeptide Y (NPY) is a neuropeptide abundantly expressed in the mammalian central and peripheral nervous system. NPY is a pleiotropic molecule, which influences cell proliferation, cardiovascular and metabolic function, pain and neuronal excitability. In the central nervous system, NPY acts as a neuromodulator, affecting pathways that range from cellular (excitability, neurogenesis) to circuit level (food intake, stress response, pain perception). NPY has a broad repertoire of receptor subtypes, each activating specific signaling pathways in different tissues and cellular sub-regions Y1, Y2, Y4, Y5, Y6. Variants in the FADS gene cluster modify the activity of polyunsaturated fatty acid (PUFA) desaturation and the lipid composition in human blood and tissue. FADS variants have been associated with plasma lipid concentrations, risk of cardiovascular diseases, overweight, eczema, pregnancy outcomes, and cognitive function.

Aim: The purpose of this study was to examine of frequency distributions of FADS1 and NPY gene frekans in patients with CRC.

Method: DNA isolation was performed from blood samples of patients with colon cancer. Then, gene frequency distributions were examined by Real-Time PCR.

Conclusion: Primers prepared specifically for the genes associated with obesity in colon cancer patients were designed, and the frequency distributions of these genes were compared. In the future, polymorphism levels will be investigated by comparing with the control group.

Keywords: Colon Cancer, FADS1, NPY

OP49

Investigation of the Effect of Paclitaxel on miR-221 Expression in Breast Cancer Stem Cells

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Breast cancer is the most common malignancy among women. Despite the development of early diagnosis methods and advances in treatment in recent years, it is still an important cause of mortality and morbidity. It is known that many cancer types, including breast cancer, are driven by a population of cells displaying stem cell characteristics. These cells, called cancer stem cells (CSCs), are thought to be responsible for chemoresistance and aggressive recurrent tumors. Therefore, there is a need for research and clinical use of new molecular biomarkers in the treatment of breast cancer. After determining that miRNAs act as regulators of gene expression, these molecules were evaluated as both potential therapeutic targets and candidate diagnostic and prognostic indicators. In the study, differences in expression levels of important let-7a, miR-155, miR-10b, miR-221, miR-222, miR-335, miR-145, miR-200c, miR-21 and miR-125b in breast cancer following paclitaxel treatment were investigated in parental MCF-7 cells and cancer stem cells (MCF-7s) derived from these cells. In this direction, the obtaining of breast cancer stem cells and the characterization of these cells were provided. Then, the cytotoxic activity of paclitaxel was determined and its effect on the spheroid structure was observed. Subsequently, parental MCF-7 and MCF-7s cells were treated with 15.93 µM dose of paclitaxel for 24 and 48 hours, and RNA isolation and cDNA synthesis were performed from the cells. After 24 hours of paclitaxel treatment, a 28.37-fold increase in miR-221 expression level in MCF-7s cells was found to be statistically significant (p=0.0007). This result, supported by further functional analyzes, may reveal that miR-221 can play an important role in breast cancer and cancer stem cell biology and can be used as an effective treatment option.

Keywords: Breast Cancer, MCF-7s, miR-221, Paclitaxel

Acknowledgments: The present work was supported by the Research Fund of Istanbul University Project No. 52677

PP1

The Anti-angiogenic Effect of the Platinum (II) Saccharinate Complex trans-[Pt (sac)2(PPh3)2] on Tube Formation and in Vivo CAM Assay

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Purpose: Despite the developments in modern medicine, cancer is still one of the leading causes of death in the worldwide and an important public health problem. Metal based chemotherapeutic drugs including platinum complexes are promising agents to treat cancer with more efficacy compared to chemotherapeutic agents. Most of the mixed ligand platinum(II) saccharinate complexes have been synthesized in recent years and have been reported to show high "anticancer" activity. This study was carried out to reveal the anti-angiogenic effects of the new platinum(II) complex with phosphine and saccharinate ligand, platinum (II) saccharinate complex trans-[Pt (sac)2(PPh3)2] (MP2 complex), which is known to have anticancer effects, in vitro and in vivo.

Method: The cytotoxic effect of platinum (II) saccharinate complex complex on human umbilical vein endothelial cells (HUVECs) was examined with the SRB and ATP assay. The anti-angiogenic activity of the MP2 complex was evaluated by in vitro tube formation assay and in vivo the chick embryo chorioallantoic membrane (CAM).

Results: According to the SRB and ATP assay, cell viability was inhibited in a dose-dependent manner at tested concentrations (1.56-100µM) of platinum (II) saccharinate complex trans-[Pt (sac)2(PPh3)2] (MP2) after 24-48 h. Especially, 12.5 µM and higher concentrations of MP2 complex was showed significant decrease on cell viability. Moreover, MP2 complex

exhibited higher cytotoxic effect compared to thalidomide and cisplatin. Also platinum (II) saccharinate complex (MP2 6.25-12.5 µM) showed strongly reducing effect on tube structure at all tested times compared to vehicle and positive controls. According to the microscopic evaluations the platinum (II) saccharinate complex trans-[Pt (sac)2(PPh3)2] (MP2), strong anti-angiogenic effect was shown at the concentration of 40 µg/pellet compared to the positive control (±)-thalidomide. At the 20 µg/pellet concentration of platinum (II) saccharinate complex (20 µg/pellet) was shown strong antiangiogenic effect, but in low concentration of platinum (II) saccharinate complex (10 µg/pellet) was shown weak effect.

Conclusion: These results suggested that the platinum (II) saccharinate complex has showed significant anti-angiogenic activity at the tested concentration both in CAM and tube formation assay. Antiangiogenic treatment has a bright future ahead for cancer therapy. Angiogenesis is considered to be one of the hallmark of cancer. Therefore, pharmaceutic companies are in competition for developing new anti-angiogenic complexes/small molecules. Also, further in vivo experiments are needed for their clinical use as an anticancer drug in worthwhile due to the anti-angiogenic effects of novel platinum (II) saccharinate complex.

Keywords: Platinum (II) saccharinate complex, Angiogenesis, CAM assay

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PP2

Investigation of Transcriptional Regulators of ATP7B and Their Role in Cisplatin Resistance in Cancer

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ATP7B is a Cu+-pump, which gets translocated from the golgi to lysosomes upon increased Cu+ levels, sequestering and eventually removing Cu+ via exocytosis. Not surprisingly, this important function requires tight regulation and changes in ATP7B activity is linked to several diseases.

While lack of ATP7B activity leads to Wilson's disease, its overexpression results in drug resistance in cancers. Therefore, understanding how ATP7B is regulated is crucial to shed light on the physiology of these conditions.

To date, there is very little information on the transcriptional regulation of ATP7B. MTF1 is the only known transcription factor, which controls its expression, yet MTF1 levels do not always correlate with ATP7B levels suggesting additional factors involved in its regulation. To find these additional factors, we initially performed an in-silico analysis using TRANSFAC/PROMO software and have found that several transcription factors may bind to ATP7B promoter. Furthermore, VISTA analysis showed that the conserved regions were mostly focused around 3000 to +1, indicating that the regulatory sequences are most likely located in this region.

To investigate which of these factors bind to the ATP7B promoter, Genomic Locus Proteomics methodology will be used. In this technique, deadCas9 protein is fused to APEX2 enzyme and guided to the ATP7B promoter via specific gRNAs. The proteins which are close to the dCas9APEX2 will be biotinylated and marked proteins will be identified by mass spectrometry. Depending on their enrichment scores, selected proteins will be investigated and confirmed with ChIP. Eventually, CRISPR knockout of the candidate proteins will be tested for their effects on cancer cell lines for cisplatin resistance.

Keywords: ATP7B, drug resistance, cancer, epigenetics

PP3

Investigation of Cell Cycle Dependent Nek2A Kinase Targets by TurboID Labeling

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Nek2A is a cell cycle regulated kinase, which is involved in several cellular processes and overexpressed in numerous cancer types. It has been associated with

chromosome instability, increased cell proliferation and drug resistance in cancers. Therefore, Nek2A has been proposed as an attractive target for cancer therapy. Our laboratory has previously shown that overexpression of Nek2A can lead to multipolar mitosis via unclustering extra centrosomes. The best characterized role of Nek2A is the phosphorylation of centriolar linkage proteins in the G2/M. However, the role of these proteins on Nek2A-mediated increase in multipolar cell divisions has not been determined. This indicates that, Nek2A may have different target proteins that have not been identified yet. The main purpose of our study is to define the cell cycle specific interaction partners of Nek2A. To achieve our goal, we use Nek2A-TurboID proximity-labelling system in synchronized cell populations and determine how Nek2A interactome changes in G1, S, or G2/M. First, we confirmed the expression and localization of TurboID-Nek2A-WT and -KinaseDead constructs in U2OS cells by Western blotting and immunofluorescence staining. Then, we used double thymidine block to arrest cells, released them, and then collected at specific time points. Results were analyzed by MaxQuant. Previously known Nek2A interacting proteins such as anaphase promoting complex were identified, indicating the specificity of the assay. Significantly enriched proteins that are in the close proximity of Nek2A, such as KIFC1, KIF2C, and ATOX1 will be evaluated as novel potential Nek2A targets, and held into further analysis to understand how Nek2A activity regulates multipolar divisions.

Keywords: Cancer, Centrosome, Cell cycle, Therapeutic target

PP4

The Rof Autophagy in DENSpm-induced Apoptosis in MDA-MB-453 Breast Cancer Cells

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Autocrine Growth Hormone (GH) triggers epithelial to mesenchymal transition (EMT) and induced metastatic profile by increasing occludin and fibronectin expression levels in MCF-7 breast cancer cells. DENSpm, one of the most studied PA analogues, has been shown to induce G1 cell cycle arrest in MALME-3 M melanoma, prostate, breast and non-small cell lung cancer cells. Autophagy is a self-degradation process of cellular components that involves elimination of misfolded or aggregated proteins and damaged organelles, such as mitochondria, endoplasmic reticulum and peroxisomes, as well as intracellular pathogen. Our aim in this study is to investigate the role of autophagy in DENSpm-induced apoptotic cell death in MDA-MB-453 cells. 10 µM DENSpm decrease cell viabillity in MDA-MB-453 wt and GH+ breast cancer cells. Although autocrine GH expression increased colony diameter, drug treatment significantly decreased colony diameter. 10 µM DENSpm exposure triggers autophagy vacuole formation by acridine orange staining. In addition, autophagy was induced by DENSpm treatment in MDA-MB-453 GH+ cells via LC3II, Ag5, Atg12 and Atg7 upregulation. In conclusion, autocrine GH expression triggers cell growth, viability, colony formation, but DENSpm significantly prevented GH-mediated aggressive profile in MDA-MB-453 cells. DENSpm-mediated autophagy induction was demonstrated in MDA-MB-453 wt and GH+ breast cancer cells.

Keywors: Breast Cancer; Autophagy; DEMSpm; Growth Hormone

PP5

Effects of Doxorubicin on In Vitro Breast Cancer Model with Lymphocyte and Monocyte Cells

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Introduction and Aim: Breast cancer is most common malignancy in females worldwide. With the prominence of immunotherapy as an alternative to chemotherapy in cancer treatment, examining the interaction of cancer

cells and immune cells has gained great importance. (1, 2). In this study, it was aimed to determine the effect of lymphocytes and monocytes on the chemotherapy efficacy and drug resistance of Doxorubicin (Dox) in breast cancer cells.

Material and Methods: A co-culture model was established with breast cancer cells and lymphocyte cells. Jurkat cells used as lymphocytes were stimulated with Phytohemagglutinin M (PHA-M). An in vitro co-culture model was also formed with unstimulated Jurkat cells. Another model was created with MDA-MB-231 breast cancer cells and THP-1 cells that are used as monocytes. In both models, cells were used at a ratio of 5:1 (immune cells: tumor cells).

Dox-induced cytotoxicity was determined by MTT assay in both all of cells and co-culture models. Apoptosis analysis was performed by flow cytometry according to the determined IC50 concentration. In addition, MDR-1 protein, which is multi-drug resistance protein, was evaluated flow cytometrically. Statistical analysis in the study was carried out using Graphpad Prism 5.03 Software.

Results: When the MTT results of the Dox were evaluated, higher IC50 values were determined in the co-culture model comparatively. However, no significant difference in IC50 values of Dox was observed between PHA-M-stimulated Jurkat cells and co-culture models with unstimulated Jurkat cells. Cell death rates were determined by flow cytometry analysis after Dox treatment. Additionally, a significant increase in MDR-1 protein expressions was detected with Dox treatment at the same concentration in the Jurkat-MDA-MB-231 co-culture model.

Conclusions: Relatively high IC50 values in the 5:1 ratio in vitro co-culture models were associated with drug resistance. Dox treatment to Jurkat: MDA-MB-231 co-culture model significantly increased drug resistance through MDR-1 protein expressions. In conclusion, we think that the number and functionality of immune cells and drug resistance may be related in cancer. This perspective will shed light on many cancer studies.

Keywords: Breast cancer, doxorubicin, cytotoxicity, drug resistance, immune cells

PP6

Mass Spectrometry-based Proteomics to Investigate Biomarkers for Mon-small Cell Lung Cancer

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Lung cancer is a heterogeneous disease that includes various histological types. Large cell carcinoma is defined as non-small cell lung cancer (NSCLC) originating from the epithelial cells of the lung and indicating no apparent histological evidence of differentiation. To date, there is still very little knowledge about available that reveal the molecular features of LCC. On the other hand, proteomic studies using constantly updated methods and technologies provide important clues about how proteins in tumor cells change and interact. Mass spectrometers, especially powerful tools in this field, are promising for a better understanding of proteins associated with cancer processes. Here, we aimed to reveal dysregulated proteins in lung tissue and serum samples from LCC patients by MS-based proteomic approaches. For quantification, we analyzed the digested peptide samples with using a label-free LC-MS/MS method. We found that extracellular matrix proteins, caveolar and cell junction proteins are differentially expressed. Our results address changes in proteins that explain the invasion and metastasis. Consequently, quantitative proteomic analyzes imply that these proteins may have an important role as potential cancer biomarkers for LCC.

Keywords: Lung cancer, large carcinoma cell, quantitative proteomics, mass spectrometry

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PP7

Investigating Differences in Polycomb Group Proteins in a Newly Developed Colorectal Cancer EMT Model

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Colorectal cancer (CRC) is one of the most common malignant tumors worldwide. Colorectal cancer is a type of cancer that is generally curable, but metastasis of the cancer adversely affects the course of the disease. An important condition seen in most malignant carcinomas is that, the cells lose their epithelial and gain mesenchymal characteristics, a process known as epithelial-mesenchymal transition (EMT). For this reason, elucidating the molecular mechanisms of epithelial-mesenchymal transformation is an important step towards understanding metastasis, which is the most important cause of cancer deaths. In this study, a spontaneously differentiating colorectal cancer cell line. HT-29, was used to develop an EMT-MET model. Three types of populations; ancestral group (aHT-29), which is 80% confluent, differentiation group (eHT-29) collected 20 days after growing in galactose media, redifferentiation group (mHT-29) passaged after day 20 and collected at day 4, were generated. Cells were collected on the specified days and the changes in epithelial (E-cadherin, CDX2) and mesenchymal (transgellin, vimentin, fibronectin) markers were examined. The results support that the ancestral group and the redifferentiation group have mesenchymal features, while the differentiation group has epithelial features. In order to elucidate the plastic nature of EMT, changes in the amounts of Polycomb group proteins (EZH1, EZH2, CBX2, CBX4, CBX6, CBX7 and CBX8), in aHT-29, eHT-29 and mHT-29 cells were analyzed. According to the results, EZH2 has decreased and CBX7 has increased eHT29 cells compared to aHT-29 and mHT-29. Differences in the epigenetic regulatory elements would provide potential targets for future diagnostic and therapeutic purposes.

Keywords: Colon cancer, epigenetic, epithelial-mesenchymal transition, polycomb protein

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PP8

Investigation of Genetic Variations of PPAR-γ Gene in Patients With Diabetic and Obesity

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Aims: Diabetes mellitus is a metabolic disease that causes hyperglycemia as a result of insufficient secretion or effectiveness of insulin and is characterized by long-term vascular complications. The pathogenesis of diabetes is mostly of autoimmune and genetic origin. Obesity, which has become a global health problem, is a disease characterized by excessive accumulation of fat in the body. Adipose tissue is an endocrine organ with metabolic functions in addition to its storage function. Obesity is associated with adipose tissue inflammation, which can translate into systemic inflammation, insulin resistance, and an increased risk of type 2 diabetes in rodents and humans. PPAR-γ is an important regulator of lean body mass, lipid and glucose metabolism. It also contributes to the improvement of metabolic indicators in type 2 diabetes, obesity and other chronic conditions. Therefore, it is aimed to examine PPAR-γ gene polymorphisms in diabetic and obese patients.

Method: In our study, 2 patient groups (80 diabetic obese and 80 nondiabetic obese) and 1 control group (79 healthy individuals) were used. 10 ml blood samples from selected cases were placed in tubes containing ethylene diamine tetra acetate (EDTA) and DNA samples were taken from peripheral blood leukocytes in the tubes. PPAR-γ gene polymorphisms were determined by isolation of the obtained DNA samples and using quantitative real time PCR (qPCR) methods.

Result: When the obese and control groups were compared, age, glucose, urea, creatinine, Triglyceride, HDL, a1c, Na, CL, and weight and body mass index values were found to be significant ($p<0.001$). Considering the results in terms of genotype, age, glucose, urea and a1c values were found to be correlated ($p<0.050$). When the descriptive data were compared in terms of post-hoc analysis according to genotype, it was determined that glucose and a1c values of GG-CG genotypes were related ($p<0.050$).

Conclusion: We found significant associations exist between increase gene polimorfizm levels of PPAR-γ in obese and control group. Therefore, we could say that the gene polimorfism increases in response to the obese and control group.

Keywords: Diabetes Mellitus, Obesity, PPAR-γ, DNA isolation, Real Time PCR

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