



Türk Moleküler  
Tıp Derneği  
1999

VI. INTERNATIONAL CONGRESS OF

# Molecular Medicine

MOLECULAR MEDICINE FROM THE UPDATES TILL THE FUTURE

22-25 May 2017 ISTANBUL - TURKEY

Istanbul University Congress and Culture Center

## CONGRESS ABSTRACT BOOK

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VI. INTERNATIONAL CONGRESS OF  
**Molecular  
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## WELCOME MESSAGE

**Dear Colleagues,**

On behalf of the Organizing Committee, Turkish Society of Molecular Medicine & Istanbul University I am very delighted to welcome you the 6th International Congress of Molecular Medicine.

This biennial congress gathers researchers and clinicians from Turkey and abroad to focus on the latest developments in molecular medicine. Also this year meeting organisers have assembled a rich congress program consisting of plenary lectures, applied workshops, oral and poster presentations & exhibition.

Major scientific topics of the congress are: New Molecular Aspects in Sports; Surgery and Molecular Medicine; Inflammatory Mechanisms in Psychiatric Disorders; Good Cholesterol – Bad Cholesterol; Molecular Future in Cancer; Unravelling the Mysteries of Proteins: Proteomics and Medicine; The Evolution of Aging and Death; Different Aspects of Gut-Brain Axis; Molecular Information Processing: Data Mining; Molecular Metabolism in Diabetes; Cellular and Molecular Aspects of Microbiota; Designing the Future: Nanotechnology in Medicine; Molecular Aspects in Cancer “From Laboratory to Clinic“.

I wish to take this opportunity to express special thanks to Istanbul University, Conference Organising and Scientific Committees, participants, lecturers, speakers, presenters and supporters.

We encourage every participant to be active and use this occasion to exchange ideas, and build collaborations. It is an opportune time and place to discuss latest developments and share the information with colleagues.

In conclusion, I would like to wish you success in your work, productive time at the congress and a very beautiful stay in Istanbul.

Sincerely yours,

**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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## Scientific Program

### 22 May 2017, Monday

- 09:00** Registration
- 09:30 - 15:00** **Workshops:**
- Bütünsel RNA Çalıştayı**  
*Real-Time PCR dün , bugün, yarın..*
- İmmünohistokimya Çalıştayı**  
*Genotoksik ve Karsinojenik maddelerin DNA Hasarı Üzerine Etkisinin Doku ve Hücre Örneklerinde Comet Assay Yöntemi İle İncelenmesi*
- R.A.M.P. Warm Up Performans Metodu Çalıştayı**
- 16:00 - 18:30** **Keynote Speech**  
**Congress Honorary Chair:** Mahmut Ak  
**Congress Chair:** Ümit Zeybek  
**Plenary Lecture:** Emin Kansu  
Future Perspectives in Cancer Therapy: Precision Medicine
- 18:30** **Cocktail**

### 23 May 2017, Tuesday

#### MAIN HALL

- 09:00 - 11:00** **New Molecular Aspects in Sports**  
**Session Chair:** Mehmet Kurtoğlu, Ümit Zeybek
- The Importance of Metabolic Assessment on The Development of Physical Performance  
*Türker Bıyıklı*
- Psychological Factors and Genetic Characteristics Affecting Performance in Sports  
*İtir Tanı Cömert*
- Doping in Sports: Gene Doping  
*İlker Yücesir*
- Understanding Exercise Motivation in Cancer Patients  
*Gözde Ersöz*
- 11:00 - 11:15** **Coffee Break**

11:15 - 12:45

**Surgery and Molecular Medicine**

**Session Chair:** Mehmet Kurtoğlu, Ümit Zeybek

Predisposing Genetic Factors for Venous Leg Ulcer Development  
*Gyozo Szolnoky*

Fast Tract Interventions After Gynecologic Abdominal Surgery  
*Fusun Terzioğlu*

Personalized Genomics-Personalized Surgery  
*Gül Baktır*

12:45 - 13:30

**Lunch Break**

13:30 - 15:30

**Inflammatory Mechanisms in Psychiatric Disorders**

**Session Chair:** Erdem Tüzün, Bedia Çakmakoğlu

Psychosis and Autoantibodies  
*Erdem Tüzün*

Inflammation in Neurobiology of Depression  
*Feyza Arıcıoğlu*

Chemokine Gene Variants Role on Psychiatric Disorders  
*Elif Sinem Bireller*

Tryptophan-Kynurenine Pathway in Schizophrenia: Role of Cytokines  
*Elif Weidinger*

15:30 - 16:15

**Session Chair:** Dildar Konukoğlu

Good Cholesterol - Bad Cholesterol  
*Canan Efendigil Karatay*

16:15 - 16:30

**Coffee Break**

16:30 - 18:00

**Molecular Future in Cancer**

**Session Chair:** Safiye Aktaş, Semra Demokan

Curcumin and Resveratrol Potentiate Doxorubicin in Upregulation of PcG-associated Protein RYBP and miR-200, miR-26b in Hepatocellular Carcinoma  
*Ahmad Bassiouny*

Importance of Molecular Heterogeneity in Cancer Management  
*Safiye Aktaş*

Transmission of Molecular Changes to Cancer Cells by Exosomes  
*Zekiye Altun*

## 24 May 2017, Wednesday

### MAIN HALL

09:00 - 11:00

#### **Unravelling the Mysteries of Proteins: Proteomics and Medicine**

*Session Chair: Aysel Özpınar, Arzu Ergen*

Preparation of Highly Purified Nuclear Protein Extracts From Cultured Cells And  
Proteomic Identification of Nuclear Proteins

*Murat Kasap*

Proteomic Analysis of Epithelial Mesenchymal Transition

*Nurhan Özlü*

Investigating Neurological Disease Mechanisms via Proteomics Analysis

*Ahmet Tarık Baykal*

Discrimination of Parathyroid Adenoma and Hyperplasia via 2d Based Proteomics

*Gürler Akpınar*

11:00 - 11:15

#### **Coffee Break**

11.15 - 13.30

#### **Session Chair: Ayşe Kevser Özden Pişkin**

The Evolution of Aging and Death

*Ali Demirsoy*

13:30 - 14:30

#### **Lunch Break**

14:30 - 16:30

#### **Different Aspects of Gut-Brain Axis**

*Session Chair: Feyza Arıcioglu*

Gastrointestinal Aspect of Gut-Brain Axis

*Neşe İmeryüz*

Kidney and Excretory Aspect of Gut-Brain Axis

*Mehmet Koç*

Metabolism and Appetite Aspect of Gut-Brain Axis

*Dilek Gogas Yavuz*

Neurologic Aspect of Gut-Brain Axis

*Aslı Tuncer*

16:30 - 16:45

#### **Coffee Break**

16.45 - 17.15

#### **Session Chair: Ümit Zeybek**

Molecular Information Processing: Data Mining Techniques to Detect Cancer with  
Odor Analysis

*Serkan Türkeli & Büşra Bayat*



## 25 May 2017, Thursday

### MAIN HALL

09:30 - 11:00

#### **Molecular Metabolism in Diabetes**

**Session Chair:** *Willy Malaisse, Ali Osman Gürol*

Predictive And Preventive Value Of Amino Acids In Type 2 Diabetes  
*Aydın Duygu*

Regulation of Insulin Transcription by Calcium-binding Proteins  
DREAM/Calsenilin and Secretagoin  
*Teodora Daneva*

Anoctamin 1, Candidate Anionic Channel Sensitive to Cell Volume in  
Insulin-Producing Cells  
*Willy Malaisse*

11:00 - 11:15

#### **Coffee Break**

11:15 - 13:15

#### **Cellular and Molecular Aspects of Microbiota**

**Session Chair:** *Tarkan Karakan*

Gut Microbiota Modulation  
*Tarkan Karakan*

Gut Microbiota, Obesity and Popular Diets  
*Banu Çaycı*

Microbiome-based Disease Biomarkers  
*Süleyman Yıldırım*

Human Microbiome and Autoimmune Diseases  
*Christina Tsigalou*

13:15 - 14:15

#### **Lunch Break**

14:15 - 15:45

#### **Designing the Future: Nanotechnology in Medicine**

**Session Chair:** *Cumhur Gündüz*

Nanocarriers and Targeted Drug Delivery for Cancer  
*Sevil Dinçer Işoğlu*

Synthesis and Characterisation of Nanomaterials For Health Applications  
*Cengiz Kaya*

Emerging Technologies in Cancer Diagnosis and Treatment  
*İsa Yıldırım*

15:45 - 16:00

#### **Coffee Break**

16:00 - 18:00

#### **Molecular Aspects in Cancer "From Laboratory to Clinic"**

**Session Chair:** *Engin Ulukaya, Elif İlkay İkitimur Armutak*

Genomics in Precision Medicine: Current Status & Future Prospects  
*Suresh C. Jhanwar*

Autophagy: Nobel Prize and New Results  
*Devrim Gözüaçık*

Isocitrate dehydrogenase Mutation in Cancer and Progress Toward  
Development of Targeted Therapeutics  
*Hüray İşlekel*

Role of Surgeon in Targetted Medicine  
*Akif Turna*

18:00

#### **CLOSING CEREMONY**

## Oral Presentation Program

23 May 2017, Tuesday

11:15 - 11:45

**SALOON 1 Mutay Aslan** - Changes in PUFA Levels and Inflammation in an Animal and Cell Model of Hepatic Endoplasmic Reticulum Stress **OP19**

**SALOON 2 Cansu Özbayer** - Association Between Rs5275 Variant of COX-2 Gene and Lung Cancer Risk **OP8**

**SALOON 3 Dilara Akçora Yıldız** - Decreased Multiple Myeloma Viability of Malignant Plasma Cells by Inhibition of Werner Helicase **OP14**

11:45 - 12:15

**SALOON 1 Esin Ak** - Radiotherapy Induced Oxidative Injury of Ileum is Alleviated by Resveratrol Treatment in Rats **OP24**

**SALOON 2 Metin Çalışkan** - Determination of EGFR, KRAS, BRAF, PIK3CA, HER2 and NRAS Gene Mutations in Parafin Block Sections from Patients Diagnosed with Non-Small Cell Lung Cancer **OP11**

**SALOON 3 Ülgen Sever** - The Role of Dat, 5-Htt, Maa and Maob of Nicotine Dependence in a Turkish Population **OP29**

12:15 - 12:45

**SALOON 1 Özlem Özdemir** - Evaluation of The Hepatoprotective Effect of Lipoic Acid Upon Exposure to 2,3,7,8-Tetrachlorodibenzo-P-Dioxin in Rat Hepatocyte Cultures **OP20**

**SALOON 2 Ceyda Tuba Şengel-Türk** - Antiproliferative Activity and Safety of Lonidamine Encapsulated PEG-block-PCL Nanocarriers against SW480 Colon Cancer Cells **OP9**

**SALOON 3 Mahmut Balkan** - Genetic and Epigenetic Factors in Male Infertility **OP6**

12:45 - 13:30 *Lunch Break*

13:30 - 14:00

**SALOON 1 Nilgün Çetin** - Fendrr and LincRNA-p21 Expression Decrease in Atherosclerotic Plaques **OP39**

**SALOON 2 Duygu Aygüneş** - The Effects of Docetaxel with Insulin in Er (+) Breast Cancer Cells on Cellular Toxicity and Molecular Mechanism **OP1**

**SALOON 3 Günnur Demircan** - Does Autophagy Have a Role in the Progress of Coronary Collateral? **OP44**

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**14:00 - 14:30**

**SALOON 1 Işıl Aksan Kurnaz** - Ets Protein Elk-1 in Brain Tumor Proliferation **OP45**

**SALOON 2 Muhammad Waqas Akbar** - Breast Cancer Cells with Stem like Features are Sensitive to Midostaurin, Resistant to Lapatinib and Show Worse Prognosis when Treated with Paclitaxel **OP25**

**SALOON 3 Sermin Biçer** - The Licensing of Biologicals and Biosimilars in Turkey and Patient Access **OP32**

**14:30 - 15:00**

**SALOON 1 Rukiye Nar** - TFII-I Interacts with E2F transcription Factors and regulates Their Association with The Co-occupied CDC27, CDKN1C, HDAC1, and DNMT1 Gene Loci **OP34**

**SALOON 2 Emine Firdevs Yıldırım** - Apoptotic Effect of Anacardic Acid and Farnesyl Transferaz Inhibitor on Metastatic Breast Cancer Cell Line (MCF-7) **OP23**

**SALOON 3 Hasan Basri Savaş** - Investigating the Effects of Artificial Food Colorings, Exposed During Prenatal Term with the Dose of NOAEL, on Saliva Glands in Adult Period **OP38**

## 24 May 2017, Wednesday

**09:30 - 10:00**

**SALOON 2 Neslihan Pınar Özateş Ay** - New Promising Stars of Acute Lymphoblastic Leukemia: Ruxolitinib and BIBR1532 **OP22**

**SALOON 3 İrem Doğan Turaçlı** - Potential Effects of Metformin in DNA BER System Based on Oxidative Status in Type 2 Diabetes **OP48**

**10:00 - 10:30**

**SALOON 1 Faruk Çelik** - Investigation of Novel Genes Associated with Endurance and Strength in Athlete **OP28**

**SALOON 2 Arzu Zeynep Karabay** - Aspirin Inhibits Bcr-Abl and Its Downstream Effectors in Chronic Myeloid Leukemia **OP18**

**SALOON 3 Elif Şahin** - Safety of Herbal Self- Medication in Diabetes **OP33**

**10:30 - 11:00**

**SALOON 1 Ali Gül** - Effect of The Polymorphisms of Uncoupling Proteins Genes Ucp1-3826 A/G and Ucp2 Exon8 Del/Ins in Childhood Obesity **OP42**

**SALOON 2 E. Sinem Bireller** - A New Perspective for The Treatment of Colon Cancer: Mesenchymal Stem Cells **OP31**

**SALOON 3 Özlem Kurnaz Gömleksiz** - Smoking and ACE D Allele: Determinants of High Serum Oxidized-LDL Levels in Coronary Heart Disease **OP27**

**11:00 - 11:15 Coffee Break**

**14:30 - 15:00**

**SALOON 1 Hümeysra Öztürk Emre** - Dynamic Thiol-Disulphide Homeostasis in Low-Grade Gliomas: Preliminary Results in Serum **OP41**

**SALOON 2 Gülsüm Seda Güleç Yılmaz** - Next Generation Sequencing and Detection of Common Mutations in Lung and Colon Cancers **OP17**

**SALOON 3 Hale Güler Kara** - Investigation of Cytotoxic, Apoptotic and Molecular Effects of Astaxanthin and Nocodazole in Mcf-7 Cell LINES **OP4**

**15:00 - 15:30**

**SALOON 1 Wen-Hui Fang** - The Potential Use of Mesenchymal Stem Cells Loaded with Small Molecule Compounds as Therapeutics in Disease **OP13**

**SALOON 2 Filiz Bakar** - Down-regulation of Annexin I is Correlated with Inflammatory Mediators in Colorectal Carcinoma **OP3**

**SALOON 3 Fatma Necmiye Kacı** - Cytotoxic Effect of Ni Doped ZnO Samples on Human Primary Glioblastoma Cell Line **OP21**

**15:30 - 16:00**

**SALOON 1 Mehmet Öztürk** - Val58 and Tyr65 Amino Acids are Critical for Catalytic Activity and Substrate Specificity of Bile Salt Hydrolase from Lactobacillus plantarum B14 **OP10**

**SALOON 2 Betül Şahin** - Evaluation of Proteomic Response of Human Tumor Cells to Sirtinol by a Novel Sample Preparation Method **OP40**

**SALOON 3 Arın Tomruk** - The Effects of Radiofrequency Fields on Caspase-Dependent Apoptosis in Human Colorectal Carcinoma Cells **OP46**

**16:00 - 16:30**

- SALOON 1 Gül Uçar** - Identification of Anaerobe Bacteria from Patients with Chronic Periodontitis using Molecular Techniques **OP5**
- SALOON 2 Nezaket Türkel Sesli** - Mechanism of Boron Derivatives for The Treatment Of Renal Cell Carcinoma **OP26**

## 25 May 2017, Thursday

**11:15 - 11:45**

- SALOON 1 Şehkar Oktay** - The Effect of Myrtus communis Extract Administration on Bile Duct Ligated Rats' Brain Tissue **OP15**
- SALOON 2 Atiye Seda Yar Sağlam** - The Effects of Sequential Administration of EF24 with Docetaxel Apoptotic Response in Metastatic Breast Cancer Cell Line **OP7**
- SALOON 3 Hacer Ezgi Karakas** - Autophagy Analysis of Tumor-Fibroblasts Crosstalk on Biochips **OP3**

**11:45 - 12:15**

- SALOON 1 Özlem O. İbrahimoğlu** - PTPN22 deficiency influences B1 and marginal zone B cell responses and accelerates leukemia development in the Eμ-TCL1 transgenic mouse model of chronic lymphocytic leukemia **OP49**
- SALOON 2 Abdulmecit Gökçe** - Silencing of ERG Transcription Factor in H596 Lung Cancer Cell Line Inhibited the Epithelial-Mesenchymal Transition Markers **OP47**
- SALOON 3 Serdar Durdağı** - Discovery of Klotho Peptide Antagonists Against Wnt3 and Wnt3a Target Proteins: Combination of Computational, Peptide Synthesis, and in vitro Analysis **OP30**

**12:15 - 12:45**

- SALOON 1 Volkan Keleş** - Using Drosophila Melanogaster as a Nonmammalian Model Organism for Understanding to Molecular Mechanisms of Clinically Important Antibiotics **OP16**
- SALOON 2 İdil Çetin** - Comparison of the Effects of Albumin Bound Paclitaxel (Abi-007) on Triple Negative Breast Cancer cCII Line MDA-MB-231 and Luminal a Breast Cancer Cell Line MCF-7 **OP50**
- SALOON 3 Kübra Şahin** - Effect of MIF rs755622 gene polymorphism on the alzheimer patients **OP35**

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**12:45 - 13:15**

**SALOON 1** **Taha Ceylani** - Bowel-brain axis affected by cefoperazone and ampicillin treatment in mice **OP12**

**SALOON 2** **Sibel Özdaş** - Nuclear Retention of P33ing1b Through Inhibition of Exportin-1 Dependent Nuclear Export in Head and Neck Cancer Cells **OP52**

**SALOON 3** **Sümeyya Deniz Çelik** - The Effect of Surfactant Protein B Gene Polymorphism in The Ethiology of Acute Bronchiolitis **OP36**

**13:15 - 14:15 Lunch Break**

**14:15 - 14:45**

**SALOON 3** **Çisem Nildem Doğan** - Association between bronchioitis infants and interleukin 8 gene polymorphism **OP37**

**14:45 - 15:15**

**SALOON 3** **İbrahim Bozgeyik** - Differential Expression of Piwil2 in Papillary Thyroid Cancer **OP51**

**15:15 - 15:45**

**SALOON 3** **Sevgi İrtegin-Kandemir** - Differential Expression Patterns of ADAMTSs and HAPLNs in Pre-eclampsia **OP43**

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## **SPEAKER SUMMARIES**



## FUTURE OUTLOOK OF CANCER THERAPY: PRECISION MEDICINE

Emin Kansu

Hacettepe University Cancer Institute, Ankara, Turkey

Cancer has been one of the most important and challenging disease in medicine. Although a significant progress has been made in the genomics and molecular biology of cancer in last fifty years patients still die of their disease. Therapeutic use of tumor antigen specific monoclonal antibodies, tyrosine kinase inhibitors, adoptive immunotherapy with LAK /TIL cells, cellular immunotherapies and recently discovered checkpoint inhibitors and CAR-T Cells can be listed as successful list of anti-cancer treatments. As we realize, the limitations of our approaches to cure cancer have been hampered due to vast array of molecular defects that define various cancers and subtypes.

Since 2012, NCI and NIH have been discovering unique therapies that can treat an individual's cancer based on specific genetic abnormalities of that person's tumor type. This is a new era of oncology practice where completely mapped genetic and molecular profile about a patient's cancer can be routinely employed for his/her therapy.

Precision Medicine is defined as “*Translation of basic science to routine testing, screening, diagnosis and therapy in cancer*”. Precision medicine uses massive data (Big Data) network that aggregates and analyzes information from large patient cohorts, healthy populations, experimental organisms and reaches toward disease mechanisms and precision diagnosis and therapy for each individual. In precision medicine, sequencing cancer genomes is only the first step in understanding the disease. Then, we have to find out which genetic changes / mutations are playing a role as “drivers” in the development of cancer. Transcription Factors (TFs) serve as “master regulators” control most of the genes in the gene signatures of cancers. If one wants to put all the data/big data in perspective system biology, experimental biologist, molecular biologist, expert in bioinformatics and clinical researcher must be employed in the team to translate cancer genome findings (bench) to the patient care (bed-side).

President Obama has expressed quite a strong conviction that science offers great potential for improving health and announced the **Precision Medicine Initiative** on January 15<sup>th</sup>, 2015 ([www.whitehouse.gov/precisionmedicine](http://www.whitehouse.gov/precisionmedicine)). This important initiative has two components, namely “*a near-term focus on cancers*” and as a second aim to “*generate knowledge applicable to the whole array of health and disease*”. There will be many steps ahead to have a success in speeding the application process and regulatory affairs of this novel therapeutic challenge in cancer medicine.

## **THE IMPORTANCE OF METABOLIC ASSESSMENT ON THE DEVELOPMENT OF PHYSICAL PERFORMANCE**

Türker Bıyıklı

Nişantaşı University, School of Physical Education and Sports, Istanbul, Turkey

Nowadays, researches about sportive performance - sportive profitability/performance development- are rapidly growing. The fundamental problem is to not put the scientific researches into practice.

So generally the practioners not use the scientific datas. In this study, a great example for sports science to work in collaboration with other disciplines, The athlete's physical site tests and the comparison of evaluation results of the genetical test panel and how they are assessed in genetical performance evaluation (periodisation) and its results have been exempld.

Athletes genetical evaluation is used in practice and in terms of developing athlete performance for future.

Besides, this is a study stressing the genetic features are required not only for sportive tendency/talent selection but also for the physical and emotional development of an athlete.

Herewith, genetic science is such a meeting point that manage of expertise performance components.

For success, all the specialists (Head Coach, Strength& Conditioning Coach, Nutrition specialist, Health specialist, Sport psychologist etc.) that are influencing the athletes are required to work together.

## PSYCHOLOGICAL FACTORS AND GENETIC CHARACTERISTICS AFFECTING PERFORMANCE IN SPORT

İtir Tari Cömert

Fatih Sultan Mehmet Vakıf University Faculty of Literature Department of Psychology, Istanbul

**Introduction:** In modern societies, individuals and societies tend to see sportsmen as role models, as those who they engage themselves, considering a sportsman not only within the limits of his performance as a sportsman, but also according to his characteristics in everyday life. All the process has pioneered in placing special care for the sportsmen, particularly the ones who play in the youth setup, to be well and healthy psychologically. The main psychological conditions, which effect the state of well-being and aesthesia sportsmen, can be categorized as depression, anxiety, and stress and attention and reaction time, which occur dependently to the former reasons. If they are not treated properly, all of these problems may have serious impacts on sportsmen, and effect the performance negatively in before, during, and after the games. Lately, following the developments in genetic studies, genetic factors for sportsmen have been a part of main research objects, along with environmental and emotional elements. In what follows, many scientist have been examining polymorphism, which is seen as an effective component that influences durability and performance. Examinations held on a particular gen, that is called “candidate gen” has constituted an important part of the studies, which is considered effective in the characteristic of a sportsmen. This study, covering the football players between the ages 13-18 in Galatasaray Football Academy Youth Setup, aims to analyze the relation between the levels of depression, anxiety, and stress of the sportsmen and their level of gene expression, which is assumed to affect their mood.

**Material Method:** The study was conducted with 61 athletes who are licensed to play sports. Depression, Anxiety and Stress Scale (DASS) were used as a data collection tool and Personal Information Form was used to determine the demographic characteristics of participants. The Personal Information Form used in the research was prepared by the researcher to determine the demographic characteristics of the athletes participating in the survey. The genetic screening part of the study was based on the genes which are thought to be related to metabolism of athletes and affect the phenotypic features PPAR DELTA, NRF2, PGC-1A, EPAS-1, HBB, GYS1, ADRB2, VEGF, CKMM, ACTN3, MLCK, ACE, AMPD1, IGF1, ABO, TNC, 5HTT, BDNF, TFAM, AGT, MAO-A, COL5A-1, and also based on the on the examination of the genetic relationship underlying the performance differences through Quantitative Real Time PCR.

**Findings:** All of the athletes participating in the survey were male. When the age groups of participants were examined, 18.0% (n:11) of the sample was 13 years old, 13.1% (n:8) was 14 years old, 29.5% (n:18) was 15 years old, 29.5% (n:18) was 16 years old, 6.6% (n:4). The mean age was  $15.05 \pm 1.3$ . When we look at the comparison of depression, anxiety, stress, reaction time and attention with 5-HHT, BDNF and MAO genes, regarding the ages of 13-16, it is observed that there is a significant relationship between reaction time and age. ( $p: .000$ )  $*p < 0.05$

**Discussion:** The aim of this study is to examine the depression, anxiety and stress levels of the players between the ages of 13 and 18 who play soccer in Galatasaray Football Academy, and the relation of the gene expression levels which are thought to affect these emotional states. The most important feature that distinguishes this study from the studies in the field is that this study is the first to use the gene study with the psychological evaluation. Numerous studies have been conducted to improve the performances of the athletes, but no research found in the literature that examines the psychological characteristics and genes that affect these characteristics.

## DOPING IN SPORTS: GENE DOPING

İlker Yücesir

Istanbul University, Sports Sciences Faculty, Department of Sport Health Sciences

Doping is one of the biggest problems in sports world. Ruining the integrity and spirit of the sport, doping has been a big trouble during 20th century. Despite enormous development of anti-doping community and organizations, it keeps being one of the most complex and detrimental problems of fair sports environment. Establishment of World Anti-Doping Agency (WADA) in 1999 and its development has changed a lot in favor of fairness. Since the early efforts seen before and during 2000 Sydney Olympic games, WADA has become the major ruling body of anti-doping world. In 2003, before 2004 WADA Code came in force, “Prohibited Classes of Substances and Prohibited Methods” of Olympic Movement Anti-Doping Code is the first document, which include “Gene Doping” into the prohibited list as a “method”. Gene doping was defined as: “*Gene or cell doping is defined as the non-therapeutic use of genes, genetic elements and/or cells that have the capacity to enhance athletic performance.*” Today, in 2017 version of annually renewed WADA’s Prohibited List, Gene Doping is set in “Methods” section as in the first document and defined as: “*The following, with the potential to enhance sport performance, are prohibited: 1. The transfer of polymers of nucleic acids or nucleic acid analogues. 2. The use of normal or genetically modified cells.*”

Effects of genetic heritage on sports performance is well known since thousands of years. Genetic advantages of a person to another are related but not limited to well-known basic athletic parameters like endurance, power, and so on. Anthropometric characteristics, intelligence, skill learning abilities and many others contribute to athletic performance of different sports to varying extends. Nevertheless, yet most suspected and hence targeted genetic variations/manipulations are enhancement of oxygen transfer, positive contribution to cell energetics, cell regeneration and muscle mass.

Enhancement of athletic performance via manipulation of human genetics seems to be possible. Gene therapy methods are expected to be most possible gene doping tools. Despite suspects of that somewhere some athletes might practice gene doping, there is no evident case yet. Research to implement gene doping testing of some possible methods are to be finalized very soon. But yet, no scientifically proven reliable tests are in routine. The 2016 Rio Olympic games were expected to be the first major event where gene doping tests to be started. It did not.

The general aspects of doping and particularly gene doping in sports and recent developments will be discussed during the congress.

## UNDERSTANDING EXERCISE MOTIVATION IN CANCER PATIENTS

Gözde Ersöz

Namık Kemal University, School of Physical Education and Sports

When recent researches concerning cancer and exercise are examined, it is understood that exercise prevents many types of cancer, improves the quality of life, alleviates the side effects (fatigue, depression etc.) during and after treatments and reduces the rates of death. American College of Sports Medicine and the American Cancer Society recommends cancer survivors accumulate 150 min/week of moderate intensity activity, 75 min/week of vigorous intensity activity or a combination of these activities (Rock et al., 2012; Schmitz et al., 2010). Although exercise is beneficial in terms of aerobic endurance, muscular strength, fatigue, depression, anxiety, self-esteem, functional ability and overall quality of life (Rock et al., 2012; Buffart, Galvão, Brug, Chinapaw, & Newton, 2014; Chipperfield, Brooker, Fletcher, & Burney, 2014; Mishra, Scherer, Snyder, Geigle, & Gotay, 2014), most cancer patients do not do physical activity regularly (Courneya & Friedenreich, 2011; Pinto & Ciccolo, 2011). One of the most important factors to encourage exercise behavior and increase the level of regular physical activity of individuals is the notion of motivation. Nowadays, decreasing physical activity habits and accompanying health problems make the need for understanding exercise motivation even more evident. The models that are usually used to explain cancer patients the notion of exercise motivation are Health Belief Model (Biddle and Mutrie, 2007), Theory of Planned Behaviour (Ajzen, 1991), Self-Determination Theory (Deci and Ryan, 2000) and Transtheoretical Model (Prochaska and DiClemente, 1984). Besides the theoretical researches in this field, practical studies have been carried out in order to increase regular physical activity in cancer patients. These studies have shown that face-to-face consultancy, telephone consultancy, exercise diary, oncologist's verbal exercise recommendation are effective for increasing exercise behaviours in cancer patients (Vallance et al., 2007; Bicego et al., 2009; Jones, Courneya, Fairey and Mackey, 2004; Patrick, Pratt and Sallis, 2009). As a consequence, increasing the physical activity levels of cancer patients, helping them include and maintain moderate intensity and regular physical activity in their daily routines is very important in terms of their decreased levels of fatigue, psychological well-being and quality of life during and after the treatment. Nevertheless, studies are very limited in this area in Turkey. In this presentation, studies on exercise motivation in cancer patients will be presented and efforts will be made to raise awareness in order to increase the amount of work done in this field in Turkey.

## PREDISPOSING GENETIC FACTORS FOR VENOUS LEG ULCER DEVELOPMENT

Győző Szolnoky<sup>1</sup>, Nikoletta Nagy<sup>1,2,3</sup>, Gábor Szabad<sup>1</sup>, Kata Filkor<sup>4</sup>, István Nagy<sup>4</sup>, Éva Dósa-Rácz<sup>1</sup>, Zsuzsanna Bata-Csörgő<sup>1,3</sup>, Márta Széll<sup>1,2,3</sup>, Lajos Kemény<sup>1,3</sup>

<sup>1</sup> Department of Dermatology and Allergology, University of Szeged, 6 Koranyi fasor, H-6720 Szeged, Hungary

<sup>2</sup> Department of Medical Genetics, University of Szeged, 4 Somogyi B utca, H- 6720 Szeged, Hungary

<sup>3</sup> Dermatological Research Group of the Hungarian Academy of Sciences, University of Szeged, 6 Koranyi fasor, H-6720, Szeged, Hungary

<sup>4</sup> Institute of Biochemistry, Biological Research Centre of the Hungarian Academy of Sciences, Szeged, Hungary

**Background:** A number of well-known acquired and putative inherited etiological factors contribute to the development of venous leg ulcer (VLU).

**Aim:** In this study we set out to perform a meta-analysis of putative genetic and acquired factors predisposing to VLU development.

**Methods:** The frequencies of four genetic factors were determined: the R506Q (Leiden) mutation of the F5 gene, the G20210A mutation of the F2 (prothrombin) gene, the 2451 A/G SNP of the fibroblast growth factor receptor 2 (FGFR2) 3' UTR, and the -308 G/A SNP of the tumor necrosis factor  $\alpha$  (TNF $\alpha$ ) promoter. We investigated the mRNA expressions of Syndecan 4 (SDC4), a heparan sulfate proteoglycan, and neuropilin 1 (NRP1), a transmembrane receptor, are both involved in normal wound healing and furthermore pro- inflammatory cytokines IL-1, IL-8, TNF $\alpha$  and anti-inflammatory mediator IL-10 as well as TAM receptors (Tyro, Axl, MerTK) and their ligands Gas6 and Protein S between VLU and control persons.

**Results:** The -308 TNF $\alpha$  and the 2451 A/G FGFR2 3' UTR SNPs exhibited higher frequencies among VLU patients. SDC4 showed significantly lower mRNA and protein expression in the uninvolved dermis of VLU patients compared with controls. IL-1 $\alpha$  is notably overexpressed in venous leg ulcer treatment non- responders to standard complex VLU therapy; in contrast, Axl gene expression is robustly stronger among VLU responders.

**Conclusions:** The aforementioned markers may be considered as candidates for the prediction of treatment response among venous leg ulcer patients.

## FAST TRACT INTERVENTIONS AFTER GYNECOLOGIC ABDOMINAL SURGERY

Füsun Terzioglu

Istinye University, Dean of Faculty of Health Science, Director of Nursing Services in MLPcare Health System

**Aims and objectives:** The aim of this study was to determine the effects of chewing gum, early oral hydration and early mobilization on time of first bowel sounds, first passage of flatus and first defecation following abdominal gynecologic surgery.

**Background:** A major complication of abdominal surgical procedures is paralytic ileus which results in patient discomfort, prolonged length of hospital stay, and increased cost of treatment.

**Design:** Prospective randomized case-control study

**Methods:** Women who underwent abdominal gynecological surgery for benign disorders under general anesthesia were randomized into 8 groups according to different combinations of interventions consisting of chewing gum, early oral hydration and early mobilization. The effects of these interventions on the time of first bowel sounds, first passage of flatus and first defecation following abdominal gynecologic surgery were investigated. The data were analyzed using chi-square tests, t test for independent samples, Tukey HSD test, pair wise comparison test, one-way analysis of variance.

**Results:** It was found that the time when bowel sounds were heard was shorter, the time first passage of flatus was shorter and first defecation occurred earlier in the 1st group of women who chew gum, was hydrated orally and were mobilized early after surgery than the other groups. It was also determined that these periods were longest in the women who did not receive any intervention and received the routine hospital care when compared with other groups. Duration of hospital stay was shorter in the women who chew gum, was hydrated orally and was mobilized early than the other groups.

**Conclusions:** Early oral feeding, early mobilization and chewing gum are effective methods in terms of preventing paralytic ileus following abdominal gynecological surgery, improving patient comfort and shortening the duration of hospitalization.

**Relevance to clinical practice:** Nurses may cause early recovery, improve the patient comfort, prevent paralytic ileus and shorten the duration of hospitalization after gynecologic abdominal surgery by recommending gum chewing, early mobilization and early hydration.

## **PERSONAL GENOMICS - PERSONALIZED SURGERY**

Gül Baktır

Istanbul Yeni Yuzyil University, Faculty of Pharmacy

Personalized medicine refers to the tailoring of medical and surgical therapies to the individual's unique molecular profile. Modern advances in DNA sequencing, mRNA expression, tissue banking, as well as metabolomics, proteomics and epigenetics are moving personalized medicine to the forefront of healthcare. Personalized medicine represents a more precise, focused approach compared to current clinical medicine, which is based upon studies collected from large, heterogeneous populations of patients.

Among many attempts to determine the essential elements needed to establish successful personalized medicine programmes, a useful model was created to be applied in centers for personalized medicine and surgery. This model includes four phases. Phase 1, "genomic profiling", builds an infrastructure to collect and store patients' molecular profile through DNA, RNA, proteomic, and epigenetic data. Phase 2, "the development of imaging diagnostics", describes the integration of the patient's molecular profile into clinical decision-making. Phase 3, "the examination of the function of selected molecular targets" uses genomic data to identify previously unknown disease-associated molecular derangements. Phase 4 is "targeted therapy" which includes medical, surgical, immunological, and/or gene therapies, by utilizing the information gained from functional analysis, based on the individual patient's personalized molecular profile. Single-gene mutations have already influenced surgical decision-making in breast, colorectal and thyroid cancer.

In this presentation, established examples for personalized medicine in surgery such as RET mutations requiring early thyroidectomy for medullary thyroid cancer, E-cadherin and BRCA1/BRCA2 mutations necessitating prophylactic gastrectomy and mastectomy, respectively, will be discussed.



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## **PSYCHOSIS AND AUTOANTIBODIES**

Erdem Tüzün

Department of Neuroscience, Aziz Sancar Institute for Experimental and Medical Research (ASDETAE), Istanbul University, Istanbul, Turkey

Cell surface antibody-associated central nervous system disorders have emerged in the last decade as a novel field in neuroimmunology. Patients with antibodies to N-methyl-D-aspartate receptor and voltage-gated potassium channel-complex manifest with prominent psychiatric symptoms and particularly psychosis early in the disease course. In this presentation neuronal cell surface autoantibodies associated with neuropsychiatric symptoms will be discussed with a special emphasis on their potential pathogenicity in psychiatric disorders. Presence of neuronal cell surface antibodies in patients with isolated first episode psychotic disorder and schizophrenia were also discussed. Moreover, a list of diagnostic criteria that might help recognition of neuronal cell surface antibody positive psychosis patients has been proposed.

## **INFLAMMATORY MECHANISMS IN PSYCHIATRIC DISORDERS: INFLAMMATION IN NEUROBIOLOGY OF DEPRESSION**

Feyza Arıcıoğlu

Marmara University, Department of Pharmacology and Psychopharmacology Research Unit, Istanbul, Turkey

Stressful experiences can precipitate depression and anxiety, and stress-induced changes in physiology include an immune component. Throughout the evolution of mammalian physiology, stress-inducing situations reliably required activation of the immune system, and vice versa. Depression is one of the most common psychosocial disorders more than 10% of adolescents and approximately 30% of those suffering from depression exhibit treatment resistance, which has been linked to an increase in circulating cytokines. Accumulating data indicate that the alterations in inflammatory markers exhibited by a subset of depressed patients represent a complex dysfunction of the immune system incorporating both the brain and the body. The paradigm is now shifting from monoaminergic hypothesis to significance of other novel mechanisms that could possibly play substantial role for the development of depression in inter-related manner. In fact, neuroinflammation, amongst other mechanisms does seem to be a key pathological component by having impact on certain pathway pathologies including glutamatergic neurotransmission, oxidative processes, neurotropic factors, neurotransmitter metabolism, and glucocorticoid functions in the central nervous system and in the periphery, thereby triggers the pathological alterations that is thought to contribute to the development of depression. Neuroinflammation has been proposed as a potential mechanism underlying brain changes; there is evidence of an increased density and activation of microglia, immune cells resident in the brain, at various stages of the illness.

Today, there is growing consensus suggesting that inflammatory processes are highly related with the occurrence of depression. Individuals with immune and/or inflammatory diseases such as rheumatoid arthritis, diabetes, systemic lupus erythematosus, psoriasis and cardiovascular diseases have been reported to have depressive symptoms. On the other hand, basic and clinical studies have shown that cytokines, as main mediators of inflammatory responses, are elevated in depression. Furthermore, certain antiinflammatory approaches can reduce depressive symptoms, whereas antidepressant treatments can alleviate the elevated levels of cytokines in some cases. Therefore it has been postulated that there might be a reciprocal relationship between ongoing inflammatory processes and depression.

Taken together by the clinical point of view, although the role of inflammation in depression and its possible clinical implications have not been fully determined yet, but still inflammation aspect of depression holds promise for predicting antidepressant treatment response and raising question to the possible significance of utilizing anti-inflammatory approaches in the treatment of depression.

## **CHEMOKINE GENE VARIANTS ROLE ON PSYCHIATRIC DISORDERS**

Elif Sinem Bireller

Istanbul Yeni Yuzyil University, Faculty of Pharmacy, Istanbul, Turkey

Chemokines are known to play major roles in driving inflammation and immune responses in several diseases including neuroinflammatory process. According to studies, chemokines have also implicated the participation of pathogenesis on psychiatric disorders such as activation of their inflammatory pathways.

For decades, researches have been started to focus on showing both alterations of inflammation process on the field of mood disorders especially Schizophrenia, Bipolar disorder-I and Obsessive-Compulsive Disorder. It is important that to find a new biomarker or associated gene variants to early prediction which should be resulted fast and easy to get clinical samples such as peripheral blood.

In this presentation, the immune system components; chemokine gene variants and possible association will be discussed particularly Schizophrenia, Bipolar disorder-I and Obsessive-Compulsive Disorder and their role as biomarkers of these disorders.

## TRYPHTOPHAN-KYNURENINE PATHWAY IN SCHIZOPHRENIA: ROLE OF CYTOKINES

Elif Weidinger

Ludwig-Maximilians University, Psychiatric Hospital, Munich, Germany

Immune alterations seem to play an important role in the pathophysiology of schizophrenia. Recurring infections lead to immune conditioning and increased cytokine release. Stress is also well-known to increase pro-inflammatory cytokines. The stress-vulnerability-inflammation hypothesis of schizophrenia states that recurrent stressors (i.e. early infections, reinfections and psychosocial stressors) lead to immune conditioning and a pro-inflammatory immune state via proliferation of primed microglia, the primary immune cells of the CNS.

In this context it is known that infections and increased levels of pro-inflammatory cytokines predict an increased risk for schizophrenia in the offspring. At the same time childhood CNS infections are associated with a 5-fold risk in schizophrenia. High levels of pro-inflammatory cytokines have repeatedly been described in the blood and CSF of schizophrenic patients. A pro-inflammatory immune state activates the enzyme indoleamine 2,3-dioxygenase of the tryptophan/kynurenine metabolism. One of the neuroactive products of the kynurenine pathway is kynurenic acid, the only known naturally occurring NMDA receptor antagonist of the human CNS. NMDA receptor antagonism is known to be associated with positive and negative symptoms as seen in schizophrenia. Kynurenic acid as an antagonist of the  $\alpha 7$  nicotinic acetylcholine receptor on the other hand might explain symptoms of cognitive impairment in schizophrenia. High levels of kynurenic acid were shown in CSF as well as in critical CNS regions of schizophrenic patients.

Interestingly, antipsychotic drugs are known to exhibit anti-inflammatory effects and were also shown to decrease levels of kynurenic acid. Furthermore, anti-inflammatory drugs, like aspirin or selective COX-2-inhibitors, show therapeutic effects in schizophrenic patients. Studies reporting on the effect of kynurenine aminotransferase isoenzyme inhibitors, which are known to reduce kynurenic acid levels, have to be waited for.

## GOOD CHOLETEROL? BAD CHOLESTEROL?

Canan Karatay

Florence Nightingale Hospital, Internal Medicine and Cadiology, Istanbul, Turkey

We've all been persuaded that there are two cholesterols but are there? Our nutritional problems started with Dr Ancel Keys. Based on selective statistical associations Dr Keys had a theory. Dr Keys had a substantial reputation and the theory was promoted by the media. An alternative theory showed that heart disease and diabetes was associated with excess sugar consumption. Plentiful supplies of affordable refined sugar are new in human evolution. Yudkin was largely ignored by the medical establishment and his ideas were ridiculed by the Food Industry, particularly sugar refiners. Now championed by Robert Lustig. Senator George McGovern's Select Committee settled a scientific debate with a political edict. Hypothesis became Dogma without the benefit of scientific proof. These dietary goals made it possible for the food industry to feed a growing population relatively cheaply. In the late 1970's there was a clear change in the trends in obesity. This coincided with huge changes in food, farming and medications. The policies encouraged us to 'eat eat less fat and more carbs'. Low fat processed foods introduced which were high in sugar HFCS, High fructose corn syrup.

A 1936 paper used post-mortem data on people who died accidentally. It covered all age groups but found no association between blood cholesterol and atherosclerosis. In 1985 a post-mortem study of middle-aged men clearly shows no association between atherosclerosis and cholesterol. Association is not causation. Cholesterol enables us to exist, it enabled a major evolutionary step in complex cellular life. There is no difference between any cholesterol molecule. All cholesterol molecules are identical and vital to our cellular functions in all tissues. Cholesterol is a vital membrane molecule without which our cells are unable to function or cannot function. Membranes in cells are hosting the Protein Machinery (enzymes, pumps and transports). The wall structures of our cells are mainly lipid with a ratio of 1 cholesterol molecule to every 4 fat molecules. Cells communicate by releasing and absorbing small molecules, ions and lipid particles through cell membrane systems. Cells obtain fatty nutrition and recycle waste by releasing and absorbing fatty particles exo- and endo- cytosis of lipid vesicles. The double lipid layer that forms cell membranes is 20% molecular cholesterol 18% is not enough for normal cell functions. Endo (incoming) and (outgoing) exocytosis., exchange of lipids vesicles with the outside if the molecules of cholesterol are reduced from 20% to 18% this process will stop. Xia et al. showed that a small reduction in cellular cholesterol shuts down insulin production. In 2008 Xia showed that a small (10%) reduction in membrane cholesterol could shut down the release of insulin. Lowering membrane cholesterol can directly cause diabetes by switching off beta-cells  
Lipid wrapped vesicles enter and leave through the cell walls. A process dependent on cell wall cholesterol. Could all active tissues and organs be closed down by a reduction in membrane cholesterol? Over time reactive refined sugars like Fructose can attach to and damage the protein label and prevent the intake of then lipids. Organs are then starved of fats, fat-soluble nutrients and cholesterol. How does anyone imagine that medication to reduce the availability of cholesterol help a fat starved organ?

A diabetes clinician told that people who control their sugar-damage by diet and exercise have improved LDL scores. Excessive use of refined sugars has been identified are the primary cause of the rise in obesity in recent decades. All research reviews have connected high fructose intake with many mature onset illnesses including diabetes and many dementias.

## **AUTOPHAGY: NOBEL PRIZE AND NEW RESULTS**

Devrim Gozuacik

Faculty of Engineering and Biological Sciences, Molecular Biology, Genetics and Bioengineering Program and, EFSUN Nanodiagnostics Center of Excellence, SABANCI University, Tuzla, Istanbul, Turkey

In our lab in Sabanci University, Istanbul, we focus on signaling events regulating mammalian autophagy in health and disease. To discover new autophagy regulators and coordinators, we performed several unbiased functional screens.

Our microRNA (miRNA) screens led to the discovery of several miRNAs targeting autophagy at various steps of the pathway. miRNAs are able to affect the expression of a number of proteins at once. Therefore, miRNA networks seem to integrate cellular stress response pathways including autophagy and apoptosis, and coordinate them to shape cell faith. Our published and unpublished results allowed us to have a better picture of the miRNA networks modulating autophagic responses in human health and disease.

Protein interaction screens performed in our lab led us to discover novel proteins involved in autophagy regulation. In fact, some of these proteins were directly interacting with the core autophagy machinery components. Unexpected direct links between autophagy and other important cellular pathways were found, allowing us to reveal novel entry points for autophagy regulation and coordination in cells. Interestingly, some of this interactions seemed to be autophagy signal specific, and our work revealed novel dynamics in autophagy regulation.

Results from our recently published and unpublished studies will be presented and physiological and pathological implications of our results will be discussed.

This work was supported by The Scientific and Technological Research Council of Turkey (TUBITAK) 1001 Grant number: 114Z982 and Sabanci University.

## **IMPORTANCE OF MOLECULAR HETEROGENEITY IN CANCER MANAGEMENT**

Safiye Aktas

Dokuz Eylul University, Oncology Institute, İzmir, Turkey

Cancer develops from single cell. However, additive mutations in proliferation process, causes different cellular populations in cancer tissue or in metastases with different properties by time. This condition is called heterogeneity. Heterogeneity might be observed in two types. Intratumoral heterogeneity is existence of tumor cell populations with different characteristics in the same tumor tissue, and intertumoral heterogeneity means that the lymph node or distant organ metastasis does not show the same properties with primary tumor. Heterogeneity might be at morphologic, physiologic or molecular level. The most important properties of cancer for heterogeneity are, proliferation capacity, angiogenesis, cell surface receptor status. This situation might cause different responses of different cells to cancer therapy.

Responsiveless to therapy, drug resistance, recurrences after targeted therapies might be caused by tumor heterogeneity. Metastasis is thought to be caused by the heterogeneous cells that gained invasion and metastasis capacity. Even the metastatic cells in different locations might have different characters than the metastatic cells of other sites.

It is possible to define heterogeneity in point of view of cancer stem cells. According to cancer stem cell hypothesis, a little amount of cells in cancer tissue have cancer stem cell properties. Cancer is formed by proliferation to different differentiation of these cancer stem cells. Among these cells some stays in senescence, stop proliferation and goes to cell death. Tumor heterogeneity is in contact with tumor microenvironment. The microenvironment induces heterogeneity. In contrast, heterogeneous cells of cancer might induce different types of stroma.

To study tumor heterogeneity, microdissection of different tumor areas that we are sure of them not to be normal tissue, are needed to be compared. Microsatellite instability, fluorescent in situ hybridization to compare known molecular aberrations, sequencing for known mutations, immunoglobulin and T cell receptor analysis for hematologic malignancies are some of procedures to analyse to understand tumor heterogeneity.

Clinical aspects of tumor heterogeneity is a very important issue. The biologic crosstalks of cells with different molecular properties in the same tumor is a contemporary issue of research. Improving next generation sequencing technologies to detect tumor heterogeneity is important. Understanding and reporting the clinical importance of overload molecular data on cancer is becoming an important problem in cancer management.

## **TRANSMISSION OF MOLECULAR CHANGES TO CANCER CELLS BY EXOSOMES**

Zekiye S. Altun

*Dokuz Eylül University, Institute of Oncology, Department of Basic Oncology, İzmir*

Exosomes are small, 30-100 nm sized, cell derived extracellular vesicles that contain potential key elements to regulate intercellular communication. Extracellular vesicles or exosomes commonly used in the determination of circulating markers are small, lipid-bound spherical structures which are formed by invagination of intracellular vesicles. In many types of cancer, cancer cells secrete exosomes into body fluids and these exosomes carry a variety of nucleic acids, including miRNA, mRNA and ncRNA of tumor origin and DNA. Exosomes containing these nucleic acids have been shown to reflect the genetic condition of the tumor and carry their own cargos to the recipient cells and make phenotypic changes. They have also carrying different types of cytokines, growth factors and proteins.

Normal cells are significantly interacting by reciprocally by means of tumorigenic potential with their vesicular content and driving the molecules related to oncogenic processes such as proliferation, invasion and metastasis, or even drug resistance. Recently, exosomes have been described as a specific mediator of interactions of tumor microenvironment. Exosomes derived from tumor cells have been shown to have both pro- and anti-tumorigenic properties. Exosomes have the capability of all of the hallmarks of the cancer cell properties. Furthermore, tumor derived exosomes can interact with immune system cells to evasion from tumor immune eradication. Tissue-specific biomarkers found in tissue-specific exosomal structures can be used for diagnosis, prognosis, and monitoring of disease. Consequently, exosomes with different kind of contents can modify normal cells to transformation to cancerous cells. They also would be an ideal targets and anticancer drug delivery vehicles.



## **CURCUMIN AND RESVERATROL POTENTIATE DOXORUBICIN IN UPREGULATION OF PcG-ASSOCIATED PROTEIN RYBP AND miR-200, miR-26b IN HEPATOCELLULAR CARCINOMA**

Ahmad Bassiouny and Amira Zaky

Department of Biochemistry, Faculty of Science, Alexandria University, Egypt

Acquired resistance to doxorubicin in hepatocellular carcinoma (HCC) is a serious therapeutic problem. The aggressiveness of HCC is in part due to its intrinsic and extrinsic drug resistance characteristics, which are also associated with the acquisition of epithelial-to mesenchymal transition (EMT). Emerging evidence also suggests that the processes of EMT are regulated by the expression status of many microRNAs (miRNA). The present study aimed to investigate the combined effects of curcumin, a natural product from turmeric, and resveratrol and compared the expression of miRNAs and the expression profile of Ring1 and YY1 binding protein (RYBP), a member of the polycomb group proteins in doxorubicin-resistant hepatic cancer rats and in HepG2 cell line. The molecular targets of miR-200, miR-26b, and miR-122 were identified using a computer algorithm and confirmed experimentally. Mir-26b expression and RYBP were downregulated in HCC tissues, compared with matched adjacent non-tumor tissues as detected by reverse transcription-quantitative polymerase chain reaction. It was inversely correlated with the grade of HCC. The combination treatment with DOX elicited a synergistic antiproliferative effect in DOX-resistant rats, upregulation of miR-200, miR-26b, miR-122 and binding protein (RYBP). This was accompanied by increased expression of the epithelial marker E-cadherin and decreased expression of the mesenchymal marker vimentin and correlated with increased PcG-associated protein RYBP. The results of the present study suggested the importance of RYBP in HCC and its possible mechanism in the metastasis of HCC.

## **PREPARATION OF HIGHLY PURIFIED NUCLEAR PROTEIN EXTRACTS FROM CULTURED CELLS AND PROTEOMIC IDENTIFICATION OF NUCLEAR PROTEINS**

Murat Kasap

Kocaeli University Medical School, Department of Medical Biology

Nuclei sits at the center of cells and orchestrates many cellular events. However, in proteomic studies, its presence is always under-represented due to poor enrichment of its proteome. In this study, we enriched nuclear proteome using a novel improved approach that allowed us to study nuclear proteins. SHSY-5Y cells were grown under standart culture conditions. From these cells, nuclear protein isolations were performed using either commercially available kits or density gradient centrifugation. The purity of the nuclear protein isolations were verified using western blot analysis and antibodies against histon, GAPDH, LaminA/C and Cyclophilin. Further analysis was performed by identifying proteins from 2DE gels and MALDI-TOF/TOF. Commercially available nuclei isolation kits failed to provide highly enriched nuclear proteome. Fractions collected were contaminated with cytoplasmic proteins as demonstrated by WB analysis using anti-GAPDH antibody. Only 30% of the identified proteins from 2DE gels were nuclear. An improved method using density gradient centrifugation was developed. Fractions collected gave bands only with anti-histone and anti-laminin antibodies but not with anti-GAPDH and anti-cyclophilin antibodies. 70% of the proteins on 2DE gels were resident nuclear proteins and 10% of the proteins were predicted to be nuclear associated. In our studies, we demonstrated that although it is not possible to obtain purified nuclear protein fractions, it is possible to obtain highly enriched nuclear fractions from cells grown in culture. This new method which provided a better lysis and separation may allow comparative nuclear proteome analysis with high coverage.

## PROTEOMIC ANALYSIS OF EPITHELIAL MESENCHYMAL TRANSITION

Nurhan Özlü

Koc University, Cell Biology and Proteomics Lab, Istanbul, Turkey

Epithelial-Mesenchymal-Transition (EMT) plays an important role during carcinogenesis and tumor formation. Its major contribution to the tumor formation is through providing epithelial cells with the ability of invasion and metastasis. By this way, epithelial cells gain the capacity to disseminate from primary tumors to allow them to grow at a distant location. Cancer progression through the process of metastasis has been the focus of extensive research for years. However, the paradigms of the EMT process are less well understood. In this regard, examining the radical biochemical changes at both protein and post-translation modification levels during EMT are critically important to identify regulatory factors effecting EMT and metastatic behavior of carcinomas. In this study, we take advantage of the comparative proteomics and phosphoproteomics methods that we developed in our previous studies to comprehensively evaluate the biochemistry of a cell and its phosphorylation events as it undergoes EMT.

## INVESTIGATING NEUROLOGICAL DISEASE MECHANISMS VIA PROTEOMICS ANALYSIS

Busra Gurel<sup>1,7</sup>, Aise Rumeysa Mazi<sup>1,7</sup>, Aysegul Sumeyye Arzuman<sup>1,7</sup>, Cansu Sevinc<sup>2</sup>, Seda Kelestemur<sup>1</sup>, Busra Ocalan<sup>3</sup>, Aysen Cakır<sup>3</sup>, Sami Aydın<sup>2</sup>, Nevzat Kahveci<sup>3</sup>, Mehmet Ozansoy<sup>1,4</sup>, Mehmet Cansev<sup>3</sup>, Ozlem Taskapilioglu<sup>5</sup>, Ismail Hakki Ulus<sup>6</sup>, Betul Sahin<sup>7</sup>, Ahmet Tarik Baykal<sup>7,8</sup>.

<sup>1</sup>Regenerative and Restorative Medical Research Center, Istanbul Medipol University, Istanbul, Turkey;

<sup>2</sup>Department of Pharmacology, Faculty of Medicine, Uludag University, Bursa, Turkey

<sup>3</sup>Department of Physiology, Faculty of Medicine, Uludag University, Bursa, Turkey

<sup>4</sup>Department of Physiology, Faculty of Medicine, Medipol University, Istanbul, Turkey

<sup>5</sup>Uludag University, Faculty of Medicine, Department of Neurology, Turkey.

<sup>6</sup>Department of Pharmacology, Acibadem University School of Medicine, Istanbul, Turkey

<sup>7,8</sup>Department of Medical Biochemistry, Faculty of Medicine, Acibadem University, Istanbul, Turkey;

As the neurodynamics group we are trying to identify various pathways that can be linked to the genesis and progression of cognitive impairment. Both in-vitro and in-vivo models are incorporated in our research. Typical biological samples studied are brain extracellular matrix, serum and brain tissue. In our recent studies we extensively studied the neurological development in the 5XFAD Alzheimer's mouse model which has five of the familial disease mutations. Through label-free differential proteom analysis with nanoLC-MS/MS of the extracellular matrix and also hippocampus, cerebellum and cortex regions at different time periods of development allowed us to visualise the proteome level changes as the neurodegenerative processes develops. Cognitive impairment is measured via Morris water maze test and amyloid beta load in the brain tissue is observed with immunohistochemical analysis. The proteome difference is also visualised by principal component analysis. Here we report our results regarding the alterations in protein expressions in the early phase of Alzheimer disease genesis.

## **DISCRIMINATION OF PARATHYROID ADENOMA AND HYPERPLASIA VIA 2D BASED PROTEOMICS**

Gürler Akpınar

Kocaeli University Medical School, Kocaeli, Turkey

To understand the pathophysiology of primary hyperparathyroidism, molecular details of parathyroid hyperplasia and adenoma have to be revealed. Such details will provide the tools necessary for differentiation of these two look-alike diseases. Therefore, a comparative proteomic study using postoperative tissue samples from the parathyroid adenoma and parathyroid hyperplasia patients was performed. DIGE and 2DE proteomic approaches coupled with MALDI-TOF/TOF analysis were used to generate in depth data.

The identities of 40 regulated proteins were revealed. Fourteen of these proteins were over expressed in the hyperplasia while 26 of them were over expressed in the adenoma.

Most of the proteins over expressed in the hyperplasia samples were mitochondrial underlying the importance of the mitochondrial activity as a potential biomarker for differentiation of parathyroid hyperplasia from adenoma.

## THE EVOLUTIONARY STORY OF THE DEATH AND AGING

Ali Demirsoy

Hacettepe University, Retired Faculty Member

About 3-4 billion years ago, a lottery was made in the whole universe and probably the top bonus hit the world. This was the emergence of protein + RNA, the first self-replicating molecule.

**Bacterias:** Also today, bacteria that are accepted as an evolved extension of that time living organisms can continue their lives indefinitely by dividing into two. Therefore, life appeared without anticipating the "death" phenomenon.

**Organic formations evolve:** During this period, with some additional measures; (for example, the formation of cell membranes, the formation of some of the cell organelles, etc) evolution towards more complex structured organisms took place. The first fear that comes instinctively into the living world is fear of hunger, not fear of death.

**Chloroplast is formed:** the amount of oxygen has increased from 01% in the atmosphere to 16% in the first stages and then to 21% in the formation of black plants.

**Mitochondria are formed:** The first cells to use oxygen as an important component of their metabolism. Some oxygenated breathing bacteria later formed the ancestor of mitochondria.

**First corpse:** Current names of the partially carcass releasing unicells: Radiolaria = rays, Foraminifera = holes and Heliozoa = sunshine.

### TRANSITION TO MULTI CELLULARITY

**Germoplazma-Somatoplazma:** In order to allow selection of new phenotypes dying (disappearing) body (somatoplasma by historical definition; as well separated to the germplasm section to maintain lineage

**Telomere: emergence and novel developments**

### MAJOR REASONS OF AGING

1. Telomere formation; Termination of telomerase activity
2. Mitochondria formation and degradation by time
3. Apoptosis: Hereditary Programmed cell deaths
4. Memory formation stimulation; Arresting the division of nerve cells; Tissue differentiation
5. Physical and chemical destructors, Worn-out body cells

### TELOMERES HEREDITARY RESULTS OF CHROMOSOME FORMATION

**Short living organisms evolves -Death Genes:** Short life living creatures, such as wheatgrass, poultry, insects, etc. Diversified by evolving much faster, long-living species, fillers, eagles have entered the process of extinction.

**Examination of telomere characteristics about aging-Structure that paves the way to death:** It is a structure that causes the genome structure to be cut into chromatins and breaks down, prevents chromosomes from joining together, forms the basis for chromosome formation and chromosomal recombination.

**Human telomere:** Human beings normally have 92 telomeres in each ends of the 46 chromosomes. Each telomere consists of 5,000 to 20,000 repeating six (hexameric) TTAGGG base sequences in DNA.

- **The lifespan of a person, called fate, is determined by telomeric size to a significant extent.**
- **Telomere:** Chromosome shortening is not seen in the cells with telomerase enzyme.

#### **Telomerase activity in different organisms**

1. In yeast cells, telomerase functions continuously, allowing yeast to function with an infinite life
2. In embryonic cells, telomerase functions for a certain period of time, preventing aging
3. In cancer cells, telomerase starts to function again and causes tumor formation.

**MITOCHONDRIA:** Invoice for High Energy Achievement: Mitochondrial aging...  
Preservation of mitochondria in reproductive cells: Egg-sperm separation

#### **PROGRAMMED DEATH**

**Apoptosis: What is necrosis, what is apoptosis?** Necrosis is the result of physical injuries and is not inherited. On the other hand, pre-designed, genetically programmed death versus special developments and environmental stimuli is called as "Apoptosis".

**MEMORY AWARD "INVOICE OF LEARNING:** After transformation to multicellularity and the central nervous system was formed, another factor limiting the length of life appeared.

#### **The emergence of the nervous system:**

**The formation of the brain limits the life span:** "The first organism which experienced programmed death was known to be PLANARIA"

**PHYSICAL AND CHEMICAL EFFECTS:** Two important astronomical factors that accelerate the approach to death - LIGHT AND TEMPERATURE

**BIOLOGICAL CLOCK:** "Circadian rhythm" and "Annual rhythm".

**Fading genes:** We are losing geological accumulation...

## GASTROINTESTINAL ASPECT OF GUT-BRAIN AXIS

Neşe İmeryüz

Marmara University Pendik Research and Application Hospital, Gastroenterology Department

Gut is called as second brain because it has enormous amount of nerves within it (intrinsic nervous system), which is comparable with that of brain in terms of amount as well as kind of neurotransmitters and hormones. Because of this complex neural hardware, gut may fulfill all responsibilities as secretory, motor and absorptive organ without any support of external nerves. Gut also has the largest surface contacting environment, noxious substances, allergens and microbes, which means that is the first place of defense. These two nervous structures, brain and gut, has a bidirectional communication to adjust their own function according to current status and needs of the other organs, physical environment, food supply, content of gut lumen, energy resources and tasks and anticipations of the whole organism. Main executives of this bidirectional communication are limbic and autonomic regions of brain, autonomous nervous system, enteric nervous system, neurotransmitters, hormones, and signaling molecules. Gut structures that trigger those regulatory mechanisms are enterocytes, enteroendocrine cells, enterochromaffin cells, and immune cells via G-protein coupled taste receptors, fatty acid receptors, toll-like receptors as well as small molecules produced by commensal gut microbiota such as butyrate. In this session I will try to overview afferent limb of the gut-brain communication and I will talk about the effects of gut-derived peptides on motor and secretory function of gut.



## **KIDNEY AND EXCRETORY ASPECT OF GUT-BRAIN AXIS**

Mehmet Koç

Marmara University, Medical Faculty, Department of Internal Diseases, Nephrology, Istanbul

The gut and brain are closely connected and this interaction may directly or indirectly regulate blood pressure, renal blood flow, water intake, excretion of electrolytes and water. Cholecystokinin (CCK), gastric insulinotropic peptide (GIP), neuropeptide-Y (NPY), bombesin, calcitonin gene related peptide (CGRP), leptin, nesfatin, apelin, relaxin, vasoactive intestinal polypeptide (VIP), hydrogen sulfide, carbonmonoxide are secreted from or produced within the gut lumen. Some of these hormones have direct effects on their specific receptors in the brain and kidney. Activation of these receptors specially affects the renal circulation, systemic blood pressure and excretory functions of the kidney. Some of these molecules activates paraventricular nucleus of hypothalamus via nuclei of vagus nerve which in turn alters renal sympathetic nerve activity.

In this talk, I mention about the gut originated neurobiological, endocrine and paracrine mechanisms affecting the kidney functions.

## **MOLECULAR INFORMATION PROCESSING: DATA MINING TECHNIQUES TO DETECT CANCER WITH ODOR ANALYSIS**

Serkan Türkeli<sup>1</sup>, Büşra Bayat<sup>2</sup>

1 İstanbul Technical University - Control and Automation Engineering Department

2 İstanbul Technical University – Chemistry Department

Our body consist of more than one hundred trillion cells. Cancer is the abnormal cell division in an uncontrolled manner. Mostly, cancer starts with one or a small group of cells. Unlike the belief that body cannot protect itself against the cancer, our immune system is capable of identify self and non-self materials such as cancer. However, it is not always possible to keep up with high division rate of cancerous cells. For that reason, there are some researches about identifying the cancer before it spreads out with the help of sensors. One of the studies focused on an electronic nose which is intended to detect cancer using the mechanism of recognizing odors and flavors. Still, describing an odor and finding the similarities is a difficult process. The purpose of this study is to explain how to detect cancers with sensors by analyzing of odors via molecular level.

## **PREDICTIVE AND PREVENTIVE VALUE OF AMINO ACIDS IN TYPE 2 DIABETES**

Aydın Duygu

Doctors Medical Center, Istanbul, Turkey

The prevalence of type 2 diabetes is apparently increasing despite the lifestyle change is well known and the most efficient clinical approach for the prevention of this pandemic. Since insulin resistance is established years before onset of type 2 diabetes, lifestyle changing may become more challenging. On the other hand it shouldn't be underestimated that intensive glucose control in patients with poorly controlled type 2 diabetes had no significant effect on the rates of major cardiovascular events, death according to studies conducted by ADVANCE Collaborative Group and VADT Investigators and published in N Engl J Med 2008 and 2009 respectively. Therefore it should be an imperative priority to develop novel predictive markers for insulin resistance and diabetes in order to ensure lifestyle changes are applicable.

Increased numbers of clinical studies reveal plasma free amino acid profiles have potential as biomarkers for assessing diabetes and related cardiovascular risk. Moreover, essential amino acid dense nutrition or specific amino acid supplementation may provide additional benefits in the management of type 2 diabetes.

To engage amino acid analysis and essential amino acid based nutrition into the clinical practice of primary health cares may be an effective method to prevent or slow down spreading of type 2 diabetes.

## REGULATION OF INSULIN TRANSCRIPTION BY CALCIUM-BINDING PROTEINS DREAM/CALSENILIN AND SECRETAGOGIN

Teodora Daneva

Institute of Biology and Immunology of Reproduction "Acad. Kiril Bratanov", Bulgarian Academy of Sciences, Sofia, Bulgaria

Pancreatic beta cells are the alone cells producing insulin in the mammalian body. Several proteins are involved in the process of insulin transcription, in particular calcium-binding proteins with typical EF-hand motives. Two of these EF-hand proteins are DREAM/Calsenilin and Secretagogin.

Downstream regulatory element antagonist modulator (DREAM) is known to be a 4-EF-hands DNA-binding transcriptional regulator. We found it to be present in pancreatic beta cells and in insulinoma cells. The expression of DREAM in  $\beta$ -cells in the islets of Langerhans regulates the promoter activity of the insulin gene by directly interacting with the sequence located between +52 bp and +81 bp downstream of the transcriptional start site of the promoter.

Secretagogin is 6-EF-hands expressed in the islet of Langerhans and various neuroendocrine cells. We found two variants of Secretagogin which differ by one amino acid at position 22. The most frequent version has glutamine (Q) at position 22, while in the other version this amino acid is arginine (R). We have found that this variation is due to mRNA editing at the posttranscriptional level, which results in a Q/R exchange at amino acid 22. The functional difference of Secretagogin-R22 versus Secretagogin-Q22 was then investigated. It was found that Secretagogin-R22 stimulates insulin transcription when measured by human insulin promoter driven luciferase assays whereas Secretagogin-Q22 has no effect. A third variant of Secretagogin (Setagin) consists of 49 amino acids. Due to a frame shift, only the first 27 amino acids are identical to secretagogin. We demonstrate that this protein truncation results in complete loss of the calcium binding capacity. Whereas Secretagogin-Q22 and Secretagogin-R22 were also found in the central nervous system and organs containing neuroendocrine cells Setagin expression was found restricted in the pancreas.

Our results suggest potential role of the naturally occurring Secretagogin variants in the regulation of calcium-sensitive insulin transcription in pancreatic beta cells. It was suggested that the different effect on insulin transcription is a result of difference between the intracellular proteins interacting with Secretagogin variants. This was elucidated using two-dimensional gel electrophoresis.

## **ANOCTAMIN 1, CANDIDATE ANIONIC CHANNEL SENSITIVE TO CELL VOLUME IN INSULIN-PRODUCING CELLS**

Willy J. Malaisse

Department of Biochemistry, Université Libre de Bruxelles, Brussels, Belgium

It is proposed that anoctamin 1 represents a candidate as an anionic channel sensitive to cell volume in insulin-producing cells. Such a proposal is based on experimental findings concerning (i) the expression of the RNA messenger for this protein and its presence documented by immunochemistry in pancreatic islets, (ii) the effect of tannic acid and another inhibitor of anoctamin 1 (T16A inh-A01) upon the volume of islet cells, the secretion of insulin, the metabolism of D-glucose in pancreatic islets, the bioelectrical activity of beta cells and the transport of chloride anions activated by calcium via channels present in plasma membrane fragments obtained from pancreatic islet beta cells.

## GUT MICROBIOTA MODULATION

Tarkan Karakan

Gazi University, Department of Gastroenterology, Ankara, Turkey

Human beings and gut microbiota are in a symbiotic relationship, and the hypothesis of a “super organism” composed of the human organism and microbes has been recently proposed. The gut microbiota fulfills important metabolic and immunological tasks, and the impairment of its composition might alter homeostasis and lead to the development of microbiota-related diseases. The most common illnesses associated with alterations of the gut microbiota include inflammatory bowel disease, gastroenteric infections, irritable bowel syndrome and other gastrointestinal functional diseases, colorectal cancer, metabolic syndrome and obesity, liver diseases, allergic diseases, and neurological diseases such as autism. In theory, every disease associated with the impairment of intestinal microflora might benefit from the therapeutic modulation of the gut microbiota. A number of attempts to manipulate the microbiota have not produced identical results for every disease. Although antibiotics and probiotics have been available for a long time, the so-called fecal microbiota transplantation, which is a very old remedy, was only recently re-evaluated as a promising therapeutic approach for microbiota impairment. A comprehensive understanding of the gut microbiota composition, in states of both health and various diseases, is needed for the development of future approaches for microbiota modulation and for developing targeted therapies.

The modulation of gut microbiota is perhaps an ancestral, innate concept for human beings. At this time, the restoration of gut microbiota impairment is a well-established concept in mainstream medicine, and several therapeutic approaches have been developed in this regard. Antibiotics, prebiotics and probiotics are the best known and commercially available options to overcome gastrointestinal dysbiosis. Fecal microbiota transplantation is an old procedure that has recently become popular again.

### **Probiotics and prebiotics**

According to the 2001 FAO/WHO definition, probiotics are “live micro-organisms, which when administered in adequate amounts confer a health benefit on the host”. The rationale for the use of probiotics for the treatment of gut microbiota-related disease is the restoration of intestinal homeostasis by beneficial microbes. Most probiotics consist of Lactobacilli and Bifidobacteria, but also yeasts such as *Saccharomyces boulardii* have been used with good outcomes.

Prebiotics were defined for the first time in 1995 by Gibson and Roberfroid as “non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth or activity of one of a limited number of bacterial species already present in the colon, thus improving host health.” To include other fields that may profit by prebiotic action this definition has been renewed by Roberfroid in 2007: “A prebiotic is a selectively fermented ingredient that allows specific changes, both in the composition or activity in the gastrointestinal microflora that confer benefits upon host well-being and health”. To be classified as a prebiotic, a food ingredient needs to fulfill the following criteria: resistance to gastric acid secretion and to hydrolysis by digestive enzymes; absorption in the upper gastrointestinal tract and fermentation by the intestinal gut microbiota; and stimulation of the growth or activity of beneficial microbes.

### **Fecal microbiota transplantation (FMT)**

FMT, also known as “fecal infusion” or “fecal bacteriotherapy”, refers to the introduction of a liquid filtrate of stools from a healthy donor into the gastrointestinal tract of a patient for the treatment of specific diseases. The administration of feces for therapeutic purposes was first

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described more than 1,500 years ago by Ge Hong. FMT came to the attention of mainstream medical science only in the late 50's: in 1958, Eiseman, a surgeon from Colorado, successfully treated four patients with pseudomembranous colitis using fecal enemas. Both the rising epidemic of *C. difficile* infection and the growing scientific interest toward the gut microbiota have recently led to the renewal of FMT. FDA approved FMT in resistant *C. difficile* infections. However, there are other experimental applications of FMT, mainly in IBD, metabolic diseases (obesity, Diabetes mellitus, insulin resistance), intractable antibiotic-associated diarrhea, constipation, IBS, psychiatric diseases, neurodegenerative diseases (Multiple sclerosis, Alzheimer disease, ALS) and autism. Even there are case series for Graft vs host disease and FMT.

As a result, future holds potential for application of these microbiome therapies in various disease states. However, there are still plenty of issues that should be clarified.

## GUT MICROBIOTA, OBESITY AND POPULAR DIETS

Banu Çaycı

Gazi University Faculty of Medicine ,Dept. of Biochemistry, Ankara, Turkey

Gut microbiota affect energy balance, inflammation state and gut barrier function, as well as integrate peripheral and central food intake regulatory signals leading to an increase in body weight. Recent evidence suggests that gut microbiota is involved in the control of body weight, energy homeostasis and inflammation, and thus plays a role in the pathophysiology of obesity. An important role of intestinal microbiota is synthesis of various biomolecules. For instance, microflora produces wide range of vitamins (C, B, folate and niacin) and essential amino acids and facilitates their absorption. Flora also promotes better absorption of calcium and vitamin D. Diet has a large role in the determination of the composition of the gut microbiota. The gut microbiota is composed of two dominant phyla, which make up over 99 % of the diversity in the distal gut and faecal bacteria: Firmicutes and Bacteroidetes. In healthy adults the ratio of Firmicutes to Bacteroidetes was reported as 10.9/1. Many studies have linked a prolonged consumption of a high-fat diet to gut microbiota changes or gut dysbiosis. The consumption of a diet high in carbohydrate but low in fat resulted in a marked increase in the faecal *Bifidobacterium* spp. numbers. High carbohydrate together with a high glycemic index diet showed a correlation with an increase in faecal Bacteroidetes, whilst a high carbohydrate but low glycemic diet led to an enhanced growth of *Faecalibacterium prausnitzii*. High-fat diets modulate the microbiome composition to increase circulatory lipopolysaccharides coinciding with general inflammation. General dysbiosis within the gut is associated with a high level of plasma endotoxin and inflammation that eventually promotes metabolic disorder. The gut microbiota that digests complex dietary carbohydrates produces many monosaccharides and short-chain fatty acids (SCFAs) such as acetate, propionate, and butyrate which are an important energy source and nutrition of the intestinal epithelium. SCFAs act in the gut as signaling molecules and are specific ligands for at least two G protein-coupled receptors, GPR41 and GPR43, mainly expressed in intestinal epithelial cells. Gpr41, which is produced by enteroendocrine cells, may be a regulator of host energy balance through effects that are dependent on gut microbiota. Activation of GPR41 increases production of peptide YY (PYY), an enteroendocrine cell hormone that normally inhibits gut motility, increases intestinal transit rate and reduces extraction of energy from the diet, thus affecting peripheral glucose utilization. Recent study has shown that Gpr43<sup>-/-</sup> mice are resistant to diet-induced obesity and insulin resistance, at least partly due to Gpr43-regulated energy expenditure. Additionally, gut microbes enhance the intestinal barrier and help eliminate potential pathogens. Prebiotics and probiotics are of interest because they have been shown to alter the composition of gut microbiota and to affect food intake, appetite, body weight and composition as well as metabolic functions through gastrointestinal pathways and modulation of the gut bacterial community.

The most frequent cause leading to the obesity development is a dysbalance between energy intake and energy expenditure. In this complex process, genetic susceptibility, environmental and lifestyle factors are involved.

the microbiota of the human gut responds rapidly to large changes in diet. A particular change in diet can have a highly variable effect on different people owing to the individualized nature of their gut microbiota.

Anaerobic bacteria synthesize biologically active substances:  $\beta$ -alanine, 5-aminovaleric and  $\gamma$ -aminobutyric acid

Normal flora of the human body participates in the metabolism of proteins, carbohydrates, lipids and



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nucleic acids; breaks down cellulose; provides epithelium with substrates of gluconeogenesis and lipogenesis; and stimulates intestinal motility monosaccharides that are produced by micro- bial fermentation and absorbed and transferred to the liver via portal vein, activate ChREBP which increases the transcription of several proteins involved in hepatic de novo lipogenesis [39]. This contributes to hepatic steatosis.

Non-digestible carbohydrates include plant-derived fibers such as xylans, cellulose, inulin, and resistant starch. GM degrades these carbohydrates for harvesting energy and providing the host with a variety of metabolites such as short-chain fatty acids (SCFAs) propionate, acetate, and butyrate. These SCFAs affect glucose, cholesterol, and lipid metabolism in different body tissues. The type of food intake by the human host influences the GM composition and diversity. The western diet (high fat) results in a reduction of Bacteroidetes and an increase in Firmicutes, especially Mollicutes .Accordingly, obese individuals are known to have a microbiota rich in Firmicutes and lower in Bacteroidetes as compared to the GM of lean individuals.

## MICROBIOME-BASED DISEASE BIOMARKERS

Süleyman Yıldırım

Istanbul Medipol University, International School of Medicine , Department of Medical Microbiology

Humans are associated with trillions of microbial cells and viruses. The dynamic gene repertoire of these microbes in a particular host niche makes up the human microbiome, which is considered as the second genome of humans. Remarkably, this non-human gene repertoire in human body recently estimated to constitute approximately two orders of magnitude more genes than that of human host, providing paradoxical resource for molecular medicine; enormously untapped yet largely uncharted gene abundance and metabolites produced by these genes. Thus, this vastly under-explored and diverse microbial world associated with the human host makes attractive target for diagnostic and therapeutic approaches in modern medicine. Biomarkers are of crucial importance in healthcare, which provide physicians with measurable indicators to diagnose a disease, to assess probable effect of treatment on patient or to monitor progress of the disease. The genomes of microbial species, both their sheer abundance within the microbial community, per se, and the genes, the pathways, and the metabolites resulting from these genomes hold untapped potential to become a new kind of biomarkers or otherwise to add value to classical clinical biomarkers in healthcare settings.

In this talk, I will briefly review recent scientific literature revolving around microbiome based novel biomarkers with a particular focus on neurodegenerative diseases, such as Alzheimer's and Parkinson's diseases. I will also describe the ongoing projects relevant to the topic in my lab and present preliminary results.

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## **HUMAN MICROBIOME AND AUTOIMMUNE DISEASES**

Christina Tsigalou

Biopathology Laboratory, University General Hospital of Alexandroupolis, Democritus University of Thrace, Dragana-Alexandroupolis 68100, Greece

Nowadays it is well established from numerous studies that the etiopathology of autoimmune diseases is multifactorial including genetics and environmental factors. On the other hand, especially the last decade, new technologies have accomplished to offer a bulk of information considering the microbiomes of human body sites. Autoimmune and inflammatory rheumatic diseases are characterized by dysbiosis of the microbiome. Recently there has been an augmented interest in the involvement of the microbiota in the pathogenesis of autoimmunity, although it is not clear yet the exact relationship of the cause and the consequence. It is more than obvious the need of broader studies to elucidate the true contribution of the microbiome to the onset, symptoms, progression and therapy for autoimmune diseases.

## **NANOCARRIERS AND TARGETED DRUG DELIVERY FOR CANCER**

Sevil Dinçer İsoğlu

Abdullah Gül University, Bioengineering Department

There are several barriers that drug molecules encountered in body beginning from kidney filtration and RES clearance to cellular trafficking. Nanocarriers have potential for the delivery of drugs by enhancing diagnostic and therapeutic activity of existing methodologies, because they possess several distinct features to overcome the obstacles mentioned above. These features bringing various physicochemical characteristics in nanocarriers include size, surface area, stability and targeting. For instance, small size allows ease of integration into physiological processes such as cell entrance and migration. High stability is critical for systemic administration and can be enhanced by hydrophilic coating with PEG, which increase blood-circulation time. Nanocarriers have advantage to be used in active targeting as well as passive targeting, which is based on EPR effect. In active targeting, the surface of nanomaterial is decorated with specific ligands recognizing membrane receptors allowing carrier to reach desired site of the body. A variety of nanocarriers are constructed by different material types, which have unique physicochemical properties for specific applications. These platforms include liposomes, inorganic particles, dendrimers, nanoparticles, micelles and stimuli-responsive systems. FDA approved nanocarrier/drug formulations, which are commercially available, exist in the form of micelles or liposomes and, many more nanotechnology-based drug formulations are under clinical phase recently. Note that, further research is required to reach the most effective and safe systems.

## **SYNTHESIS AND CHARACTERIZATION OF NANOMATERIALS FOR HEALTH APPLICATIONS**

Cengiz Kaya

Materials Science and Nanoengineering, Faculty of Engineering and Natural Sciences, Sabanci University, Tuzla, Istanbul, Turkey

Various oxide based nanostructures, such as ZnO, TiO<sub>2</sub>, CuO, Ag-TiO<sub>2</sub> and Fe<sub>3</sub>O<sub>4</sub> were synthesized with different morphologies using hydrothermal processing. Structure and morphology of the nanostructures were controlled by altering processing conditions. Carbon coated iron oxide nanoparticles were also synthesized by addition of hydrocarbons like glucose and ascorbic acid and characterized in detail. It is shown that the resultant products properties are effected from the initial concentration of raw materials.

Nano size Ag-TiO<sub>2</sub> composite particles with various Ag contents were also synthesized at 180 °C for 2h. The effects of Ag content on the particle size, structure and morphology of the synthesized particles were investigated. Stable ethanol based colloidal suspensions containing Ag-TiO<sub>2</sub> particles were prepared and coated onto 3-D metallic filters by electrophoretic deposition (EPD) using a deposition time of 5 min. and an applied voltage of 30 V D.C. It is shown that the particle size of Ag-TiO<sub>2</sub> is increased with increased Ag content and with the addition of 15 wt.% Ag to TiO<sub>2</sub> changes the spherical morphology into needle-like shape. It is shown that all of the nanostructured materials have strong antimicrobial behavior.

## EMERGING TECHNOLOGIES IN CANCER DIAGNOSIS AND TREATMENT

İsa Yıldırım

Istanbul Technical University, Electronics and Communication Engineering Dep., Istanbul, Turkey

The use of nano particles (NPs) in cancer imaging and therapeutic applications has shown great progress over the last decade. NPs with less than  $1\mu\text{m}$  size have an ability to travel through blood vessels and capillaries ranging in  $3\text{-}8\mu\text{m}$ . Multi shell magnetic smart NPs having a magnetic core and a metallic shell show an ability to provide MR contrast between malign and benign tissues providing early diagnosis. In addition to contrasting ability, targeting, accumulation, heating and/or retrieving at the end of therapy are also possible with an externally applied magnetic field. Thermal therapy activated by externally applied magnetic field may generate heating above body temperature, thus killing the malignant cells by denaturation. The effective use of magnetic NPs in thermal therapy depends on maximizing localized magnetic NP heating while not damaging healthy tissues surrounding cancerous cells. Additionally, NPs having high  $Z$  ions can be used as contrast agent in CT imaging along with x-ray driven radiotherapy. From all these aspects, these NPs will be multi functional providing early diagnosis and therapy of cancers, with their sensitivity to the interaction with magnetic field and x-ray radiation.

## **GENOMICS IN PRECISION MEDICINE: CURRENT STATUS & FUTURE PROSPECTS**

Suresh C. Jhanwar

Memorial Sloan-Kettering Cancer Center, Departments of Pathology & Medicine, 1275 York Avenue, New York, NY-10065, USA

Cancer as a genetic disease is by now well recognized. Genomic analysis of cancer cells, therefore, has greatly enhanced our ability to identify genetic alterations associated with various cancer types, including both lympho-hematopoietic as well as solid tumors. Chronic myeloid leukemia (CML), based on the specific diagnostic genetic abnormality has served as a prototype disease to clearly demonstrate the significance of the genomic analysis of cancer in identifying targeted therapy. Such a success has provided extraordinary opportunities to investigate the role of genetic abnormalities and the pathways amenable to targeted therapy, not only in blood cancers but solid tumors such as Lung, colon, Renal, Breast carcinomas as well as other epithelial and mesenchymal tumors. The main focus of this presentation is to illustrate the role of genomic analysis in targeting lung cancer, based on abnormalities or the pathways deregulated in tumor cells from individual patients. Lung cancer is one of the most common epithelial cancers associated with cigarette smoking and other environmental carcinogens. According to current estimates, 1.3 million cases of lung cancer are expected to be diagnosed worldwide annually, resulting in one million deaths annually. Since the discovery that patients' tumors with specific mutations in the EGFR may be sensitive to targeted therapeutic approach and the subsequent realization that such mutations in the gene are not as prevalent, several cancer centers including ours initiated intense efforts to find other mutations or genomic alterations, which may serve as targets of specific therapy. Such efforts have successfully resulted in a battery of genes such as KRAS, ALK, C-MET, HER-2/neu, ROS1, etc, which have helped oncologists to triage the patients for personalized therapies. A significant proportion of patients with lung cancer, however, do not show any of the above genetic abnormalities.

Approximately 90% of lung cancers exhibit RB1 mutation/deletion and/or KRAS mutations, therefore, the signaling pathways, which regulate multistep tumorigenesis in lung cancer, are important for the treatment of histologic subtypes of lung cancer, which includes NSCLC & SCLC. Equally important was the findings that similar signaling pathways are also shared by other solid tumor types including colon cancer. We have investigated the role of these pathways to target these cancers and develop new strategies to treat lung, and related cancers. In addition, our translational studies in other tumor types such as NF2 related malignancies, Glioblastoma and renal cancer revealed pathways amenable to targeted therapies. Selected examples representing each of these tumor types will be discussed to illustrate the critical role of translational research in developing novel therapeutic approaches for the successful and durable responses in some of these cancer types.

## ISOCITRATE DEHYDROGENASE MUTATION IN CANCER AND PROGRESS TOWARD DEVELOPMENT OF TARGETED THERAPEUTICS

Hüray İşlekel<sup>1,2</sup>

<sup>1</sup>Dokuz Eylül University, Institute of Health Sciences, Molecular Medicine Dept.

<sup>2</sup>Dokuz Eylül University School of Medicine Medical Biochemistry Dept. İzmir/Turkey

Isocitrate dehydrogenase 1 and 2 (IDH1 and IDH2) are key metabolic enzymes that reversibly convert isocitrate to  $\alpha$ -ketoglutarate ( $\alpha$ KG) with concomitant reduction of NADH to NADPH in the cytoplasm and mitochondria respectively. Somatic heterozygous hotspot IDH1 and IDH2 mutations have been identified in various tumor types, including gliomas (80%), myeloid malignancies (20%) such as acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS), colangiocarcinoma (20%), condrosarcoma (60%) and others. IDH1 and IDH2 mutations cause enzymatic loss of wild type functions. In addition mutant IDH gain a neoenzymatic (gain of function) activity resulting in the conversion of  $\alpha$ KG and NADPH to the oncometabolite, D-2-hydroxyglutarate (2-HG) and NADP. The subsequent accumulation of 2-HG results in epigenetic dysregulation via inhibition of  $\alpha$ KG-dependent histone and DNA demethylases, and a block in cellular differentiation. IDH1 mutations were initially reported in 2009 in a small number of glial tumors and it was noted that the glioblastomas harbouring IDH 1 mutations were mostly secondary glioblastomas (those that had arisen through progression of a lower grade glioma), occurred mostly in younger patients and were associated with higher survival rate. The most common mutation is R132H (arginine to histidine) which is observed in 80-90% of IDH1 mutations. There is now growing preclinical and clinical evidence suggesting that IDH mutations are involved in neoplasia. Furthermore, preclinical studies assessing small molecule inhibitors of mutant IDH1/2 enzymes have provided proof of concept that this approach decreases intracellular 2-HG levels, reverses epigenetic dysregulation and induces cellular differentiation. Phase I studies of mutant IDH inhibitors are currently ongoing in patients with IDH-mutant hematologic and solid tumors. Inhibition of mutant IDH shows promise as a treatment approach in hematologic malignancies, with further development ongoing in solid tumors and glioma. The mutant IDH inhibitors may have clinical utility both as single agents and in combination strategies that target additional oncogenic pathways. However, care should be taken while using these agents in radiotherapy patients since they may limit irradiation efficacy.



## ROLE OF SURGEON IN TARGETED MEDICINE

Akif Turna

Department of Thoracic Surgery, Cerrahpasa Medical Faculty, Istanbul University, Istanbul

Lung cancer has recently become the number-one cause of cancer deaths worldwide. The predicted death from non-small cell lung cancer is 155 870 in 2017 in USA. Patients with metastasis or N2/3 disease have dismal prognosis and resectional surgery is generally futile in these subsets. On the another hand, earliest stages indicated better survivals which were not satisfactory. Patients with cIA tumor have 61% 5-year survival, whereas the 5-year survival of cases with pIA tumors is 67%. Despite all anatomic parameters, 'non-anatomic' parameters can be proposed to be important in predicting survival of patients with non-small cell lung cancer. We firstly introduced the importance of perineural invasion. Certain histopathological factors such as histological type, grade, lymphatic invasion, blood vessel invasion, necrosis were found to be prognosticators in some studies. Blood vessel invasion and lymphatic vessel invasion have been reported to be important prognostic factors in patients with resected NSCLC with intrapulmonary metastases. The most of the research with regard to the association between many different biologic and/or histologic markers and prognosis in NSCLC emphasizes the potential contribution of markers to understanding the heterogeneity of survival patterns for specific anatomic and histologic subsets of patients with this disease. In addition, epigenetic changes may have occurred that are important in the tumorigenesis process, including changes in expression of genes encoding growth factor receptors (e.g., HER-2/neu and epidermal growth factor receptor[EGFR], MET, hepatocyte growth factor receptor, and insulin-like growth factor genes); BCL-2 and the telomerase gene. Today, EGFR, ROS and ALK mutations are of great importance for indicating the necessity of new targeted agents. In the growing era of personalized medicine for the treatment of NSCLC, it has been becoming increasingly important that sufficient quality and quantity of tumor tissue are available for morphologic diagnosis and molecular analysis. As new treatment options emerge that might require more frequent and possibly higher volume biopsies, the role of the thoracic surgeon will expand, and it will be important for thoracic surgeon to work within a multidisciplinary team to provide optimal therapeutic management for patients with NSCLC.

As conclusion, it has become obvious that, the current staging system for resected NSCLC despite its wide acceptance, is far from perfection. In addition to accepted TNM system, many authors emphasize the importance of molecular and histopathological factors in prognosis prediction in patients with NSCLC and also, thoracic surgeon's role in providing tissue is crucial in order to offer targeted therapies to the patients. It is invaluable that, thoracic surgeon should acknowledge the new molecular treatment options in addition to 'state-of-the-art' surgical interventions.

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## ORAL PRESENTATION

## ORAL PRESENTATION – 01

### THE EFFECTS OF DOCETAXEL WITH INSULIN IN ER (+) BREAST CANCER CELLS ON CELLULAR TOXICITY AND MOLECULAR MECHANISM

Duygu Aygüneş<sup>1</sup>, Hale Güler Kara<sup>1</sup>, Aslı Tetik Vardarlı<sup>1</sup>, Canfeza Sezgin<sup>2</sup>

<sup>1</sup> : Ege University, Medical Faculty, Medical Biology Department

<sup>2</sup> : Biruni University, Medical Faculty, Department of Internal Diseases

**Background / Aim:** Changes in glucose metabolism in the cells are one of the important issues investigated in many diseases, including cancer, in recent years. It is known that insulin, which is one of the primary elements in glucose regulation, plays an active role in the course of many diseases besides diabetics.

We aimed to investigate the effects of insulin with docetaxel in the MCF-7 breast cancer cell lines as an ER (+) breast cancer model, in order to determine the changes in the use of insulin in combination with chemotherapy. Accordingly, the effects of different doses of insulin (2,5 to 20 µg / mL) in combination with different doses of docetaxel (32,5 to 130 nM) were compared to only with insulin or docetaxel treated cells. Untreated cells were accepted as controls.

**Materials and Methods:** xCELLigence Real-Time Cell Analysis System was performed to measure cell toxicity and viability. Gene expression analysis with RT-QPCR was performed to understand the molecular mechanism underlying changes in the cells.

**Results:** In our study, it was found that low-dose insulin with docetaxel was significantly cytotoxic compared to only docetaxel-treated, high-dose insulin with docetaxel-treated and insulin-only groups in the MCF-7 breast cancer cell line.

RT-QPCR analysis was performed to investigate which molecular mechanisms triggered the cells when docetaxel with low dose insulin, which was more favorable than docetaxel alone. Accordingly, in the low dose insulin and docetaxel group, significant gene expression differences were found in the AKT1, BRCA1, CDH1, APAF1, MYC, CDKN1C, PTEN, EGFR, MAPK1 and BIRC5 genes according to the only docetaxel group.

**Discussion and Conclusion:** Our study is the first study in Turkey that combines insulin with chemotherapeutics. Together with this study, it has been shown that low doses of insulin in combination with chemotherapeutics may positively affect disease progression in ER (+) breast cancer.

*Keywords: Insulin, docetaxel, MCF-7, breast cancer*

## ORAL PRESENTATION – 02

### DOWN-REGULATION OF ANNEXIN I IS CORRELATED WITH INFLAMMATORY MEDIATORS IN COLORECTAL CARCINOMA

Filiz Bakar<sup>1</sup>, Dilsa Mizrak<sup>2</sup>

<sup>1</sup> : Ankara University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey

<sup>2</sup> : The University of Texas M.D. Anderson Cancer Center, Department of Gastrointestinal Medical Oncology Houston, TX, USA

**Background:** Colorectal cancer is one of the most common malignancies worldwide and the epidemiological studies report that colorectal cancer renders 9% of cancer related mortalities. The relation between inflammation and cancer has long been reported in several studies. In the last decades, the researchers have identified a new protein family called Annexins and among the members of the family, annexin-1 has been shown to have effects on inhibition of the synthesis of PLA<sub>2</sub> and eicosanoids. At present study, we aimed to evaluate the relation of Anx1 protein with inflammatory microenvironment of patients with colorectal cancer.

**Materials and Methods:** 114 patients who were diagnosed as colorectal cancer and 98 healthy volunteers as control were included for this study. The mRNA expression of Annexin I and PLA<sub>2</sub> were analyzed by Real Time PCR technique. The correlation analyses between Annexin I plasma levels and IL-6, cPLA<sub>2</sub>, sPLA<sub>2</sub> and Interleukins were also performed.

**Results:** Annexin I was downregulated in patient group with 0.3914 fold change when compared to control (p<0.0001). PLA<sub>2</sub> mRNA expression was also lower than control (p=0.001). The decrease of Annexin I plasma levels in patient group was significantly correlated with the increase of interleukin-1 $\alpha$  and interleukin-6 and prostaglandine-E<sub>2</sub> levels (p<0.05).

**Discussion:** The inflammation-cancer relation theory is based on the observations such the formation of tumors in chronic inflammation sites, the existence of inflammatory cells, chemokines and cytokines in tumor tissues, the activation and/or inhibition of some molecular targets or similar pathways in both inflammation and carcinogenesis processes. The studies have shown that some members of Annexin family display antiinflammatory effects which explained with a membrane-substrate interaction process since annexins compete with PLA<sub>2</sub> on membrane binding process and thus decrease the consumption of substrate. We also observed a significant alteration on prostaglandine mRNA levels inversely correlated with the increase of plasma levels of prostaglandine E<sub>2</sub> metabolites.

**Conclusion:** At present study, the colorectal cancer has been evaluated for several inflammatory markers and Annexin I protein has been shown to contribute to the inflammatory state of colorectal cancer.

*Keywords: Annexin I, Inflammation, Colorectal Cancer, PLA<sub>2</sub>, Interleukins*

*Note to the Scientific Committee: This study was supported by Ankara University Research Foundation (2015-13B3336002).*

## ORAL PRESENTATION – 03

### AUTOPHAGY ANALYSIS OF TUMOR-FIBROBLASTS CROSSTALK ON BIOCHIPS

Hacer Ezgi Karakas<sup>a,1</sup>, Junyoung Kim<sup>b,1</sup>, Juhee Park<sup>c</sup>, Jung Min Oh<sup>c</sup>, Yongjun Choi<sup>b,c</sup>, Devrim Gozuacik<sup>a,d,2</sup>, Yoon-Kyoung Cho<sup>c,b,2</sup>

<sup>a</sup> Sabanci University, Istanbul, Turkey

<sup>b</sup> UNIST, Ulsan, Republic of Korea

<sup>c</sup> IBS, Ulsan, Republic of Korea

<sup>d</sup> EFSUN Nano Diagnostics Center of Excellence, Sabanci University, Istanbul, Turkey

<sup>1</sup> These authors contributed equally to this work.

<sup>2</sup> Corresponding authors: dgozuacik@sabanciuniv.edu and ykcho@unist.ac.kr

**Background/Aim :** Autophagy is an evolutionary conserved stress response mechanism which creates alternative sources of building blocks and energy to cells. Although induced autophagy in fibroblasts, major component of stroma, has an important role for the proliferation and metastasis of cancer, initial signal(s) of induced autophagy in fibroblasts during their crosstalk with cancer cells is not clearly understood, yet. Here, we present a biochip system to mimic a simple tumor microenvironment and to monitor communication between cancer-fibroblasts through modulation of autophagy.

**Materials & Methods :** In this study, transgenic GFP-LC3 mouse embryonic fibroblast (MEF) cells and stably RFP expressing MDA-MB-231 (MDA) breast cancer cells were used. For autophagy analysis under microscope, over 20 GFP-LC3 dots per MEFs was called as GFP-LC3 dot positive cells. Biocompatibility and autophagy analysis of PDMS membrane in biochip was performed with live/death assay and autophagy analysis methods.  $1.0 \times 10^4$  MDA cells, infected with shGFP (CNT) or shTGF $\beta$ 1 viruses, were loaded on the top reservoir of biochip and cells were trapped into the pore by shaking motion and suction pressure. Trapped MDA cells were arrayed on a MEF monolayer and autophagy analysis was performed using Nikon A1R microscope.

**Results & Discussion:** Transforming growth factor (TGF $\beta$ 1) was tested as a communication signal between cancer-fibroblasts. First, effect of TGF $\beta$ 1 on autophagy in MEFs was analyzed using microscope and immunoblot analysis. According to our results, autophagy in fibroblasts was induced in the presence of TGF $\beta$ 1 and was kept basal level in the absence of TGF $\beta$ 1. Next, autophagy in MEFs around single MDA-trapped or empty holes in biochip systems was analyzed. Captured single MDA cells induce autophagy in fibroblast cells near to the holes. To test the biochip system for screening, the effect of mixed CNT-MDA and shTGF $\beta$ 1-MDA cancer cells on autophagy in fibroblast cells was tested in biochip system. CNT-MDA cells induced autophagy in fibroblast cells around the holes upto 40%. shTGF $\beta$ 1-MDA cells have caused basal autophagy level in surrounding fibroblast cells similar to empty hole result. Genomic DNA analysis confirmed the unbiased screening result with 81% accuracy. These results showed that specificity of TGF $\beta$ 1-induced autophagy was 90%. Due to allowing cancer cells retrieval back from chip system, this biochip system is suitable for large-scale unbiased omics such as single cell genomic, transcriptomics and even metabolomics analysis.

**Conclusion:** We propose that our biochip platform can be used as a promising tool for autophagy quantification during tumor-stroma interaction, especially for high-throughput screening of paracrine factors that are secreted from heterogeneous tumor cell populations.

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*Keywords: Autophagy, TGF $\beta$ 1, tumor, fibroblasts, biochip*

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## ORAL PRESENTATION – 04

### INVESTIGATION OF CYTOTOXIC, APOPTOTIC AND MOLECULAR EFFECTS OF ASTAXANTHIN AND NOCODAZOLE IN MCF-7 CELL LINES

Hale Güler Kara<sup>1</sup>, Pinar Buket Atalay<sup>2</sup>, Duygu Aygüneş<sup>1</sup>

<sup>1</sup> Ege University, Medical Faculty, Medical Biology Department

<sup>2</sup> Maltepe University, Medical Faculty, Medical Biology Department

**Background / Aim:** Breast cancer is a complex disease with different clinical, histopathological and molecular backgrounds and it is known as the second cause of cancer-related deaths among women. In the course of treatment, alternative treatments have started to be used frequently, besides the classical treatments. Astaxanthin that has sighted important interest in recently is a ketocarotenoid. Astaxanthin has a strong antioxidant capacity and anticancer activity. Nocodazole is a microtubule depolymerizing agent. This study aimed to determine the effects of nocodazole and astaxanthin as single agents and in combination, in terms of cytotoxicity, apoptosis and molecular basis in MCF-7 breast cancer cell lines.

**Materials and Methods:** WST-1 cytotoxicity assays were performed to determine IC<sub>50</sub> values of nocodazole and astaxanthin in MCF-7 cell lines. IC<sub>50</sub> values were applied to cells as single agent and in combination as 24, 48, 72 hour experimental groups and compared with untreated control group. After application of specific IC<sub>50</sub> values to cell lines, apoptosis experiments were performed with Annexin V and Mitocapture methods. To determine the molecular regulation of cytotoxicity and apoptosis, gene expression analysis was performed by real-time RT-PCR.

**Results:** In our study, it was found that nocodazole and astaxanthin are significantly cytotoxic when they are single agents. However, when in combination, their cytotoxicity is not significant compared with untreated control group in MCF-7 cell line. We found that nocodazole as single agent is more effective than combination. Our apoptosis and molecular results confirmed cytotoxicity data. Significant variations have been found in CDH1, PTEN, CCND1, BIRC5 genes for nocodazole group compared to astaxanthin and combination groups.

**Discussion and Conclusion:** In our study, we have found that astaxanthin and nocodazole, have anti-proliferative effects on MCF-7 cell line. However, their effects were not synergistic for this cell line. Nocodazole appears to be more effective than astaxanthin and combination groups in terms of cytotoxicity, apoptosis and molecular mechanism. In our future studies, we aim to investigate which pathways are responsible for these effects, and the effects of each agent will be enlightened in new studies that will include other cell lines.

*Keywords: Astaxanthin, Nocodazole, MCF-7 cell line, Breast cancer*

## ORAL PRESENTATION – 05

### IDENTIFICATION OF ANAEROBE BACTERIA FROM PATIENTS WITH CHRONIC PERIODONTITIS USING MOLECULAR TECHNIQUES

Gül Uçar<sup>1</sup>, Yasemin Bulut<sup>2</sup>, Sebahat Fındık Aydın<sup>3</sup>, Zülal Aşçı Toraman<sup>4</sup>, Hakan Kamalak<sup>5</sup>

<sup>1</sup> İstanbul Rumeli University Vocational School

<sup>2</sup> Firat University, Faculty of Medicine, Department of Medical Microbiology, Elazığ-Turkey

<sup>3</sup> Elazığ Oral and Dental Health Center

<sup>4</sup> Firat University, Faculty of Medicine, Department of Medical Microbiology, Elazığ-Turkey

<sup>5</sup> Firat University, Faculty of Dentistry, Department of Restorative Dentistry, Elazığ-Turkey

The objectives of this study were molecular detection of anaerobic agents from the subgingival plaque samples and to determine whether there is any relationship between the frequency of these agents in the patients and some parameters such as plaque index (PI), gingival index (GI), and probing depth (PD) that are important in determining the course of the periodontitis. For this purpose, in 2013, crevicular fluid samples were taken from 37 periodontitis patients at the Elazığ Dental Hospital and 33 otherwise healthy people by placing paper points to the periodontal pockets. Next, DNA was isolated from these samples. The DNA samples were tested by Polymerase chain reaction (PCR)-Reverse hybridization method. According to the results of PCR-Reverse hybridization, the agents detected from the 37 periodontitis patients were 94% *Tannerella forsythia* and *Fusobacterium nucleatum*, 86% *Capnocytophaga species*, 78% *Campylobacter rectus*, 70% *Treponema denticola*, 56% *Parvimonas micra* and *Eikenella corrodens*, 51% *Porphyromonas gingivalis*, 21% *Eubacterium nodatum* and 16% *Aggregatibacter actinomycetemcomitans*. On the other hand, 54% *Fusobacterium nucleatum*, 15% *Capnocytophaga species*, 3% *Tannerella forsythia* and *Eikenella corrodens* were found within the control group. When distribution of the microorganisms were looked into, the difference between the two groups were found significant ( $p < 0,01$ ). Significant differences were detected in PI, GI, PD values between the groups. ( $p < 0,001$ ). Analyzing the relation between PD and the frequency of the occurrence of bacteria, there were a significant relation between PD and the presence of *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Tannerella forsythia*, *Treponema denticola*, *Parvimonas micra*, *Campylobacter rectus* and *Eikenella corrodens* ( $p < 0,05$ ,  $p < 0,01$ ,  $p < 0,001$ ) while no significant relation was found in *Provetella intermedia*, *Fusobacterium nucleatum*, *Capnocytophaga species*, and *Eubacterium nodatum* ( $p > 0,05$ ). In studies conducted so far, it has been reported that the culture method has some limitations and difficulties such as the detection of anaerobic bacteria, preservation of bacterial viability during bacterial sampling and determination of bacterial numbers, where as PCR analysis has been reported to be more successful in these cases.

Identification of 11 periodontopathogenic microorganisms by PCR-Reverse hybridization method was successfully performed within the same day. There is a strong correlation between clinical parameters important for determining the course of chronic periodontitis and anaerobic bacteria it is appropriate to use the PCR-Reverse hybridization can be used to detect this relationship faster, and more specifically and accurately.

**Keywords:** Chronic Periodontitis, Anaerobic Bacteria, Plaque Index, PCR-Reverse Hybridization

**Note to the Scientific Committee:** This work was supported by Firat University Scientific Research Projects Unit (TF.13.55).

**Ethics Committee Decision Number:** 02.052013-07/04



## ORAL PRESENTATION – 06 GENETIC AND EPIGENETIC FACTORS IN MALE INFERTILITY

Mahmut Balkan<sup>1</sup>

<sup>1</sup>: Department of Medical Biology and Genetic, Faculty of Medicine, Dicle University, 21280, Diyarbakır, Turkey

Male factor infertility is a multifactorial complex disorder that affects about 7% of male from the general population. In about 50 % of these cases, the causes of male infertility are unknown and categorized as idiopathic. In approximately 15 percent of these idiopathic infertility cases, the etiology is related to known genetic disorders, including chromosomal aberrations and single gene mutations. It appears that at least half of idiopathic male infertility cases remain undiagnosed and are have some unidentified genetic basis and may be linked to unknown genetic and epigenetic abnormalities. In this study, I review current literature regarding genetics and epigenetics aspects of idiopathic male infertility. The understanding of the etiology of male factor infertility will provide great insight into the genetics of these cases and this may lead to further developments in the creation of specific targeted treatments for cases.

## ORAL PRESENTATION – 07

### THE EFFECTS OF SEQUENTIAL ADMINISTRATION OF EF24 WITH DOCETAXEL APOPTOTIC RESPONSE IN METASTATIC BREAST CANCER CELL LINE

Atiye Seda Yar Saglam<sup>1</sup>, Zubeyir Elmazoglu<sup>2</sup>, Handan Kayhan<sup>3</sup>, Hacer Ilke Onen<sup>1</sup>, Akin Yilmaz<sup>4</sup>, Emine Sevda Menevse<sup>1</sup>

<sup>1</sup>Department of Medical Biology and Genetics, Faculty of Medicine, Gazi University, Besevler, Ankara, Turkey

<sup>2</sup>Department of Medical Pharmacology, Faculty of Medicine, Gazi University, Besevler, Ankara, Turkey

<sup>3</sup>Department of Adult Hematology, Faculty of Medicine, Gazi University, Besevler, Ankara, Turkey

<sup>4</sup>Department of Medical Biology, Faculty of Medicine, Hitit University, Corum, Turkey

**Background / Aim:** Breast cancer is the most common cancer among women worldwide, and leading cause of cancer-related deaths. Docetaxel, a taxane class agents, has become one of the most important chemotherapeutic agents in the past several years. Docetaxel causes microtubule stabilization during mitotic spindle. Currently, more effective treatment options have been investigated by combining new molecules with the classic chemotherapy agents for breast cancer. One of these molecules is EF24, which is a synthetic curcumin analog. We aimed to investigate possible antiproliferative and apoptotic effects of EF24 and docetaxel alone as well as with their sequential administration on MCF-7 breast cancer cells.

**Materials and Methods:** 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) and Lactate dehydrogenase (LDH) tests were performed to determine the effect of EF24 and docetaxel on cell viability and cytotoxicity. Apoptotic cell death methods were performed using Flow cytometry assay, with selected appropriate doses of the cells. Besides, relative mRNA levels of *cMYC* and *cFOS* genes were determined by quantitative Real-time PCR (qRT-PCR) method.

**Results:** The viability of MCF-7 cells decreased significantly after treatment with sequential administration of docetaxel followed by EF24 treatments, compared to docetaxel alone. Sequential administration of docetaxel followed by EF24 decreased cell viability to a higher extent than either agents alone, in a dose dependent manner. Compared to docetaxel alone treatment, EF24 pretreatment overwhelmingly increased apoptosis level in MCF-7 cells. The percentage of apoptotic and necrotic cells were determined by the flow cytometer analysis. Moreover, real-time PCR analyses showed that *cMYC* and *cFOS* mRNA levels changed markedly after sequential treatment.

**Discussion:** In our previous study, we showed that EF-24 pretreatment elevated the apoptotic response of classical chemotherapeutic agents on malignant pleural mesothelioma cells. To the best of our knowledge, this is the first study showing that EF-24 pretreatment increased the apoptotic rates of MCF-7 cells following treatment with docetaxel.

**Conclusion:** These data suggest that sequential administration of EF24 with docetaxel could be useful as a potential chemotherapeutic agents in the management of breast cancer. Further analyses using *in vitro* and *in vivo* models are needed to confirm these findings.

*Keywords: Docetaxel, EF24, metastatic breast cancer cell line, MCF-7, apoptosis*

## ORAL PRESENTATION – 08

### ASSOCIATION BETWEEN RS5275 VARIANT OF COX-2 GENE AND LUNG CANCER RISK

<sup>1</sup>Cansu Ozbayer, <sup>2</sup>Aysegül Bayramoğlu, <sup>3</sup>Hasan Veysi Gunes, <sup>4</sup>Muzaffer Metintas, <sup>3</sup>Hulyam Kurt

<sup>1</sup>School of Health Sciences, Dumlupınar University, Kutahya, Turkey

<sup>2</sup>Department of Nutrition and Dietetics, Faculty of Health Sciences, Artvin Coruh University, Artvin, Turkey

<sup>3</sup>Department of Medical Biology, Medical Faculty, Eskisehir Osmangazi University, Eskisehir, Turkey

<sup>4</sup>Department of Pulmonary Diseases, Medical Faculty, Eskisehir Osmangazi University, Eskisehir, Turkey

Lung cancer is the leading cause of cancer death in the worldwide and the most important risk factor for lung cancer is smoking. Tobacco smoke leads to the formation of lung diseases by the induction of pulmonary inflammation.

Chronic inflammation triggers DNA damage and oncogenic mutations, cause tumor formation and tumor progression. One of the important components of the inflammatory response is cyclooxygenase-2 (COX-2). It has been reported that COX-2 promotes inflammation and cell proliferation, and many cancers often overexpress this enzyme. Accordingly, the aim of our study is to determine the relationship between rs5275 (-8473T/C) gene polymorphism with lung cancer risk.

For this purpose, the rs5275 variant of COX-2 gene was investigated by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) in 100 healthy control individuals and 160 lung cancer patients. After the genomic regions were amplified by PCR, amplicons were digested with the *BclI* enzyme and visualized by agarose gel electrophoresis.

A significant difference was found between control group and patients with lung cancer as for genotype frequencies ( $\chi^2=6.80$ ,  $p=0.009$ ). Additionally, when the genotype frequencies of the lung cancer patients and the controls were compared, there was a statistically significant increase in TC (%61.95) and CC (%11.03) frequency in the lung cancer patients ( $p<0.05$ ).

Our results support the importance of continued investigation into COX-2 and related pathways for the development of new treatments and the potential use of COX-2 as a molecular marker for lung cancer.

*Keywords:* COX-2 gene; rs5275; polymorphism; lung cancer

*Ethics committee approval no:* 2013/102 (15 Feb 2013)

## ORAL PRESENTATION – 09

### ANTIPROLIFERATIVE ACTIVITY AND SAFETY OF LONIDAMINE ENCAPSULATED PEG-BLOCK-PCL NANOCARRIERS AGAINST SW480 COLON CANCER CELLS

Ceyda Tuba Sengel-Turk<sup>1</sup>, Filiz Bakar<sup>2</sup>

<sup>1</sup>Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Technology, 06100, Ankara, Turkey

<sup>2</sup>Ankara University, Faculty of Pharmacy, Department of Biochemistry, 06100, Ankara, Turkey

**Background:** Lonidamine, a derivate of indazole-3-carboxylic acid, has generally been used as an anticarcinogenic agent against several tumors. However, its use in cancer treatment is limited due to the low water solubility and low bioavailability. These limitations could be overcome by designing the nanocarriers of lonidamine. The aim of this research is to prepare a novel poly(ethylene glycol)-block-poly( $\epsilon$ -caprolactone) (PEG-b-PCL) nanocarriers of lonidamine and to evaluate its cytotoxic and apoptotic activity against SW480 colon adenocarcinoma cells.

**Materials and Methods:** Lonidamine encapsulated PEG-b-PCL nanocarriers were produced with a nonionic surfactant, Vitamin E TPGS, using a nanoprecipitation technique. The influence of the usage concentrations (0.015-0.030-0.060%) of the Vitamin E TPGS on the physicochemical characteristics of the nanocarriers was investigated in the field of entrapment efficiency, mean particle size and size distribution, surface charge and drug release profiles. The effects of produced nanocarriers on cell viability, apoptosis and cell cycle arrest in SW480 cells were also performed.

**Results:** The entrapment efficiency of all nanocarriers was determined over 80%. The mean particle size of nanocarriers was found to be in the range of  $149.3 \pm 2.913$  and  $312.3 \pm 15.65$  nm with negative surface charges. When the percentage of Vitamin E TPGS increased, the polydispersity index of the nanocarriers was expanding. The nanoparticles produced with 0.015%, 0.030% and 0.060% of the Vitamin E TPGS have displayed significant cytotoxicity with  $IC_{50}$  values of  $48.85 \mu\text{M}$ ,  $71.46 \mu\text{M}$  and  $74.22 \mu\text{M}$ , respectively.

**Discussion:** PEG-b-PCL nanocarriers containing both 0.015% and 0.030% Vitamin E TPGS had small particle diameters with narrow size distribution whereas the nanocarriers produced with a content of 0.060% Vitamin E TPGS had bigger particles with a bimodal size distribution. Cytotoxicity results indicated that all formulations inhibited cell proliferation efficiently in a dose-dependent manner. The produced nanoparticle prepared with 0.015% Vitamin E TPGS represented the most apoptotic efficiency than others. Cell cycle analysis demonstrated that the compounds have showed a significant arrest in G0/G1 phase of cell cycle when compared to control ( $p < 0.001$ ).

**Conclusion:** Among the investigated percentages of Vitamin E TPGS, 0.015% (w/v) was found the most suitable emulsifier concentration for efficiency of lonidamine encapsulated PEG-b-PCL nanocarriers against SW480 cells.

*Keywords: Apoptosis, Lonidamine, PEG-block-PCL nanoparticles, SW480 cells.*

## ORAL PRESENTATION – 10

### VAL58 AND TYR65 AMINO ACIDS ARE CRITICAL FOR CATALYTIC ACTIVITY AND SUBSTRATE SPECIFICITY OF BILE SALT HYDROLASE FROM *LACTOBACILLUS PLANTARUM* B14

Mehmet Öztürk<sup>1</sup>, Cansu Önal<sup>1</sup>, Zekiye Kılıçsaymaz<sup>1</sup>

<sup>1</sup> : Department of Biology, Faculty of Arts and Science, Abant İzzet Baysal University, Bolu, Turkey

**Background/Aim:** Bile salt hydrolases (BSH) are synthesized by some intestinal microbiota and released into mammalian gut. BSH catalyzes the hydrolysis of taurine and/or glycine -conjugated bile salts into amino acid residues and the free bile acids that provide the decreasing of the blood cholesterol level and also formation of the toxic and mutagenic secondary bile acids. Accumulation of these secondary bile acids in feces, blood and bile are associated with specific diseases of the intestinal system such as gallstone formation and colon cancer. Microbial BSH enzymes differ between species with respect to pH optima, enzyme kinetics and substrate specificity. This study aims to better understand the substrate specificity of clinically significant BSH enzyme. Detection of which amino acids relate with substrate preference of BSH allows us to detect the microorganisms those produce toxic secondary bile salts.

**Material and Methods:** The codons of the Val-58 and Tyr-65 amino acids of BSH, supposed to be responsible for substrate preference, were substituted for the codons of Asn-58, Phe58, Met58, Cys-65, Phe-65 and Leu-65 amino acids respectively by site directed mutagenesis. Mutant recombinant BSHs (mrBSH) were expressed and characterized in *E. coli* BLR(DE3) strain. The substrate specificity and stability of the mrBSHs were examined along with six different human bile salts by ninhydrin assay and SDS-PAGE respectively.

**Results:** Ninhydrin test results indicated that wild-type recombinant BSH (wrBSH) hydrolyzed six major human bile salts with an apparent preference towards glycine-conjugated to tauro-conjugated bile salts. However, while the Asn-58 and Phe58 mutations did not affect much the activity and substrate specificity of the BSH, Met58 decreased 30% activity of BSH. On the other hand, Cys-65 Phe65 and Leu-65 mutations altered the substrate preference of BSHs against to glycocholic acid, glycodeoxycholic acid, glycochenodeoxycholic acid, taurocholic acid, taurodeoxycholic acid and taurochenodexychoic acid respectively. All mutations did not affect the stability of the BSHs.

**Discussion:** Although available kinetic data suggest that BSHs recognize their substrate predominantly at amino acid moieties, our findings support the suggestion that BSHs recognize their substrates by their motifs of substrate binding pocket of BSHs. However, further PCR-based site-directed mutagenesis, structure-driven computational and theoretical approaches are required for the precise determination of BSH's substrate specificities and the selection of probiotic since excessive deconjugation of specific bile salts has been implicated in negative health outcomes to the host.

**Conclusion:** Val58 and Tyr65 are probable key residues of the substrate binding pocket and Tyr65 plays a critical role in selectivity of bile salts as substrate for the BSH enzyme.

*Keywords:* Bile salts, Bile salt hydrolase, *Lactobacillus*, site-directed mutagenesis, substrate specificity

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## ORAL PRESENTATION – 11

### **DETERMINATION OF *EGFR*, *KRAS*, *BRAF*, *PIK3CA*, *HER2* AND *NRAS* GENE MUTATIONS IN PARAFIN BLOCK SECTIONS FROM PATIENTS DIAGNOSED WITH NON-SMALL CELL LUNG CANCER**

Metin Çalışkan<sup>1</sup>, Gökay Bozkurt<sup>2</sup>, Nezi Meydan<sup>3</sup>, İbrahim Meteöğlü<sup>4</sup>, Nur Selvi Günel<sup>1</sup>

<sup>1</sup> Department of Medical Biology, School of Medicine, Ege University, Bornova, Izmir 35100, Turkey

<sup>2</sup> Department of Medical Genetics, School of Medicine, Adnan Menderes University, Efeler, Aydın 09100, Turkey

<sup>3</sup> Department of Medical Oncology, School of Medicine, Adnan Menderes University, Efeler, Aydın 09100, Turkey

<sup>4</sup> Department of Medical Patology, School of Medicine, Adnan Menderes University, Efeler, Aydın 09100, Turkey

The leading cause of cancer deaths is lung cancer and %85 of this type of cancer forms of Non-Small Cell Lung Cancer (NSCLC). Improvements in cancer treatment have been recorded with the identification of genetic changes in tumor tissue and with the use of repressor molecule against oncoproteins resulting from these changes in recent years. The identification of genetic changes in cases of cancer and the generation of special personalized treatment have become extremely important. Determining of genetic changes, identifications of those rates and correlations in Turkey's society may thus contribute to establish priorities and guide for clinicians who treat patients. In our study, we aimed to determine Epidermal Growth Factor Receptor (*EGFR*), V-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog (*KRAS*), neuroblastoma RAS viral (v-ras) oncogene homolog (*NRAS*), v-Raf murine sarcoma viral oncogene homolog B (*BRAF*), phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit alpha (*PIK3CA*), human epidermal growth factor receptor 2 (*HER2*) gene mutations as well as the ratio and correlation of these mutations in sections which were taken from the paraffin blocks of tumor of patients with NSCLC. DNA was isolated from paraffin block sections of patients with NSCLC by use of commercial "AmoyDx FFPE DNA Kit". Mutations were determined using AmoyDx commercial mutation kit with Cobas z (Roche) Real Time PCR instrument.

In the present study, a total of 80 patients with a diagnosis of NSCLC were enrolled. All cases were investigated for *EGFR*, *KRAS*, *BRAF*, *PIK3CA*, *HER2* and *NRAS* gene mutations. In 46, 2% of patients had at least one mutation. Mutations in *EGFR*, *KRAS*, *BRAF*, *PIK3CA*, *HER2* ve *NRAS* genes were detected as 7(8,7%), 23(28,7%), 1(1,2%), 6(7,5%), 0(%), 1(1,2%) respectively. In addition, mutations in *KRAS* and *PIK3CA* genes were determined in 1,2% of cases. These results showed that Turkish people has similarity in terms of mutations in Caucasian people. Only mutations in *PIK3CA* gene were identified over given the results. We think that mutations in *PIK3CA* gene must be well considered in diagnosis and treatment of NSCLC. Also, no mutation was found in 43(53,7%) of all cases. There is a need to investigate molecular factors in these cases which stimulate tumor development.

**Keywords:** NSCLC; *EGFR*; *KRAS*; *BRAF*; *PIK3CA*; *HER2*; *NRAS*

*Ethical committee decision: Adnan Menderes University, Faculty of Medicine, Ethics Committee for Non-Interventional Clinical Investigations 30.10.2014 ordinary meeting Decision on 11th.*

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## ORAL PRESENTATION – 12

### **BOWEL-BRAIN AXIS AFFECTED BY CEFOPERAZONE AND AMPICILLIN TREATMENT IN MICE**

Taha Ceylani<sup>1</sup>, Rafiq Gurbanov<sup>3</sup>, Hikmet Taner Teker<sup>1</sup>, Ewa Jakubowska-Doğru<sup>1</sup>, Ayşe Gul Gozen<sup>1</sup>

<sup>1</sup>Department of Biological Sciences, Middle East Technical University, 06800, Ankara, Turkey

<sup>2</sup>Department of Molecular Biology and Genetics, Muş Alparslan University, 49250, Muş, Turkey

<sup>3</sup>Department of Molecular Biology and Genetics, Bilecik Şeyh Edebali University, 11230, Bilecik, Turkey

**Background/Aim:** Over use of antibiotics which are known profoundly change the bowel microbiota by removing symbiotic bacteria may also influence brain functions leading to the development of anxiety like behaviour and depression syndromes, and even cognitive deficits. The aim of this study is addresses this issue by using an animal model.

**Material and Methods:** 21 days old male Balb/C mice was used. Two broad spectrum antibiotics (ampicillin and cefoperazone 1g/l) used to perturb the bowel microbiota. After treatment period all mice subjected to related cognitive tests and gut microbiota profile determined using denaturing gradient gel electrophoresis system (DGGE).

**Results:** DGGE profile revealed that, each antibiotic regime perturbed the bowel microbiota by differently reducing their composition. All antibiotic-treated groups showed lower exploratory and locomotor activities. Ampicillin receiving group demonstrated higher anxiety. Cefoperazone/Ampicillin administration lead to depression-like behaviour compared to untreated group.

#### **Discussion**

The existence of bowel microbiota have role to manage anxiety-like behaviour. According to the specific alteration in the composition of gut microbiota the stress responses also changed.

**Conclusion:** Repeated administration of antibiotic at juvenile age alters bowel microbiota composition and also these changes are antibiotic specific. Ampicillin caused greater perturbances in microbial profile compared to cefoperazone. These changes were associated with behavioural deviations such as an increase of anxiety-like behaviour and behavioural despair.

*Keywords: Bowel microbiota, DGGE, Cognitive deficits, Balb/C mice*

*Ethics Committee's approval number: 49783314-/32 (Ankara University)*

## ORAL PRESENTATION – 13

### **THE POTENTIAL USE OF MESENCHYMAL STEM CELLS LOADED WITH SMALL MOLECULE COMPOUNDS AS THERAPEUTICS IN DISEASE**

Wen-Hui Fang<sup>1</sup>, Shant Kumar<sup>2</sup>, David Smith<sup>3</sup>, Glenn Ferris<sup>1</sup>, Mark Slevin<sup>1</sup>

<sup>1</sup>School of Healthcare Science, Faculty of Science and Engineering, Manchester Metropolitan University, Manchester, UK

<sup>2</sup>School of Biomedicine, Faculty of Medicine and Human Sciences, University of Manchester, Manchester, UK

<sup>3</sup>Cockcroft Building, University of Salford, Salford, UK

The potential use of stem cells as therapeutics in disease has gained momentum over the last few years and recently phase-1 clinical trials showed favourable results in treatment of a small cohort of acute stroke patients. Similarly, they have been used in pre-clinical models-drug-loaded for the effective treatment of solid tumours.

Firstly, we characterised uptake and release of a novel p5-CDK5 inhibitory peptide by human adipose-derived mesenchymal stem cells (hAD-MSCs) and showed release levels capable of blocking aberrant CDK5 signalling pathways, through phosphorylation of CDK5 and p53. These pathways represent the major acute mechanism stimulating apoptosis after stroke and hence modulation of this could benefit patient recovery.

Secondly, we investigated whether hAD-MSCs can be used as potent and safe tumour tropic vehicles for conventional drug delivery to tumours. The results showed that paclitaxel and carboplatin, the first line chemotherapeutic drugs for lung cancer treatment, produced a strong anti-proliferative effect on three lung cancer cells (HCC827, A549 and H520) whereas hAD-MSCs were strongly resistant to paclitaxel and relatively resistant to carboplatin, respectively. The conditioned media from paclitaxel or carboplatin primed hAD-MSCs produced a dose dependent growth inhibition of lung cancer cells, whereas conditioned media from untreated hAD-MSCs were not effective. LC-MS/MS analysis further confirmed the time dependent release of drugs by primed hAD-MSCs. The kinetics of doxorubicin internalization into hAD-MSCs revealed the appreciable internalization of doxorubicin by hAD-MSCs after 1 hour of priming and the intense staining in cytoplasm at the end of priming (24 hours). The distribution of doxorubicin in cytoplasm decreased after 24 hours, suggesting a possible excretion. Furthermore, transwell assays showed that conditioned media from lung carcinomas induced the migration of hAD-MSCs.

Our work indicates a potential use for drug-loaded stem cells as delivery vehicles for stroke therapeutics and in addition as anti-cancer receptacles particularly, if a targeting and/or holding mechanism can be defined.



## ORAL PRESENTATION – 14

### DECREASED MULTIPLE MYELOMA VIABILITY OF MALIGNANT PLASMA CELLS BY INHIBITION OF WERNER HELICASE

Dilara Akcora Yildiz<sup>1</sup>, Tülin Özkan<sup>2</sup>, Mehmet Özen<sup>3</sup>, Mehmet Gündüz<sup>3</sup>, Meral Bektaş<sup>3</sup> and Asuman Sunguroğlu<sup>2</sup>

<sup>1</sup> Department of Biology, Art&Science Faculty, Mehmet Akif Ersoy University, Burdur, TURKEY

<sup>2</sup> Department of Medical Biology, Faculty of Medicine, Ankara University, Ankara, TURKEY

<sup>3</sup> Department of Hematology, Faculty of Medicine, Ankara University, Ankara, TURKEY

**Background/Aim:** Multiple Myeloma (MM) is a plasma cell malignancy characterised by proliferation of monoclonal plasma cells in the bone marrow. Despite several therapeutic approaches, including stem cell transplantation, high-dose chemotherapy and the usage of novel agents such as bortezomib, MM still remains an incurable disease. Extensive genomic instability is a major hallmark of MM cells and promoted by unfaithful DNA repair. Werner Syndrome (WRN) helicase is a member of RecQ helicase family and contributes to DNA replication, recombination and repair. The aim of this study was to examine the effect of inhibition of WRN activation in decreasing the MM cell viability by disturbing DNA repair.

**Materials and Methods:** In this study, WRN mRNA levels were determined in human MM cell lines (NCI H929, RPMI 8226 and U266), three samples of control PBMCs, fourteen newly diagnosed (ND) CD138+ myeloma, seventeen ND CD138- non-tumorigenic, fourteen relapsed/refractory (RR) CD138+ myeloma and eleven RR CD138- non-tumorigenic cells obtained from bone marrow aspirates of MM patients by quantitative RealTime PCR. Following treatment of MM cells with NSC19630, a WRN helicase inhibitor, for 48 hours, cell viability, cell cycle progression and apoptosis were assessed by MTT and flow cytometry. DNA damage levels were examined by alkaline comet assay and immunoblotting of  $\gamma$ -H2AX phosphorylation.

**Results:** We found a decreased expression of WRN in MM cell lines compared with PBMCs. Although we showed an increased expression of WRN in both ND and RR CD138+ myeloma plasma cells compared to their CD138- non-tumorigenic cells, its expression seems to be not involved in MM disease progression. Furthermore, by using NSC19630 a specific WRN helicase inhibitor, we showed a decreased proliferation and an increased apoptosis in MM cells. In addition, NSC19630 perturbed cell cycle and decreased phosphorylation of G1/S specific CyclinE1 in MM cells. In our study, the efficacy of Melphalan (an alkylating agent) cytotoxicity was not enhanced by the co-treatment with NSC19630.

**Discussion:** We reported here for the first time the inhibition of WRN activity impairs apoptosis in MM. In line with our study, decreased expression of WRN was detected in MM cells. However, high RECQ1, WRN and RECQ4 expression are associated with an adverse prognosis in MM was reported, indicating depletion of their activity could be important for the treatment of MM.

**Conclusion:** These results suggests that WRN seems to be important in MM cell viability and its inhibition impairs cells growth and induces apoptosis in MM cells.

**Keywords:** Multiple Myeloma, WRN helicase, DNA repair, apoptosis

**Ethics Committee's Approval Number:** The experiments with human cells were approved by the Ethical Committee of Ankara University School of Medicine (Protocol 04-176-13).

**Note to the Scientific Committee:** This research has been supported by The Scientific and Technological Research Council of Turkey (No:113Z383).

## ORAL PRESENTATION – 15

### THE EFFECT OF *MYRTUS COMMUNIS* EXTRACT ADMINISTRATION ON BILE DUCT LIGATED RATS' BRAIN TISSUE

Sehkar Oktay<sup>1</sup>, Burcin Alev-Tuzuner<sup>1</sup>, Unsal Veli Ustundag<sup>1</sup>, Hazal Ipekci<sup>1</sup>, Ebru Emekli-Alturfan<sup>1</sup>, Tugba Tunali-Akbay<sup>1</sup>, Goksel Sener<sup>2</sup>, Aysen Yarat<sup>1</sup>

<sup>1</sup>Department of Basic Medical Sciences, Faculty of Dentistry

<sup>2</sup>Department of Pharmacology, Faculty of Pharmacy, Marmara University, Maltepe, Istanbul, Turkey

**Background:** Brain is a sensitive organ which is affected by BDL (Bile Duct Ligation). Brain damage, cognitive deficit and edema can develop in progression of BDL. *Myrtus communis* (MC) is one of the most important medicinal species from *Myrtaceae* family. Its fruits and leaves have been reported to show antioxidant and anti inflammatory effects.

**Aim:** The aim of this study was to evaluate the possible effect of MC extract on BDL rats' brain tissue on oxidant-antioxidant system.

**Materials and Methods:** Female Sprague-Dawley rats were divided into four groups as follows: 1- Sham operated and saline treated control group (n=6), 2-Sham operated and MC extract treated control group (n=6), 3-Bile duct ligated (BDL) and saline treated group (n=8), 4- BDL and MC extract treated group (n=7). Under anesthesia, bile ducts of Sprague Dawley rats were ligated. Control+MC and BDL+MC groups received a daily dose of MC extract (50mg/kg dissolved 1 ml in saline) by orogastric tube for 28 days after BDL. Control and BDL groups received 1 ml saline. Animals were sacrificed, brain tissues were taken and examined. Glutathione (GSH), lipid peroxidation (LPO) levels and superoxide dismutase (SOD), catalase (CAT), glutathione-S-transferase(GST), total nitric oxide (NO) levels were determined in brain tissue samples.

**Results:** Decreased GSH levels and increased CAT activities in the BDL group were the significant findings of the study. However, there was a trend for an increase in LPO levels although not significant. MC did not change the parameters investigated in this study.

**Discussion:** In the brain tissue of BDL rats, decreased GSH levels shows the consumption of this antioxidant to prevent the LPO increase. Moreover the increased CAT activities might be due to the response of the brain to support the disturbed antioxidant system.

**Conclusion:** MC did not exert its protective effect on the oxidant-antioxidant system in brain tissue in this model.

*Keywords:* Bile duct ligation, oxidative stress, brain, *Myrtus communis*,

## ORAL PRESENTATION – 16 USING *DROSOPHILA MELANOGASTER* AS A NONMAMMALIAN MODEL ORGANISM FOR UNDERSTANDING TO MOLECULAR MECHANISMS OF CLINICALLY IMPORTANT ANTIBIOTICS

Volkan Keleş<sup>1</sup>, Meltem Erdem<sup>1</sup>, Cehun Küçük<sup>1</sup>, Ender Büyükgüzel<sup>1</sup>, Kemal Büyükgüzel<sup>1</sup>

<sup>1</sup>Bülent Ecevit University

**Background/Aim:** *Drosophila melanogaster* have been frequently used as non-mammalian model organism for understanding to molecular mechanisms of diseases including cancer, diabetes, obesity and their associated complications as well as toxicology, pharmacology and agricultural purpose. Furthermore, the insect have been recently used to determine pathogenity of some infection agents and effectiveness of antibacterial, antiviral, antifungal, anthelmintic and even antidiabetics. Most of basic metabolic mechanisms such as lipid storage and mobilizing, sugar hemostasis and food intake in response to nutritional status have similarity between insects and mammals. *Drosophila* has short generation time, and is easy species for genetic tools like genome studies, and inexpensive cost associated with maintaining of stocks.

**Materials and Methods:** We reared *D. melanogaster* larvae on artificial diet in our laboratory at  $25 \pm 2$  °C, 60-70% of relative humidity and in a photoperiod of 12 h day light. The effects of clinically used drugs including old generation antibacterials, streptomycin and neomycin; and more potent new generation gyrase inhibitor, gemifloxacin; and antihelmintics such as niclosamide were investigated by rearing the first instars on artificial diet including different concentrations of these antibiotics. To evaluate effectiveness of these antibiotics, we determine changes in life table parameters (survivorship, developmental time to adult emergence and adult biological fitness including life span, fecundity and fertility), and oxidative, antioxidative and immune responses in different developmental stages of the insects

**Results:** We found that tested antibiotics and chemicals at high dietary levels decreased survivorship by 50% and prolonged developmental day to adult emergence. Gyrase inhibitor, gemifloxacin, at the highest dietary concentrations (900 mg/L) decreased survivorship of 3<sup>rd</sup> instars from 88% in the control diet to 7%, and prolonged to developmental time by over 2 days. Highest dietary concentrations of antihelmintic, niclosamide resulted in only 11% percent adults and decreased adult longevity to from 42 to 2 days. Dietary gemifloxacin at 300 mg/L increased MDA content and GST activity, decreased PCO levels. Similar effects on life table parameters and oxidative and antioxidative response of the fruit fly were obtained by streptomycin dietary exposure.

**Discussion:** We infer from these results, fruit fly can be used as non-mammalian organisms to determine secondary molecular mechanism of the clinically important drugs, and also chemicals except for their primary mode of action.

**Conclusion:** Our results also showed that the effectiveness of new drugs developed and chemical synthesized can be tested on fruit fly as model organism before directly using them for human and animal welfare and also for agricultural purpose for environment and nontargets welfare.

*Keywords:* *D. melanogaster*, nonmammalian models, antibiotics, chemical insecticides

## ORAL PRESENTATION – 17

### NEXT GENERATION SEQUENCING AND DETECTION OF COMMON MUTATIONS IN LUNG AND COLON CANCERS

Gülüm Seda Güleç Yılmaz<sup>1</sup>, Uzay Görmüş<sup>2</sup>, Birsen Pınar Yıldız<sup>3</sup> Emre Murat Altunkılıç<sup>4</sup>, Altay Burak Dalan<sup>5</sup>  
Turgay İsbir<sup>6</sup>

<sup>1</sup> Yeditepe University, Istanbul, Turkey,

<sup>2</sup> İstinye University Faculty of Medicine Department of Medical Genetics, Istanbul, Turkey,

<sup>3</sup> Yedikule Chest Disease and Chest Surgery Educational and Research Hospital, Istanbul, Turkey,

<sup>4</sup> Yeditepe University Institute of Health Sciences Department of Molecular Medicine, Istanbul, Turkey,

<sup>5</sup> Yeditepe University Faculty of Medicine Department of Medical Biochemistry, Istanbul, Turkey

<sup>6</sup> Yeditepe University Faculty of Medicine Department of Medical Biology, Istanbul, Turkey

DNA sequencing has revolutionised biological and medical research, and have a similar impact on the practice of medicine. In spite of advances in other 'omic' technologies, DNA sequencing and analysis have played the leading role to date. The next-generation sequencing (NGS) provides a new approach between genotype and phenotype. NGS offers new technologies beyond the limites of genetics. NGS Method consists of several steps: firstly gDNA is degraded in fragments, then amplification is done by emPCR, which is performed within the formed beads containing several thousand copies of the same template sequence. EmPCR beads are chemically attached to a chip desined for sequencing. Solid-phase amplification is composed of two basic steps: initial priming and extending of the single-stranded, single-molecule template, and bridge amplification of the immobilised template with immediately adjacent primers to form clusters. Next step is sequencing and imaging. Data analysis performed by the available software programmes and bioinformatic analysis. Being aware of the importance of individual genetic changes for early diagnosis, choosing proper therapeutics and decreasing mortality due to therapies, in this study of NGS, we had lung and colon cancer groups. Former one is the most common, latter is the third common cancer worldwide. In our study we analyzed patients of each group to determine the similar genetic changes. PGM and AmpliSeq Colon and Lung Cancer Panel were performed to detect the possible gene variations on KRAS, EGFR, BRAF, PIK3CA, AKT1, ERBB2, PTEN, NRAS, STK11, MAP2K1, ALK, DDR2, CTNNB1, MET, TP53, SMAD4, FBX7, FGFR3, NOTCH1, ERBB4, FGFR1, FGFR2 genes for 504 hotspot regions. We recognized previously undefined mutations in both cancer groups to be researched in more crowded patient groups. Our results can be pioneer for determining tendency to those cancer types as well as having possible prognostic and/or therapeutic follow-up values.

## ORAL PRESENTATION – 18 ASPIRIN INHIBITS BCR-ABL AND ITS DOWNSTREAM EFFECTORS IN CHRONIC MYELOID LEUKEMIA

Arzu Zeynep Karabay<sup>1</sup>, Asli Koc<sup>1</sup>, Yalda Hekmatshoar<sup>2</sup>, Aynur Karadag<sup>3</sup>, Tulin Ozkan<sup>2</sup>

<sup>1</sup>Ankara University Faculty of Pharmacy Department of Biochemistry

<sup>2</sup>Ankara University Faculty of Medicine Department of Medical Biology

<sup>3</sup>Ankara University Institute of Biotechnology

**Background / Aim:** Chronic myeloid leukemia is a hematopoietic stem cell disease characterized with the existence of Philadelphia chromosome, a bcr-abl fusion gene and its product bcr-abl oncoprotein which accounts for nearly %15-20 of all adult leukemias. Bcr-abl oncoprotein is responsible for constitutive tyrosine kinase activity which is the main orchestrator of various signaling events causing abnormal proliferation and activation of survival pathways of cancer cells including Akt and JAK-STAT. Imatinib is considered as the first line therapy for CML patients, however nearly 40% of patients have demanded higher doses of Imatinib or a different therapy due to impaired drug tolerance or drug resistance. Aspirin has been gaining serious attention for its acclaimed anti-cancer activities in recent years and its effects were examined in different cancer cell line models. In this study we tested the effects of Aspirin (2.5 and 5 mM) on Bcr-Abl and the members of Akt, JAK-STAT and m-TOR pathways.

**Materials and Methods:** K562 cell line and its Imatinib (5uM) resistant counterpart were cultured containing 10% fetal bovine serum, 100 U/ml of penicillin and 100 mg/ml streptomycin sulfate and incubated at 37°C in a humidified atmosphere of 5% CO<sub>2</sub>. Cells were treated with Aspirin (2.5 and 5 mM) for 72 hours before collection and lysis for western blot assay. Protein concentration of lysates was measured before denaturing gel electrophoresis. Proteins on gels were then transferred to PVDF membranes and incubated with proper antibodies before chemiluminescent visualisation. Western blot was performed for Bcr-Abl and the members of Akt, JAK-STAT and m-TOR pathways.

**Results (quantitative and / or statistical data):** We found that Aspirin treatment (2.5 and 5 mM) inhibited Akt, mTOR and JAK-STAT activation significantly ( $p < 0.05$ ) in both Imatinib sensitive and resistant K562 cells. Bcr-Abl oncoprotein was also found to be drastically and significantly ( $p < 0.05$ ) effected by Aspirin treatment.

**Discussion:** Various studies performed with different cell lines have reported different modulatory effects for Aspirin on key signaling effectors of cell viability such as mTOR. Since different pathways are responsible for the emergence of cancerous profiles in various cell models, we can conclude that Aspirin inhibits proliferation of CML cells probably as a result of its inhibitor activity on Bcr-Abl.

**Conclusion:** Our results suggest that Aspirin has the potential to act as a modulatory agent on components of key biochemical pathways involved in cell viability in both Imatinib sensitive and resistant CML.

*Keywords: Aspirin, CML, apoptosis*

## ORAL PRESENTATION – 19

### CHANGES IN PUFA LEVELS AND INFLAMMATION IN AN ANIMAL AND CELL MODEL OF HEPATIC ENDOPLASMIC RETICULUM STRESS

Mutay Aslan<sup>1</sup> (Presenter), Ebru Kıracı<sup>1</sup>, Özlem Yılmaz<sup>2</sup>, Betül Ünal<sup>3</sup>, Esmâ Kırımlıoğlu Konuk<sup>4</sup>, Filiz Özcan<sup>1</sup>, Hazal Tuzcu<sup>1</sup>

<sup>1</sup>Department of Medical Biochemistry, <sup>2</sup>Human Gene and Cell Therapy Center, <sup>3</sup>Department of Pathology and <sup>4</sup>Department of Histology, Akdeniz University Faculty of Medicine, Antalya 07070, Turkey

**Background:** The presence of endoplasmic reticulum (ER) stress is as an important contributing factor in various liver diseases, including alcoholic liver disease, nonalcoholic steatohepatitis, drug-induced liver injury, acute-on-chronic liver failure and hepatocellular carcinoma. Thus, investigating the ER stress response in both animal models and cell cultures can help to understand the pathology of these diseases. This study aimed to determine hepatic polyunsaturated fatty acids (PUFAs) and inflammatory response in an animal and cell model of ER stress.

**Materials and Methods:** Rats were divided into control, tunicamycin (TM) treated and TM + tauroursodeoxycholic acid (TUDCA) treated groups. Hepatic ER stress was induced by TM and the ER stress inhibitor TUDCA was injected 30 minutes before induction of ER stress. Liver THLE-3 cells were treated with TM to induce ER stress and TUDCA was administered in advance to decrease cytotoxic effects. Necroinflammation was evaluated in liver sections while cell viability was determined via MTT assay. ER stress was confirmed by immunofluorescence and western blot analysis of C/EBP-homologous protein (CHOP) and 78-kDa glucose-regulated protein (GRP78). Arachidonic acid (AA, C20:4n-6), dihomo-gammalinolenic acid (DGLA, C20:3n-6), eicosapentaenoic acid (EPA, C20:5n-3) and docosahexaenoic acid (DHA, C22:6n-3) in liver tissue and THLE-3 cells were determined by LC-MS/MS. Phospholipase A2 (PLA2), cyclooxygenase (COX) and prostaglandin E2 (PGE2) were measured in tissue and cell samples via ELISA.

**Results:** Hepatic ER stress was accomplished by TM and was alleviated by TUDCA. Tunicamycin treatment significantly decreased PUFAs in both liver tissue and THLE-3 cells compared to controls. Activity of PLA2, COX and PGE2 levels were significantly increased in TM treated rats and THLE-3 cells compared to controls. Tauroursodeoxycholic acid lead to a partial restoration of liver PUFA levels and decreased PLA2, COX and PGE2.

**Discussion:** In summary, we report that TM treatment results in significantly decreased PUFA levels and leads to significantly increased activity of cPLA2, COX and PGE2 levels in rat liver and human hepatocytes. We also shows that TUDCA increases PUFA levels and alleviates cPLA2, COX and PGE2 levels in liver tissue of TM treated rats

**Conclusion:** To our best knowledge, this is the first study reporting decreased PUFA levels in ER stress and supports the use of omega-3 fatty acids in liver diseases demonstrating ER stress. This study was supported by a grant (#214S223) from The Scientific and Technological Research Council of Turkey (TUBITAK).

*Keywords: Liver, endoplasmic reticulum stress, polyunsaturated fatty acids.*

*Ethics Committee's approval number: 2014.09.08. All experimental protocols conducted on rats were performed in accordance with the standards established by the Institutional Animal Care and Use Committee at Akdeniz University Medical School.*

*Note to the Scientific Committee: This study was supported by a grant (#214S223) from The Scientific and Technological Research Council of Turkey (TUBITAK).*

## ORAL PRESENTATION – 20

### EVALUATION OF THE HEPATOPROTECTIVE EFFECT OF LIPOIC ACID UPON EXPOSURE TO 2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN IN RAT HEPATOCYTE CULTURES

Özlem Özdemir<sup>1</sup>, Hasan Türkez<sup>1</sup>, Abdulgani Tatar<sup>2</sup>, Ivana Cacciatore<sup>3</sup>, Antonio Di Stefano<sup>3</sup>

<sup>1</sup>Department of Molecular Biology and Genetics, Faculty of Science, Erzurum Technical University, Erzurum, Turkey

<sup>2</sup>Department of Medical Genetics, Faculty of Medicine, Ataturk University, Erzurum, Turkey.

<sup>3</sup>Department of Pharmacy, University "G. d'Annunzio" Chieti-Pescara, Chieti, Italy

**Background / Aim:** The 2,3,7,8-tetrachlorodibenzo-p-dioxin or known as TCDD in short is a persistent toxic compound that is highly bio-accumulative in nature. It was clearly proven that TCDD induced dose-dependent hepatotoxicity and promoted liver cancer via forming fat accumulation, inflammation, and fibrosis. Conversely,  $\alpha$ -lipoic acid (ALA) was considered as hepatoprotective and potent antioxidant in amelioration of chemical exposure-induced hepatotoxicity in some recent publications. The aim of the present study was to assess the potential protective effects of ALA against TCDD-induced alterations in cell viability, DNA damage as well as the oxidant-antioxidant status for the first time.

**Materials and Methods:** The primary cultured rat hepatocytes were isolated, and then TCDD (10  $\mu$ M) were applied in the presence and absence of LA (0 to 200  $\mu$ M) for 48 and 72h. The cell viability was determined by lactate dehydrogenase (LDH) release assay. The micronucleus (MN) and total antioxidant capacity (TAC) assays were performed for genotoxic and oxidative alterations, respectively. Data were analyzed using ANOVA test followed by Duncan's post hoc test.

**Results:** The application of TCDD into the cultures caused a significant ( $p < 0.01$ ) decrease in cell viability and TAC level as compared to control value. In addition the treatment with TCDD caused increases of MN formation. And, treating the cells with ALA in combination with TCDD mitigated hepatocyte cell death, causing a significant reduction in LDH level and a significant increase in TAC level as compared to the TCDD-group. Moreover, the cytogenetic (MN scoring) investigation further corroborated these biochemical observations.

**Discussion:** Our findings indicate that ALA provides a significant protection against TCDD-induced liver damage in vitro.

**Conclusion:** As a conclusion, the obtained results from this study could be used to monitor the safe and effective ALA concentration for protecting against toxicity by other environmental contaminants or carcinogens.

*Keywords: TCDD, Ameliorative action,  $\alpha$ -lipoic acid, Antioxidant status, Cytotoxicity, Rat hepatocyte cultures.*

## ORAL PRESENTATION – 21 CYTOTOXIC EFFECT OF Ni DOPED ZnO SAMPLES ON HUMAN PRIMARY GLIOBLASTOMA CELL LINE

Fatma Necmiye Kacı<sup>1</sup>, Arzu Görmez<sup>1</sup>, Tuba Yetim<sup>2</sup>

<sup>1</sup>Department of Molecular Biology and Genetics, Faculty of Science, Erzurum Technical University, Erzurum-TURKEY

<sup>2</sup>Department of Chemical Engineering, Engineering and Architecture Faculty, Erzurum Technical University, Erzurum-TURKEY

**Background / Aim:** In this study, ZnO, different ratios of ZnO/Ni doped oxide films by using the zincate method was growth on the ceramic sample surface to obtain the cytotoxic effects of the films. For this purpose untreated, ZnO coated, 10% Ni doped ZnO coated and 30% Ni doped ZnO coated samples were used.

**Materials and Methods:** In zincate method, Zn(OH)<sub>2</sub> was precipitated by using the zinc acetate and ammonium hydroxide at pH 8. The precipitate was filtered and the pH is adjusted to 11 for obtaining the ammonium zincate. The samples were coated with this solution by dip coating. After the drying and sintering operations, the surface was coated zinc and zinc/nickel doped oxide film.

In order to detect cytotoxic effects of untreated, ZnO coated, 10% Ni doped ZnO coated and 30% Ni doped ZnO coated samples on U87-MG cell line, a human primary glioblastoma cell line, was demonstrated by MTT cell proliferation assay and LDH assay. LDH has been widely used to evaluate the presence of damage and toxicity of tissue and cells. Moreover, cell viability was also shown microscopically in Trypan blue exclusion test.

**Results:** As a results of MTT proliferation assay, there were dose- and time- dependent decreases in cell proliferation in response to all samples. IC<sub>50</sub> values were calculated from cell proliferation plots and found to be especially 10% Ni doped ZnO coated sample is more effective than the others on U87-MG cell line. Also MTT results were confirmed with LDH results.

**Discussion:** All results showed that the effects of ZnO coated, 10% Ni doped ZnO coated samples on human primary glioblastoma cell line had significant decreases in proliferation.

**Conclusion:** In summary, we can say that the optimum rate of Ni doped ZnO coated samples can be used as a supplement of cancer drugs. As a next step, use of nickel doped zinc oxide nanoparticles for cancer treatment can be envisaged.

*Keywords: Ni doped, ZnO, Cytotoxicity, MTT, LDH, U87-MG*



## ORAL PRESENTATION – 22 NEW PROMISING STARS OF ACUTE LYMPHOBLASTIC LEUKEMIA: RUXOLITINIB AND BIBR1532

Neslihan Pınar Özateş Ay<sup>1</sup>, Bakiye Göker Bağca<sup>1</sup>, Fatma Doğan<sup>1</sup>, Cumhuriyet Gündüz<sup>1</sup>, Çığır Biray Avcı<sup>1</sup>

<sup>1</sup>Ege Üniversitesi Tıp Fakültesi Tıbbi Biyoloji Anabilim Dalı

Acute lymphoblastic leukemia (ALL) is a hematologic malignancy arises from abnormality of differentiation and proliferation of lymphoid progenitor cells in bone marrow or other lymphoid tissues. Although the incidence is higher in children, induction of ALL triggers similar molecular mechanism with adult such as abnormal expression of proto-oncogenes or tumor suppressors, chromosomal disorders causing a fusion protein which is responsible for tyrosine kinase activity and damaged transcription factors, and abnormal chromosomal duplications. JAK/STAT signaling pathway is one of the most appropriate targets in the treatment of leukemia, as it plays a role in the response to growth factors and cytokines. Ruxolitinib is an inhibitor of Janus kinase family of protein tyrosine kinases (JAKs) that it is used for the therapy of myelofibrosis and polycythemia vera. On the other hand, telomerase inhibitors are the other important anticancer agents with antiproliferative and antigrowth manner. BIBR1532 has been used as a quite effective inhibitor of hTERT since the day it was discovered. In this study, we aimed to investigate the cytotoxic effects of these two promising agents with WST-8 analysis on adult acute lymphoblastic leukemia cell line CCRF-CEM compared to the untreated control group. The IC<sub>50</sub> doses of ruxolitinib and BIBR1532 were detected as 12,89 µM and 22,53 µM, respectively for 72<sup>nd</sup> hour on CCRF-CEM cell line.

Combination trials have shown that when two agents are used together, their apoptotic effects are increased remarkably and also significant changes in expression levels of the genes involved in this pathway were found.

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## ORAL PRESENTATION – 23

### **APOPTOTIC EFFECT OF ANACARDIC ACID AND FARNESYL TRANSFERAZ INHIBITOR ON METASTATIC BREAST CANCER CELL LINE (MCF-7)**

Emine Firdevs Yildirim<sup>1</sup>, Atiye Seda Yar Saglam<sup>1</sup>, Zubeyir Elmazoglu<sup>2</sup>, Handan Kayhan<sup>3</sup>, Hacer Ilke Onen<sup>1</sup>

<sup>1</sup>Department of Medical Biology and Genetics, Faculty of Medicine, Gazi University, Besevler, Ankara, Turkey

<sup>2</sup>Department of Medical Pharmacology, Faculty of Medicine, Gazi University, Besevler, Ankara, Turkey

<sup>3</sup>Department of Adult Hematology, Faculty of Medicine, Gazi University, Besevler, Ankara, Turkey

**Background/Aim:** Epigenetic alterations including DNA methylation, histone modifications and non-coding RNAs may contribute to the development of cancer. Histone modifications include acetylation, methylation, phosphorylation, ubiquitination and sumoylation. The acetylation of histones is regulated by two enzyme families; histone acetyltransferases (HATs) and histone deacetylases (HDACs). The structure and expression patterns of HATs and HDACs are altered in many cancer types. Anacardic acid is a histone acetyl transferase (HAT) inhibitor. LB42708, a farnesyltransferase and geranylgeranyltransferase inhibitor, causes cell cycle arrest. Metastatic breast cancer is the second leading cause of cancer-related deaths in women. Currently, a more effective treatment strategy for metastatic breast cancer is still investigated. In our study, we aimed to determine the apoptotic effects of anacardic acid pretreatment following anacardic acid in combination with LB42708 in MCF-7 cells.

**Material and Methods:** After 2 hours of anacardic acid (25  $\mu\text{mol/l}$ ) pretreatment, MCF-7 cells were incubated with various concentrations of LB42708 (5-50  $\mu\text{mol/l}$ ) for an additional 24 hours. The viability of cells at 26 hours was evaluated by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay. Cell toxicity and apoptosis levels were determined by lactate dehydrogenase (LDH) assay and cleaved caspase 3 levels, respectively. Apoptosis was confirmed with flow cytometry.

**Results:** When compared to LB42708 alone administration, pretreatment anacardic acid for 2h, and then LB42708 for additional 24h in the continued presence of anacardic acid caused a significant decreased in the cell viability of MCF-7 cells. Anacardic acid was significantly sensitized in MCF-7 cells in response to LB42708 treatment. Little or no cytotoxicity was determined in cells that were treated with all agents. Moreover, LB42708 in combination with anacardic acid administration, decreased the cell cytotoxicity to <1%. When corresponded to control cells, LB42708 alone and in combination with anacardic acid administration increased the levels of active caspase 3.

**Discussion:** We showed that pretreatment of anacardic acid sensitize MCF-7 tumor cells to a farnesyltransferase inhibitor (LB42708) *in vitro*. Similar results were also found in various cancer cell lines.

**Conclusion:** In this pre-clinical study, we demonstrated for the first time that pretreatment with anacardic acid may lead to effective response to caspase-dependent apoptosis on metastatic breast cancer cell line (MCF-7) by making cells more susceptible to farnesyltransferase inhibitor (LB42708).

*Keywords: LB42708; anacardic acid; metastatic breast cancer cell line; farnesyltransferase inhibitor*

## ORAL PRESENTATION – 24

### **RADIOTHERAPY INDUCED OXIDATIVE INJURY OF ILEUM IS ALLEVIATED BY RESVERATROL TREATMENT IN RATS**

Ismet Burcu Turkyilmaz<sup>1</sup>, Esin Ak<sup>2</sup>, Feriha Ercan<sup>3</sup>, Beste Melek Atasoy<sup>4</sup>, Goksel Sener<sup>5</sup>, Refiye Yanardag<sup>1</sup>

<sup>1</sup>Istanbul University, Faculty of Engineering, Department of Chemistry, Istanbul, Turkey

<sup>2</sup>Marmara University, Faculty of Dentistry, Department of Histology and Embryology, Istanbul, Turkey

<sup>3</sup>Marmara University, Faculty of Medicine, Department of Histology and Embryology, Istanbul, Turkey

<sup>4</sup>Marmara University, Faculty of Medicine, Department of Radiation Oncology, Istanbul, Turkey

<sup>5</sup>Marmara University, Faculty of Pharmacy, Department of Pharmacology, Istanbul, Turkey

**Background/Aim:** Radiotherapy is extensively used for the treatment of a wide variety of tumors, but its short and long-term complications limit the therapeutic success. Radiation-induced enteritis with several intestinal symptoms such as nausea, vomiting, diarrhea and anorexia is a well-recognized side effect after therapeutic irradiation. The aim of this study was to examine the potential radioprotective effects of resveratrol on the irradiation induced oxidative damage in the ileum.

**Materials and Methods:** Sprague-Dawley rats were exposed to a single dose of 20 Gy prostate-confined irradiation and given either vehicle or resveratrol (10 mg/kg, orally) once daily. Rats were decapitated at either one week (early) or ten weeks (late) following irradiation. Ileal tissues were taken for biochemical analyses such as xanthine oxidase (XO), glutathione peroxidase (GPx) and glutathione reductase (GR). All tissues were also examined histologically under a light microscope.

**Results:** XO activities were found to be increased while GPx and GR activities were decreased in both early and late radiation group. Administration of resveratrol reversed XO and GPx activity in these groups, but it did not affect GR activity in late radiation group. According to the histopathological evaluation both early and late irradiation groups, desquamation of apical epithelial cells, severe inflammatory cell infiltration were observed in both early and late irradiation groups. Resveratrol treatment produced mild degeneration in the apical epithelial cells and inflammatory cell infiltration was observed in both early and late irradiation groups.

**Discussion:** Currently, radiation-induced enteritis has still remained an important obstacle for healing in cancer patients having radiotherapy. Our results revealed that resveratrol treatment reduces irradiation-induced oxidative organ injury through its possible antioxidant properties.

**Conclusion:** Resveratrol might be an ideal adjunct to radiotherapy by precluding the development of radiation-induced tissue damage.

*Keywords: Resveratrol, Ileum, Radiation, Enzyme Activities, Histology*

## ORAL PRESENTATION – 25

### **BREAST CANCER CELLS WITH STEM LIKE FEATURES ARE SENSITIVE TO MIDOSTAURIN, RESISTANT TO LAPATINIB AND SHOW WORSE PROGNOSIS WHEN TREATED WITH PACLITAXEL**

Muhammad Waqas Akbar<sup>1</sup>, Murat Isbilen<sup>1</sup>, Nevin Belder<sup>1</sup>, Özgür Şahin<sup>1</sup>, Ali Osmay Güre<sup>1</sup>

<sup>1</sup>Department of Molecular Biology and Genetics, Bilkent University, Ankara, Turkey

**Aim:** Breast cancer (BC) is among the most common causes of cancer deaths. The aim of this study was to determine if BC could be classified into stem- and non-stem-like groups (as suggested in the literature before) and whether such sub groups showed differential sensitivity to targeted therapeutic agents.

**Materials and Methods:** We used gene expression data from CCLE<sup>1</sup> (56 cell lines) and CGP<sup>2</sup> (39 cell lines) databases to classify them into cancer stem like (CSC-like) and non-cancer stem like (non-CSC like) cells using a previously reported gene list *in silico*<sup>3</sup>. Additionally these cells were also molecularly subtyped into Luminal, Basal A and B subgroups which showed us that Luminal and Basal A subtype are non-CSC like while Basal B subtype is CSC like<sup>4</sup>. Then we identified differentially expressed gene between CSC like and non-CSC like cells. Using these genes, drugs were selected which target differentially CSC like (i.e. Midostaurin) and non-CSC like cells (i.e. Lapatinib) *in silico*. These findings were then validated *in vitro*. Then we increased cell's stemness by culturing in 3D conditions, which resulted into increased sensitivity to Midostaurin and resistance to Lapatinib as expected. Additionally when we decreased stemness by knocking down ZEB1 and SNAI2, cells became resistant to Midostaurin and sensitive to Lapatinib. Lastly upon survival analysis, our selected genes show worse prognostic value among Paclitaxel treated patients.

**Conclusion and Discussion:** Our findings propose that our selected genes, can be used to identify CSC rich tumors and those can be targeted using Midostaurin. A combinational therapy of Midostaurin with conventional drugs might lead to a better outcome targeting both CSC and non-CSC tumor population. Additionally Lapatinib which is currently used for HER2+ patients showed sensitivity to other non-CSC like cells such as some triple negative breast cancer cells.

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## ORAL PRESENTATION – 26

### MECHANISM OF BORON DERIVATIVES FOR THE TREATMENT OF RENAL CELL CARCINOMA

Nezaket Türkel Sesli<sup>1</sup>, Sıdıka Tapşın<sup>1</sup>, Fikrettin Şahin<sup>1</sup>

<sup>1</sup>Department of Genetics and Bioengineering, Faculty of Engineering, Yeditepe University, Istanbul, Turkey

**Background/Aim:** Cancer is the most common cause of mortality after heart and cardiovascular diseases and occurs due to molecular alternation of signaling molecules and deregulation in the control mechanisms that causes abnormal growth and proliferation of the cells. Cancer induces 14.1 million new cases and 8.2 million deaths per year and approximately 3% of all malignant tumors in adults emerge in the kidney. The most common form of kidney cancer, Renal cell carcinoma (RCC) is the most lethal form of malignancy including the list of breast, prostate and bladder cancer. Because of its drug resistance and highly metastatic capability, current techniques to treat this cancer type are generally ineffective. In recent years, boron derivatives have been started to use as a targeted drug for cancer cells. Nevertheless, the mechanism of boron on cancer has not been clearly established, yet. In this study, the mechanism of two boron derivatives, sodium pentaborate pentahydrate (NaB) and boric acid (BA) has been investigated on ACHN and A498 renal carcinoma cell lines and human primary renal proximal tubule epithelial cells (RPTEC).

**Materials and Methods:** Effects of boron derivatives on proliferation, cell cycle, cell death (apoptosis, autophagy and necroptosis) and metastasis were analyzed by cell viability assay, cell proliferation EdU assay, quantitative real-time PCR analysis, Annexin-V apoptosis assay, MDC autophagy assay and scratch assay analysis.

**Results:** IC<sub>50</sub> values of NaB and BA were determined for A498, ACHN cancer cell lines and RPTEC cell lines and in the further experiments these values were used. Proliferation rate of cancer cells were dramatically decreased by both derivatives, while cell death mechanisms were activated. Furthermore, cell migration were ceased significantly in both cancer cell lines, although ACHN cell line were more sensitive compared to A498 cell line.

**Discussion/Conclusion:** This study showed for the first time that, different boron derivatives might be an effective treatment for renal cancer. Remarkably, NaB was much more effective form of boron derivative on renal cancer and to our knowledge any study has not been conducted using NaB as therapeutic agent in cancer field in literature, yet.

*Keywords: Boron derivatives, renal cancer, proliferation, cell cycle, cell death, metastasis*

## ORAL PRESENTATION – 27

### SMOKING AND ACE D ALLELE: DETERMINANTS OF HIGH SERUM OXIDIZED-LDL LEVELS IN CORONARY HEART DISEASE

Özlem Kurnaz-Gömleksiz<sup>1,2</sup>, C. Selim İsbir<sup>3</sup>, Hülya Yılmaz-Aydoğan<sup>1</sup>

<sup>1</sup> Istanbul University Institute of Experimental Medicine, Department of Molecular Medicine, İstanbul, Turkey

<sup>2</sup> Istanbul Gelisim University, Department of Nutrition and Dietetics, İstanbul, Turkey

<sup>3</sup> Marmara University, Pendik Training and Research Hospital, Department of Cardiovascular Surgery, İstanbul, Turkey

**Background:** Nowadays, high plasma levels of oxidized LDL (ox-LDL) have been added to traditional risk factors in atherogenesis. It was reported that ox-LDL levels increased in coronary artery disease (CAD). Ox-LDL plays a role in endothelial dysfunction and induces the proatherogenic genes. Ox-LDL activates either Renin-Angiotensin-Aldosterone (RAS) system or their receptors in the endothelial cells. AngiotensinII (AII) which is one of the most powerful vasoconstrictors known to date and the RAS components, is produced from AngiotensinI(AI) via Angiotensin-converting enzyme (ACE). ACE I/D gene variations is responsible for inter-individual variations in plasma ACE and AII levels. High AII promotes foam cells formation via stimulation of ox-LDL uptaking mediated LOX-1 receptor in endothelial cells and macrophages. Therefore, the potential interaction between AII and oxidized-LDL in the pathogenesis of atherogenesis requires a more detailed investigation.

**Materials and Methods:** ACE I/D variations were studied in 50 subjects with CAD and 34 healthy controls. Serum lipids and ox-LDL levels were measured by enzymatically and Elisa method, respectively.

**Results:** In CAD patients comparing to the controls, smoking ( $p=0.028$ ), body-mass index ( $p=0.05$ ) were higher. While serum lipid levels were not found different in controls with ACE D-allele compared to subjects with II, ACE D-allele carriers have higher oxLDL levels than non-carriers in CAD group ( $p=0.013$ ). There was no statistically difference in I-allele carriers compared to in DD in both groups. In smoker patients with D-allele, ox-LDL levels were higher than in non-smoker patients with ACE II ( $341.74\pm 65.12$  vs.  $186.16\pm 28.58$ ,  $p=0.037$ ). It was observed that ox-LDL levels increased in patients with ACE-I&non-smoking < ACE-II&non-smoking < ACE-D&non-smoking < ACE-I < ACE-DD&non-smoking < ACE-D < ACE-I&smoking < ACE-D&smoking in order.

**Discussion:** Intracellular encapsulation of ox-LDL and AII-dependent acceleration of LDL oxidation may contribute to plaque instability by accelerating the conversion of VSMC to foam cells. Some studies suggested that in individuals with ACE D-allele, high ACE expression in heart may act in increasing local production of AII and predisposing to left ventricular hypertrophy, a strong risk factor for CAD. In another study on hypertensive patients, it was found an association ACE D-allele and high ox-LDL levels. In the present study, we showed that ACE D-allele may increase ox-LDL levels and smoking may rise the effects of ACE D-allele on ox-LDL levels.

**Conclusion:** We suggested that either smoking or ACE D-allele may increase the ox-LDL levels. Moreover, the coexistence of smoking and ACE D-allele further increases the excess in ox-LDL levels. Smoking may enhance the increasing effect of ACE D-allele on ox-LDL levels.

*Keywords: Oxidized LDL, ACE I/D gene variations, Coronary artery disease, Smoking*

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## ORAL PRESENTATION – 28

### INVESTIGATION OF NOVEL GENES ASSOCIATED WITH ENDURANCE AND STRENGTH IN ATHLETE

<sup>1</sup>Celik F, <sup>1</sup>Kahraman-Timirci O, <sup>1</sup>Zeybek U, <sup>1</sup>Tunoglu S, <sup>2</sup>Yucesir I, <sup>3</sup>Bayraktar B, <sup>4</sup>Korkmaz O, <sup>5</sup>Kurtoglu M

<sup>1</sup>Istanbul University, Department of Molecular Medicine, Aziz Sancar Institute of Experimental Medicine, Istanbul, TURKEY

<sup>2</sup>Istanbul University, School of Physical Education and Sports, Istanbul, TURKEY

<sup>3</sup>Istanbul University, Istanbul Faculty of Medicine, Department of Sports Medicine, Istanbul, TURKEY

<sup>4</sup>Marmara University, Department of Information Technology in Sports, Istanbul, TURKEY

<sup>5</sup>Istanbul University, Istanbul Faculty of Medicine, Department of General Surgery, Istanbul, TURKEY

**Background:** Different factors affecting athletic performance are well established: intensity and type of training, anthropometric characteristics as well as an important psychological component. However, the contribution of the genetic background has been less investigated. The aim of the present study was to investigate the influence of insulin-like growth factor 1 (IGF-1), vascular endothelial growth factor (VEGF), peroxisome proliferator-activated receptor-delta (PPAR $\delta$ ), creatine kinase-isoenzyme MM (CK-MM) and angiotensinogen (AGT) genes associated with endurance and strength on the physical capability and sports performance.

**Materials and Methods:** Quantitative real-time polymerase chain reaction (qRT-PCR) analysis was used to determine the expression patterns of IGF1, VEGF, PPAR $\delta$ , CK-MM and AGT genes in 73 athlete. We selected >2 cut-off values for gene expression fold changes.

**Results:** When we analyzed gene expression levels, we showed that there are correlation athletic performance datas and IGF-1 and AGT gene expression patterns.

**Conclusion:** This genetic background plays an important role in sporting potential and causes some individuals to be better adapted to specific physical training. This should be considered in athlete development to identify which sporting specialties should be trained for talent promotion.

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## ORAL PRESENTATION – 29

### THE ROLE OF DAT, 5-HTT, MAOA AND MAOB OF NICOTINE DEPENDENCE IN A TURKISH POPULATION

Ülgen Sever<sup>1</sup>, Mehmet Atilla Uysal<sup>2</sup>, Özge Pasin<sup>3</sup>, Yedikule Smoking Cessation Polyclinic Working Group<sup>2</sup>, Sacide Pehlivan<sup>1</sup>

<sup>1</sup>Department of Medical Biology, İstanbul University, İstanbul Faculty of Medicine, İstanbul, Turkey

<sup>2</sup>Yedikule Hospital For Chest Diseases and Thoracic Surgery Training and Research Hospital, İstanbul, Turkey

<sup>3</sup>Department of Biostatistics, İstanbul University, İstanbul Faculty of Medicine, İstanbul, Turkey

**Aims and Scopes:** Nicotine, which is the active substance of tobacco dependence, by affecting the dopaminergic neurons stimulates the release of dopamine and brain serotonin levels to increase due to nicotine were shown in the literature. It has been reported that range of synaptic dopamine and serotonin levels can be associated with susceptibility to various psychological disorders and addiction. Dopamine transporter protein (DAT), serotonin transporter protein (5-HTT), Catechol-O-Methyltransferase (COMT) and Monoamine Oxidase A and B (MAOA and MAOB) are involved in the regulation of dopamine and serotonin levels in the synaptic cleft. We aimed to compare gene variants of DAT and 5-HTT which were located on the autosomal chromosomes; MAOA and MAOB which were located on X chromosome, between smoker (and clinical parameters) and non-smoker individuals.

**Materials and Methods:** 164 (90 M-Male, 74 F-Female) smokers and 128 (61 M, 67 F) non-smokers were included in the study. DNA was isolated from peripheral blood samples. The variants of DAT/40bp VNTR, MAOA/uVNTR, and 5HTTLPR were investigated by PCR method; the variants of MAOB/A644G was studied by PCR-RFLP method, and agarose gel was used for analysis. All data were analyzed using software SPSS version 21.0 ( $p < 0.05$  was considered statistically significant).

**Results and Discussion:** Mean age was  $42.87 \pm 13.24$  for smokers and  $33.98 \pm 12.34$  for non-smokers. It was not determined any significant difference between the groups when compared regarding genotype / allele frequency of DAT/40bp VNTR, MAOB/A644G, and 5HTTLPR variants. It was observed that 4R variant of MAOA significantly increased in male smokers, while 3.5R variant significantly increased in male non-smokers ( $p=0.003$ ). When the genotypes were compared there was no significant difference in the number of cigarettes per day, smoking initiation age and Fagerstrom Test for Nicotine Dependence (FTND) score. In males; 3.5R variant of MAOA may play a protective role against smoking dependence, while 4R variant may be associated with predisposition to smoking dependence.

*Keywords:* Nicotine dependence, DAT, 5-HTT, MAOA, MAOB

*Acknowledgements:* This study was supported by İstanbul University BAP thesis project (2414-50595) support program and Yeşilay postgraduate scholarship program.



## ORAL PRESENTATION – 30

### **DISCOVERY OF KLOTHO PEPTIDE ANTAGONISTS AGAINST WNT3 AND WNT3A TARGET PROTEINS: COMBINATION OF COMPUTATIONAL, PEPTIDE SYNTHESIS, AND IN VITRO ANALYSIS**

Serdar Durdagi<sup>1</sup>, Shaher Bano Mirza<sup>1,2</sup>, Ramin Ekhteiari Salmas<sup>1</sup>, Aykut Uren<sup>3</sup>, Adriano Mollica<sup>4</sup>

<sup>1</sup>Department of Biophysics, School of Medicine, Bahcesehir University (BAU), Istanbul, Turkey

<sup>2</sup>Department of Biosciences, COMSATS Institute of Information Technology (CIIT, Islamabad, Pakistan

<sup>3</sup>George Town University, Medical Center, Lombardi Comprehensive Cancer Center, USA

<sup>4</sup>Universita degli Studi G. , Department of Pharmacy, Italy

The Klotho is known as lifespan enhancing protein involved in antagonizing the effect of Wnt proteins. Wnt proteins are stem cell regulators, and uninterrupted exposure of Wnt proteins to the cell can cause stem and progenitor cell senescence, which may lead to aging. Keeping in mind the importance of Klotho in Wnt signaling, *in silico* approaches have been applied to study the important interactions between Klotho and Wnt3 and Wnt3a (wingless-type mouse mammary tumor virus (MMTV) integration site family members 3 and 3a). The main aim of the study is to identify important residues of the Klotho that help in designing peptides which can act as Wnt antagonists. For this aim, a protein engineering study is performed for Klotho, Wnt3 and Wnt3a. During the theoretical analysis of homology models, unexpected role of number of disulfide bonds and secondary structure elements has been witnessed in case of Wnt3 and Wnt3a proteins. Different *in silico* experiments were carried out to observe the effect of correct number of disulfide bonds on 3D protein models. For this aim, total of 10 molecular dynamics (MD) simulations were carried out for each system. Based on the protein-protein docking simulations of selected protein models of Klotho with Wnt3 and Wnt3a, different peptides derived from Klotho have been designed. Wnt3 and Wnt3a proteins have three important domains: Index finger, N-terminal domain and a patch of ~10 residues on the solvent exposed surface of palm domain. Protein-peptide docking of designed peptides of Klotho against three important domains of *palmitoylated* Wnt3 and Wnt3a yields encouraging results and leads better understanding of the Wnt protein inhibition by proposed Klotho peptides. *In vitro* are carried out to verify effects of novel designed peptides as Wnt antagonists.

*Keywords: Klotho, Wnt3, Wnt3a, protein-protein docking, molecular dynamics (MD) simulations, peptide design, protein engineering, homology modeling*

## ORAL PRESENTATION – 31

### A NEW PERSPECTIVE FOR THE TREATMENT OF COLON CANCER: MESENCHYMAL STEM CELLS

Elif Sinem Bireller<sup>1</sup>, Baris Ertugrul<sup>2</sup>, Ilknur Kozanoglu<sup>3</sup>, Yusuf Baran<sup>4,5</sup>, Bedia Cakmakoglu<sup>2</sup>

<sup>1</sup> Department of Pharmaceutical Microbiology, Faculty of Pharmacy, Istanbul Yeni Yuzyil University, Istanbul, Turkey

<sup>2</sup> Istanbul University, Institute for Aziz Sancar Experimental Medicine Research, Department of Molecular Medicine, Istanbul, Turkey.

<sup>3</sup> Department of Hematology, Baskent University, Adana, Turkey.

<sup>4</sup> Faculty of Life and Natural Sciences, Abdullah Gul University, Kayseri, Turkey

<sup>5</sup> Department of Molecular Biology and Genetics, Izmir Institute of Technology, Urla, Izmir, Turkey.

**Background:** Colon cancer is the third most common cancer among the leading cause of cancer related death in the world. Treatment options for colon cancer are surgery, chemotherapeutic agents, and radiotherapy. Although there are many choices for colon cancer treatments, drug resistance reduces the success of especially chemotherapeutic agents; alternative therapies are still a popular topic. Mesenchymal stem cells (MSCs) are the new approach for several diseases including cancer. MSCs are adult stem cells that have multipotent differentiation potential. Last years, MSCs has turned out popular for cancer treatment. Likewise, there are studies about animal models, which have tumor model treating by injected MSCs into the animal.

**Materials and Methods:** MSCs was isolated from mouse adipose tissue and characterized by FACS Canto II (BD Bioscience, USA). MSCs concentration and usage period on colon cancer cell lines; HT-29, HCT-116, RKO were optimized by time and dose dependent manner by WST-1 cell proliferation assay. Antiproliferative and apoptotic effects of subsequently determined by changes in caspase-3 activity and also the localization of phosphatidylserine in the plasma membrane by Annexin V.

**Results:** There were significant changes in caspase-3 activity on HT-29, RKO colon cancer cells. There were not being found any change in caspase-3 activity on HCT-116 cell line. It was also resulted that apoptotic cell population was increased in response to MSCs in especially, HT-29, HCT-116 colon cancer cells in a time- and dose-dependent manner.

**Discussion:** In this research, we have found to answer that apoptosis level what if adipose derivated MSCs given as an anticancer agent on the different colon cancer cell lines and a healthy cell line for the first time. We suggested that MSCs might be a new treatment option by its differentiation and repair capacity. Further studies need to clarify its role in detailed with HCT-116, HT-29, RKO and also their *in vivo* conditions.

**Conclusion:** In conclusion, our study might be lead new window for treatment options by a view on without using immunosupresion to using him/her own adipose tissue to isolate him/her own MSCs. MSCs activity also needs to be supported with molecular expression levels and also *in vivo* analyses to be a candidate for the treatment of colorectal carcinoma.

*Keywords:* colon cancer, mesenchymal stem cell, cell death.

*Acknowledgements* This work was funded by Istanbul University Scientific Research Project number 39247.

## ORAL PRESENTATION – 32 THE LICENSING OF BIOLOGICALS AND BIOSIMILARS IN TURKEY AND PATIENT ACCESS

Sermin Bicer<sup>1</sup>, Serhat Kılıç<sup>2</sup>, Ahmet Mengi<sup>3</sup>

<sup>1</sup> Department of Pharmacology, Faculty of Pharmacy, Istanbul Yeni Yuzyil University, Istanbul, Turkey

<sup>2</sup> Faculty of Pharmacy, Istanbul Yeni Yuzyil University, Istanbul, Turkey

<sup>3</sup> Department of Biochemistry and Pharmaceutical Biotechnology, Faculty of Pharmacy, Istanbul Yeni Yuzyil University, Istanbul, Turkey

Biological medicinal products (biologics) contain biological substances that are produced by or extracted from a biological source and needs a combination of physico-chemical-biological testing together with the production process and its control for its characterisation and the determination of its quality. Biologics include recombinant therapeutic proteins, monoclonal antibodies, medicinal products derived from human blood and human plasma, immunological medicinal products and advanced therapy medicinal products. Currently these drugs are effectively used to treat a variety of medical conditions with a consistently increasing diversity and indication spectrum. Biological products, for which patents have already expired, are licensed under the name 'biosimilars' by regulatory authorities. Biosimilar products are only similar in composition to a reference product and therefore, not called generic forms of biological products compared to conventional medicines. Because of their special production processes and complex structures, the licensing criteria and approval process of biological and biosimilar products are of critical importance. Turkey has established a licensing system compatible with the European Union for the authorization of biological and biosimilar medicinal products. However, on contrary to conventional products, biological and biosimilar products are expensive products and create increasing cost to the reimbursement system. Some biological and biosimilar products are under prescription control and also obligatory safety monitoring (pharmacovigilance). These specific conditions regarding biologics and biosimilars may create some different practices during the licensing and reimbursement process in Turkey and for patients' access.

In this scope, the status of biological and biosimilar products in Turkey from regulatory perspective including safety monitoring were evaluated referring to the conventional products. Furthermore, some limitations applied to these products are underlined from patient' access perspective and government policies supporting local development and production of biologics and biosimilars are emphasized.

*Keywords: Biological product, biotechnological product, biosimilar product, recombinant DNA technology*

## ORAL PRESENTATION – 33 SAFETY OF HERBAL SELF- MEDICATION IN DIABETES

Elif Şahin<sup>1</sup>, Elif Sinem Bireller<sup>2</sup>, Gül Bakır<sup>1</sup>, Engin Özhatay<sup>3</sup>

<sup>1</sup>Department of Pharmacology, Faculty of Pharmacy, Istanbul Yeni Yuzyil University, Istanbul, Turkey

<sup>2</sup>Department of Pharmaceutical Microbiology, Faculty of Pharmacy, Istanbul Yeni Yuzyil University, Istanbul, Turkey

<sup>3</sup>Department of Pharmaceutical Botany, Faculty of Pharmacy, Istanbul Yeni Yuzyil University, Istanbul, Turkey

Plants have been using by humans since ancient times prophylactically and therapeutically against several diseases. Some plants which are used traditionally have shown pharmacological and toxicological properties in ethnopharmacological scientific studies. However, the common public belief is that plants and herbal products are harmless and would not cause side effects poses a serious risk in terms of public health. Diabetes mellitus (DM) is the most common metabolic disease affecting the world population. A lot of plants are known to be used traditionally according to ethnobotanical studies by their hypoglycemic activity. In this study, it is aimed to identify the plants with hypoglycemic effects which have some risks when used during pregnancy.

For this purpose, ethnobotanical and ethnopharmacological studies were evaluated and the plants used for hypoglycemic effect in Turkey, their pharmacological and toxicological properties were determined by literature search.

Our results demonstrate that some plants like *Trigonella foenum- graecum* (Çemen), *Momordica charanti* (Kudret Narı), *Artemisia absinthium* (Pelin Otu), *Teucrium polium* (Acı Yavşan – Kısamahmut otu), *Urtica dioica* (Isırgan), *Berberis crataegina* (Diken Üzüümü- Karamuk), *Thymus sp.* (Kekik), *Viscum album* (Ökse Otu) and *Malva sylvestris* (Ebegümeçi) have a wide traditional use for their hypoglycemic effects. On the other hand, scientific researches have shown that, these plants have some side effects on central nervous system, gastrointestinal system and cardiovascular system additionally serious side effects such as hepatotoxicity, abortus, stimulations of menstruation, genetic defect on fetus. Therefore these herbal medicinal products should not be used by diabetics, most importantly by diabetic pregnant women who prefer herbal medicines.

In addition, unreliable herbal sources and the availability of these herbal medicinal products as unregulated botanical preparations (lack of purity, classification, preparation and standardization) pose an additional risk for public health.

In conclusion, without advice of health professionals, the use of plants and herbal medicinal products for diabetes self-treatment during pregnancy can have serious consequences for mother and baby. For this reason, plants should be used by pregnant women with the advice of clinicians and pharmacist. It is necessary to educate pregnant women to avoid self-medication with plants and herbal products.

*Keywords:*, Diabetes Mellitus (DM), Hypoglycemic plants, Herbal medicinal products, Pregnancy

## ORAL PRESENTATION – 34

### TFII-I INTERACTS WITH E2F TRANSCRIPTION FACTORS AND REGULATES THEIR ASSOCIATION WITH THE CO-OCCUPIED CDC27, CDKN1C, HDAC1, AND DNMT1 GENE LOCI

Rukiye Nar<sup>1</sup>, Yong Shen<sup>2</sup>, Alex Xiucheng Fan<sup>2</sup>, Mahmoud Aryan<sup>2</sup>, Mir A. Hossain<sup>2</sup>, Ming Tang<sup>2</sup>, Jianrong Lu<sup>2</sup>, John Strouboulis<sup>3</sup>, Jörg Bungert<sup>2</sup>

<sup>1</sup>Department of Medical Biochemistry, College of Medicine, Ahi Evran University, Kirsehir, Turkey

<sup>2</sup>Department of Biochemistry and Molecular Biology, Center for Epigenetics, Genetics Institute, Shands Cancer Center, Powell-Gene Therapy Center, University of Florida, USA

<sup>3</sup>Institute of Molecular Biology and Biotechnology, Foundation of Research and Technology-Hellas, Heraklion, Crete, Greece

**Background/Aim:** Transcription factor TFII-I (gene symbol *GTF2I*) is a multifunctional protein involved in gene expression regulation. The *GTF2I* gene as well as two closely related genes are located together on chromosome 7. Haploinsufficiency of this region on chromosome 7 causes Williams Beuren (WB) syndrome, which is characterized by facial and neurological defects. Previous studies implicated TFII-I in the regulation of cell-cycle and stress-response genes (1,2). In the current study we analyzed interactions between the repressor E2Fs, E2F4 and E2F6, and TFII-I.

**Materials and Methods:** We analyzed the coassociation of TFII-I and E2Fs in more detail using bioinformatics, chromatin immunoprecipitation, and co-immunoprecipitation experiments in K562 Human erythroleukemia cell line. To reduce expression of TFII-I (*GTF2i*), K562 cells were transfected with the plasmid pGIPZ-shTFII-I.

**Results and Discussion:** The data show that TFII-I and the repressor E2Fs, E2F4 and E2F6, interact and bind to several genes implicated in the response to cellular stress, including the DNMT1, and HDAC1 genes as well as genes implicated in cell cycle regulation, including CDC27, and CDKN1C. Inhibition of TFII-I expression led to a decrease in the association of E2F4 and E2F6 with the DNMT1, HDAC1, CDC27, and CDKN1C gene loci in human erythroleukemia K562 cells. Furthermore, depletion of TFII-I also caused a decrease in expression of these genes.

**Conclusion** The results uncover novel interactions between TFII-I and E2Fs and suggest that TFII-I and E2Fs play positive roles in the expression of cell cycle and stress-response genes.

*Keywords: TFII-I, E2F, ATF3, Gene Regulation, Cell Cycle*

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## ORAL PRESENTATION – 35

### EFFECT OF MIF rs755622 GENE POLYMORPHISM ON THE ALZHEIMER PATIENTS

Kubra Sahin<sup>1</sup>, Aydın Rustemoglu<sup>1</sup>, Volkan Solmaz<sup>2</sup>, Durdane Aksoy<sup>3</sup>

<sup>1</sup>Department of Medical Biology, Medical Faculty, Gaziosmanpaşa University, Tokat, Turkey

<sup>2</sup>Department of Medical Biology, Medical Faculty, Trakya University, Edirne, Turkey

<sup>3</sup>Department of Medical Biology, Medical Faculty, Gaziosmanpaşa University, Tokat, Turkey

**Background/Aim:** The Alzheimer (AD) is a chronic neurodegenerative and inflammatory disease. Acute phase response generated from degeneration in the brain. This condition causes rapidly increasing of proteins called cytokines, which stimulate the body's defense mechanisms. Macrophage migration inhibitory factor (MIF) gene, localized in chromosome 22q 11.23, encodes a cytokine secreted by lymphocytes which inflammatory agent of natural and acquired immune response. Previously studies showed that, the polymorphisms of promotor of the MIF gene to play a role in pathogenesis of autoimmune/inflammatory diseases such as rheumatoid arthritis and systemic lupus erythematosus. The aim of this study to investigated the association between AD and MIF gene rs755622 polymorphism.

**Materials and Methods:** In this study were investigated on 215 patients with AD and 131 health individuals in terms of MIF gene rs755622 polymorphism. The genotyping of MIF gene rs755622 locus were determined using Real-Time PCR method.

**Results:** The frequency of GG, GC, and CC genotypes of MIF gene rs755622 polymorphism were found for patients and control groups as 0.7070, 0.2698, 0.0232 and 0.6107, 0.3511, 0.0382, respectively. Although the overall genotype distributions of MIF rs755622 polymorphism are different from patient and control groups, these differences was not statistically significant ( $p=0,061$ ). In terms of individual genotype frequencies, especially frequency of the GG genotype differ from patient and control groups (0.7070 and 0.6107). But, these differences was not statistically significant ( $p=0,077$ ; OR,95%CI=1.54,0.97-2.43). In similar manner, despite of the G allele was observed more higher in patients than controls (0.8419 ve 0.7863), statistically difference were not found ( $p=0,067$ ; OR,95%CI=1,45,0.98-2,14).

**Conclusions:** In spate of the fact that, the our results was showed any association between MIF gene rs755622 polymorphism and AD, because of we were studied relatively small control group, and some p- values were found near significant border, the obtained results are needed to supported other new research with more much samples.

*Keywords: Alzheimer, MIF gene, rs755622, polymorphism.*

*The study protocol was approved by the Local Ethics Committee of Gaziosmanpaşa University Faculty of Medicine (Project Number:15-KAEK-019).*

*Note to the Scientific Committee: This study was supported by Gaziosmanpaşa University Scientific Research Projects Fund (Project Number: 2015/68).*

## ORAL PRESENTATION – 36

### THE EFFECT OF SURFACTANT PROTEIN B GENE POLYMORPHISM IN THE ETHIOLOGY OF ACUTE BRONCHIOLITIS

Sumeyya Deniz Celik<sup>1</sup>, Omer Ates<sup>1</sup>, Saime Sezer Sondas<sup>1</sup>, Sahin Takcı<sup>2</sup>, Buket Altıntaş Seyyah<sup>2</sup>

<sup>1</sup>Department of Medical Biology, Medical Faculty, Gaziosmanpaşa University, Tokat, Turkey

<sup>2</sup>Department of Neonatology, Medical Faculty, Gaziosmanpaşa University, Tokat, Turkey

**Background/Aim:** Acute bronchiolitis has usually been defined as a disease characterized by acute wheezing in infants or children. The disease is caused by respiratory syncytial virus which is most common etiologic agent. Prematurity, young age, male gender, underlying lung disease (such as bronchopulmonary dysplasia), neuromuscular disease, heart disease, exposure to tobacco smoke, young maternal age, short duration/no breastfeeding, maternal asthma and poor socioeconomic factors are risk factors for acute bronchiolitis. Surfactant proteins (SPs) consists of a variety of lipids and a number of proteins, which is essential for normal lung functions. Surfactant protein B (SP-B) is one of the four known SPs, essential for the biogenesis of pulmonary surfactant and formation of lamellar bodies. Previously studies show that genetic polymorphisms in the SP-B gene have been associated with severe respiratory syncytial virus infection. This study aimed to investigate the association between SP-B polymorphism and acute bronchiolitis in Turkish infants.

**Materials and Methods:** The present study analyzed the genotype distribution and allele frequency for the C1580T polymorphism using the polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) technique in 103 patients with acute bronchiolitis and 102 healthy individuals.

**Results:** The genotype and allele distribution of SP-B C1580T polymorphism have not been associated with acute bronchiolitis ( $p=0.856$  and  $p=0.374$ , respectively).

**Discussion:** Our results suggest that polymorphic variation in SP-B gene is not involved in susceptibility to acute bronchiolitis.

**Conclusions:** Further work on the relevance of this gene in a larger cohort is required to validate our observations.

*Keywords: Surfactant Protein B, Acute bronchiolitis, Genetic polymorphism*

*The study protocol was approved by the Local Ethics Committee of Gaziosmanpaşa University Faculty of Medicine (Project Number: 83116987/2).*

*Note to the Scientific Committee: This study was supported by Gaziosmanpaşa University Scientific Research Projects Fund (Project Number: 2015/59).*

## ORAL PRESENTATION – 37

### ASSOCIATION BETWEEN BRONCHIOITIS INFANTS AND INTERLEUKIN 8 GENE POLYMORPHISM

Cisem Nildem Dogan<sup>1</sup>, Omer Ates<sup>1</sup>, Sahin Takcı<sup>2</sup>

<sup>1</sup>Department of Medical Biology, Medical Faculty, Gaziosmanpaşa University, Tokat, Turkey

<sup>2</sup>Department of Neonatology, Medical Faculty, Gaziosmanpaşa University, Tokat, Turkey

**Background/Aim:** Acute bronchiolitis is a viral disease that generally occur in winter seasons. In Turkey, it has been mostly seen in December- January. This disease is common in children under 2 years old, and it can be seen in wide age range, too. Major causes of the disease are viruses that bring lower respiratory infection. Respiratory syncytial virus (RSV) is the most common of these. However, rhinovirus, influenza, human metapneumovirus (hMPV), parainfluenza 3 (PIV 3), coronavirus and bocavirus also cause bronchiolitis. The most common viruses in Turkey are rhinovirus, RSV-A-B and hMPV. Neutrophils have been found in bronchoalveolar fluids of infants with bronchiolitis as the dominant cell type. In addition, some studies have show that RSV stimulates airway epithelial cells to produce large amounts of interleukin-8. This may give clue about which chemoatraktant stimulate the neutrophils. Furthermore, some studies showed that identical twins were more likely to have bronchiolitis than fraternal twins. Thus, these experiments shed light on genetic studies. This research aimed to investigate the possible relationships between IL-8 -251A/T gene polymorphism and acute bronchiolitis.

**Materials and Methods:** Blood samples were taken from 104 patients with acute bronchiolitis and 104 samples from the babies that brought to hospital for rutin controls. We use polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) to find genotype distribution and allele frequency of IL-8 -251A/T polymorphism.

**Result:** According to the statistical analyses, -251A / T gene polymorphism is not related to with acute bronchiolitis (P=0.8315, P=0.421 respectively).

**Discussion:** IL-8 -251A/T polymorphism was worked in different populations. In some studies not found that association between -251A/T polymorphism with acute bronchiolitis. Our results showed that IL-8 have no relationship with acut bronchioltis in Turkey.

**Conclusions:** Focusing on younger infants with bronchitis and using larger sampling numbers may produce clearer results in future studies.

*Keywords: Acute bronchiolitis, IL-8, PCR-RFLP, gene polymorphism*

*The study protocol was approved by the Local Ethics Committee of Gaziosmanpasa University Faculty of Medicine (Project Number: 15-KAEK-206)*



## ORAL PRESENTATION – 38

### **INVESTIGATING THE EFFECTS OF ARTIFICIAL FOOD COLORINGS, EXPOSED DURING PRENATAL TERM WITH THE DOSE OF NOAEL, ON SALIVA GLANDS IN ADULT PERIOD.**

Fatih GÜLTEKİN<sup>1</sup>, Hasan Basri SAVAŞ<sup>1</sup>, Kayhan BAŞAK<sup>2</sup>, Firdevs AYLAK<sup>3</sup>, Duygu KUMBUL DOĞUÇ<sup>3</sup>

<sup>1</sup> Alanya Alaaddin Keykubat University, Medical Faculty, Medical Biochemistry Department, Antalya, Turkey.

<sup>2</sup> Dr.Lutfi Kırdar Kartal Education and Research Hospital, Pathology Department, Istanbul, Turkey.

<sup>3</sup> Suleyman Demirel University, Medical Faculty, Medical Biochemistry Department, Isparta, Turkey.

Artificial food colorings as a part of food additives are widely used in today's daily life. Prior to permitting the use of additives many toxicological researches have been made. Although some studies had been carried out on the teratogenic effects of synthetic colors, researches about their adulthood effects caused by exposing to the safe levels during intrauterine term were very limited. We aimed to investigate the effects of exposure to artificial food colorings during intrauterine period on saliva glands in adult period. A total of 30 Wistar albino female rats were included in this study. Animals were equally divided into two groups as follows: Controls (n = 15) and food colorings given group (n = 15). A mixture of nine artificial food colorings (erythrosine, ponceau 4R, allura red AC, sunset yellow FCF, tartrazine, amaranth, brilliant blue, azorubine and indigotin) at NOAEL dose was given to the treatment group and tap water was administered to the control group in daily basis via oral gavage way beginning from one week prior to pregnancy till delivery. When the offsprings become adults, they were sacrificed and the possible histopathological and immunohistochemical effects of artificial food colorings on saliva glands were investigated. In our study, anti-MMP2, anti-TIMP1, anti-TIMP2, anti-TIMP3 expressions were found high in the experimental group ( $p < 0.05$ ). These results suggest that intrauterine exposure to synthetic food colorings may induce deterioration of tissue structure of the salivary glands during adulthood, thereby increasing susceptibility to many diseases including chronic inflammation, deterioration of tissue integrity, and malignancy. As an important consequence of our research, staying away from food colorings will be an important preventive measure for many diseases, starting with chronic inflammation, leading to cancer for pregnant in terms of future life of infants.

*Keywords: Artificial food colorings, saliva gland, food additives.*

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*Ethical issue: All of the study's procedures were approved by the Suleyman Demirel University Head of the Local Ethics Committee of Animal Experiments. (Approving date: 24.04.2012, number: 02).*

## ORAL PRESENTATION – 39

### **FENDRR AND LincRNA-p21 EXPRESSION DECREASE IN ATHEROSCLEROTIC PLAQUES**

Nilgün Çetin<sup>1</sup>, Arzu Özcan<sup>1</sup>, Ergün Pınarbaşı<sup>1</sup>, Sabahattin Göksel<sup>2</sup>

<sup>1</sup> Department of Medical Biology, Faculty of Medicine, Sivas, Turkey

<sup>2</sup> Department of Cardiovascular Surgery, Faculty of Medicine, Cumhuriyet University, Sivas, Turkey

**Background:** Cardiovascular disease is the most important cause of mortality worldwide and its underlying reason is atherosclerosis. Recently lncRNAs effecting atherosclerotic progression were reported in vascular smooth muscle cells, endothelial cells and monocytes suggesting that lncRNAs play an important role in atherosclerosis.

**Materials and Methods:** In this study we investigated the role of two lncRNAs, FENDRR and LincRNA-p21, by comparing their expression levels in coronary artery plaques and normal mammalian artery of 20 atherosclerotic patients using qRT-PCR technique.

**Results:** We found that FENDRR and lincRNA-p21 expression decreased by approximately 2 and 7 fold in coronary artery plaques respectively when compared to mammalian artery that is known to have no plaque development.

**Discussion:** Our study is the first study carried out with mammalian artery tissues of the same patients as a control. It is also the first expression study of FENDRR.

**Conclusion:** Our data may provide helpful insight regarding further study of lncRNAs associated with atherosclerosis.

*Keywords: Atherosclerosis, lncRNA, FENDRR, lincRNA-p21*

*The study has been approved by the ethics committee of Cumhuriyet University, Sivas, Turkey (No: 2015-03/63) and informed consent was obtained from all patients who participated in the study.*

*Not to scientific committee: This work was supported by the Cumhuriyet University Scientific Research Unit under Grant number T-643.*

## ORAL PRESENTATION – 40

### EVALUATION OF PROTEOMIC RESPONSE OF HUMAN TUMOR CELLS TO SIRTINOL BY A NOVEL SAMPLE PREPARATION METHOD

Betul Sahin<sup>1,2</sup>, Michael P Myers<sup>1</sup>

<sup>1</sup>International Centre for Genetic Engineering and Biotechnology, Trieste, ITALY

<sup>2</sup>Acibadem University, Istanbul, Turkey

**Background / Aim:** This work develops and evaluates a novel method for mass spectrometry based proteomics, with the goal of increasing the number of protein identifications, while also allowing quantitative analysis to be performed. The sample preparation approach I developed uses classical SILAC labeling coupled to a “novel” scheme for enriching cysteine containing peptides which generated by oxidizing the cysteine and cystine residues of proteins. With this novel method we aimed to study the proteomic profiles changes of H1229 cancer cells following sirtinol treatment. Sirtinol, which targets members of the sirtuin family, has been proposed as a treatment for cancer. In fact sirtinol induces senescence in H1299 cells, and we wanted to observe the long term therapeutic effects of sirtinol at the proteome level. This work will give a better understanding of the mode of action of these compounds, as well as revealing the biological mechanisms of their effects.

**Materials and Methods:** Protein sample was oxidized with 3% performic acid and optimized ERLIC (electrostatic repulsion hydrophilic interaction chromatography) was performed using PolyWAX™ resin 3M Empore™ SPE extraction disk. Sirtinol treated H1299 cells were used for the validation of the hybrid protocol. Senescence-associated beta-galactosidase (SA-β-gal) activity was checked to detect senescent cells. (Mascot is used for peptide/protein identification and ProteoIQ software is used for quantitative analysis.

**Results:** The optimized hybrid protocol yielded approximately 3 times the proteins identifications from H1299 cells, when compared to the standard protocol. Quantification of this data revealed that 140 proteins are downregulated and 88 proteins are upregulated following sirtinol treatment of H1299 cells. Moreover, an additional benefit of the protocol was an increase in the total number of post translational modifications (PTMs) identified using the hybrid approach.

**Conclusion:** By developing hybrid method I get the ease of labeling and enhanced quantitative performance of SILAC protocols with the added benefit of the reduction in sample complexity seen with ICAT protocols. The hybrid method is useful for increasing the number of protein identifications from complex samples. It is an accurate and straightforward method for comparative studies. This method is especially useful for drug analysis studies or other binary comparisons.

*Keywords: proteomics, method development, sirtinol*

## ORAL PRESENTATION – 41

### **DYNAMIC THIOL-DISULPHIDE HOMEOSTASIS IN LOW-GRADE GLIOMAS: PRELIMINARY RESULTS IN SERUM**

BERRIN BERCIK INAL<sup>1</sup>, HUMEYRA OZTURK EMRE<sup>2</sup>, OGUZ BARAN<sup>3</sup>, MERDİN AHMEDOV<sup>4</sup>,  
AHMET FARUK OZDEMİR<sup>4</sup>, RAHSAN KEMERDERE<sup>4</sup>, VEYSEL ANTAR<sup>3</sup>, SEDA ATES<sup>5</sup>, TANER  
TANRIVERDİ<sup>4</sup>

<sup>1</sup>Clinical Biochemistry Laboratory, and <sup>3</sup>Department of Neurosurgery, Ministry of Health, Samatya Training and Research Hospital, Istanbul, Turkey.

<sup>2</sup>Clinical Biochemistry Laboratory, Ministry of Health, Haseki Training and Research Hospital, Istanbul, Turkey.

<sup>4</sup>Department of Neurosurgery, Cerrahpasa Medical Faculty, Istanbul University, Istanbul, Turkey.

<sup>5</sup>Department of Obstetrics and Gynecology, Bezm-i Alem Vakif University, Medical Faculty, Istanbul, Turkey.

**Background:** Maintaining of precise balance between oxidation and antioxidation is important in both physiological and pathological states. Any pathological condition leads to redox reactions and toxic molecules, known as reactive oxygen species (ROS). Thiols are anti-oxidant molecules and contain a sulfhydryl group (-SH). Under stress conditions in which ROS are produced, thiols can undergo oxidation reaction to form disulphide bonds. Abnormal dynamic thiol-disulphide homeostasis is involved in the pathogenesis of several neurodegenerative disorders and some brain tumors. The aim of this study is to investigate dynamic thiol-disulphide homeostasis in patients with low-grade gliomas.

**Materials And Methods:** Serial serum samples were collected in 13 patients operated on low-grade gliomas before and after surgery and 13 control serum samples were obtained from venous cord blood from healthy women during caesarian section. In this study, a novel method developed by Erel, et al. is used for assay of thiol-disulphide homeostasis in serum samples.

**Results:** Total thiol, native thiol and disulphide bond formation were measured and compared with the controls. Total thiols, native thiols and disulphide bond formation significantly increased in patients before surgery compared to the controls ( $p < 0.05$ ). Although no significant difference was found between the patients and controls regarding the ratios disulphide/total thiol, disulphide/native thiol, and native thiol/total thiol ( $p > 0.05$ ), the balance seemed to shift to oxidative side.

**Discussion:** Depending on the results from the present study we certainly underlined that thiol-disulphide dynamics, or in common term, precise balance between oxidation-antioxidation mechanisms have been disrupted in patients with LGGs. Comparing with the controls, significant high serum levels of TT, NT, and DS bond formation in the patients suggest that the balance shifted to oxidative side. Furthermore higher mean levels obtained from the ratios (DS/NT, DS/TT, NT/TT) in patients before surgery and significant differences compared to the controls favor of oxidative side that is the balance has shifted to DS bond formation. NT, and DS bond formation have decreased and the differences did not reach significant levels compared to the controls after surgery although DS formation levels seems to be increased at the first week of surgery.

**Conclusion:** Thiol-disulphide homeostasis is disrupted in patients with low-grade gliomas and oxidation may play a role in the process of this disease. Supplementation with antioxidants before and after surgery may be taken into consideration.

*Keywords: Disulphide bond, Gliomas, Native thiol, Oxidation, Total thiol.*

## ORAL PRESENTATION – 42

### EFFECT OF THE POLYMORPHISMS OF UNCOUPLING PROTEINS GENES UCP1-3826 A/G AND UCP2 EXON8 DEL/INS IN CHILDHOOD OBESITY

Ali Gul<sup>1</sup>, Resul Yılmaz<sup>2</sup>, Ömer Ateş<sup>3</sup>, Tuba Kasap<sup>2</sup>, Şahin Takçı<sup>2</sup>, Emel Ensari<sup>3</sup>

<sup>1</sup>Gaziosmanpasa University School of Medicine, Department of Pediatrics, 60250, Tokat, Turkey,

<sup>2</sup>Gaziosmanpasa University School of Medicine, Department of Pediatrics, Tokat, Turkey

<sup>3</sup>Gaziosmanpasa University School of Medicine, Department of Biology and Genetics, Tokat, Turkey

**Background and Aims:** Obesity, one of the most common disorders observed in clinical practice, has been associated with energy metabolism-related protein genes such as uncoupling proteins (UCPs). Herein, we evaluated UCPs as candidate genes for obesity and its morbidities.

**Materials and Methods:** A total of 268 obese and 185 nonobese children and adolescents were enrolled in this study. To determine dyslipidemia, hypertension, and insulin resistance, laboratory tests were derived from fasting blood samples. UCP1-3826 A/G, UCP2 exon8 del/ins (D/I), and UCP3-55C/T variants were also genotyped, and the relationship between the polymorphisms of these UCPs and obesity morbidities were investigated. Blood samples were collected from each subject, and DNA was extracted from peripheral blood samples using a GeneAll® Exgene™ Blood SV Genomic DNA Kit. UCP1-3826 A/G and UCP2 exon8 del/ins (D/I), gene polymorphisms were analyzed by a polymerase chain reaction (PCR)-based restriction fragment length polymorphism (RFLP) method.

**Results:** The mean ages of the obese and control groups were 11.61±2.83 and 10.74±3.36 years, respectively. The respective genotypic frequencies of the AA, AG, and GG genotypes of UCP-1 were 46.3%, 33.2%, and 20.5% in obese subjects and 46.5%, 42.2%, and 11.4% in the controls ( $p = 0.020$ ). G alleles were more frequent in obese subjects with hypertriglyceridemia (42.9%) ( $p = 0.048$ ) than in those without, and the GG genotype presented an OR for obesity of 2.02. The polymorphisms of UCP-2 exon 8 del/ins did not influence obesity risk. The carriers of both the GG homozygote of the UCP1 and the del/del homozygote of the UCP2 generally showed an OR of 2.69 for obesity ( $p = 0.014$ ).

**Discussion:** Nakano et al. (1) reported that A/G heterozygotes present higher BMIs than A/A and G/G homozygotes in young Japanese males. In contrast to this study and in agreement with Evans et al.(2), however, we found that GG homozygotes were associated with higher BMI. Some researchers have reported no association between BMI and the UCP1-3826 G polymorphism(2, 3). In the present study, in agreement with the study of Ochoa et al.(4), UCP2 exon 8 del/ins polymorphisms were not linked to obesity

**Conclusion:** The GG genotype of the UCP1-3826 A/G polymorphism appears to contribute to the onset of childhood obesity in Turkish children. The GG genotype of UCP1, together with the del/del genotype of the UCP2 polymorphism, may increase the risk of obesity with synergistic effects.

*Keywords:* Obesity, children, polymorphism, uncoupling protein, dyslipidemia.

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## ORAL PRESENTATION – 43

### DIFFERENTIAL EXPRESSION PATTERNS OF ADAMTSS AND HAPLNS IN PRE-ECLAMPSIA

Sevgi Irtegun-Kandemir<sup>1</sup>, Irmak Icen-Taskın<sup>2</sup>, Gulsum Pektanc<sup>1</sup>, Mehmet Ali Tekin<sup>1</sup>, Kadir Demircan<sup>3</sup>

<sup>1</sup>Department of Medical Biology, Faculty of Medicine, Dicle University, Diyarbakır, Turkey

<sup>2</sup>Department of Biology, Faculty of Science, Firat University, Elazığ, Turkey

<sup>3</sup>Recently off

**Background/Aim:** Preeclampsia (PE) is one of the major reasons of perinatal and maternal morbidity and mortality influencing 5%–10% of pregnant women worldwide. Poor trophoblast invasion and inadequate spiral artery remodelling are the typical characteristic of PE. ADAMTSs are included in the degradation and reassembly of ECM process which is required for trophoblasts invasion and spiral arteries remodelling in normal placental development. Uncovering the key elements involved in placental dysfunction is critical for comprehension of the pathogenesis of PE. In this study, we aimed to determine the expression levels of ADAMTSs and their molecular partners, TIMP-3 and HAPLNs in the placental tissues from women with PE.

**Materials and Methods:** A total of 10 control placentas and 10 pre-eclamptic placentas were included in this study. The expression levels of ADAMTSs, HAPLNs and TIMP-3 were examined in two groups by Western blot.

**Results:** The expression levels of ADAMTS-4, -8, -10, -12, -13, -14, -16 and -19 were considerably reduced, while the expression levels of HAPLN-1, -2, -4, ADAMTS-18 and TIMP-3 were significantly elevated in pre-eclamptic placentas in comparison to those in controls.

**Discussion:** We reported here for the first time the expression patterns of all ADAMTS subtypes, TIMP-3 and HAPLNs in pre-eclamptic placentas. The expression of ADAMTS-1, -2, -4, -5, -6, -7, -9, -10 and -12 subtypes has been shown to be expressed in the human placenta. ADAMTS-12 is critical in the regulation of trophoblast invasion and ADAMTS-12 level was shown to be decreased in PE patients' serum supported by our study. There are a number of placenta related diseases associated with overexpression of TIMP-3 and abnormal TIMP-3 methylation in preeclampsia supported by our study with overexpression of TIMP-3 in pre-eclamptic placentas. We also evaluated expression of HAPLNs which are responsible for the generation and stabilization of the hyaluronan and proteoglycan aggregates degraded by proteases including ADAMTS subtypes. Attenuated expression of HAPLNs in malignant gliomas demonstrates similar characteristics with trophoblastic invasion which failures in PE in regards to decreased invasive phenotype distinguished in pre-eclamptic placentas.

**Conclusion:** Our study suggests that ADAMSTs and their molecular partners TIMP3 and HAPLNs might be related to the placental dysfunction in the context of PE.

*Keywords:* ADAMTSs, TIMP-3, HAPLNs, preeclampsia, placenta

*Etik kurul sayı:* 99950669/142

## ORAL PRESENTATION – 44

### DOES AUTOPHAGY HAVE A ROLE IN THE PROGRESS OF CORONARY COLLATERAL ?

Günnur Demircan<sup>1</sup> Özgür Kaplan<sup>2</sup> Şule Beyhan Özdaş<sup>1</sup>

<sup>1</sup>Istanbul Bilim Üniversitesi Tıp Fakültesi Tıbbi Biyoloji ve Genetik Anabilim Dalı

<sup>2</sup>Istanbul Bilim Üniversitesi Tıp Fakültesi Kardiyoloji Anabilim Dalı

**Aim:** Autophagy is a self-protective mechanism of living cells or organisms under various stress conditions. In this study level of autophagy enzyme in patients with coronary artery disease(CAD) are measured. Then we investigated whether role of a autophagy exists in the progress of coronary collateral.

**Materials And Methods:** Sixty patients were included in this prospective observational controlled study. Patients were divided into 2 groups: Group 1- patients with collateral (n=40); Group 2- normal controls patients (n=20). Blood samples of all patients were collected during coronary angiography process. The enzyme-linked immunosorbent assay (ELISA) kit for autophagy related protein 5(ATG5) in the plasma was studied for two groups of blood sample.

**Results:**Age, gender, prevalence of diabetes mellitus, hypertension, body-mass-index (BMI) and dyslipidemia were similar amongs the groups. Autophagy levels are significantly different between the groups( $12,3 \pm 4,5$  ng/ml ;  $6,2 \pm 1,8$  ng/ml ;  $p < 0.001$ , respectively). Significant positive correlations were found between level of autophagy and reentrop score ( $r = 0.282$ ,  $p < 0.047$ ), collateral way ( $r=0.429$ ,  $p<0.001$ )

**Discussion:** In the present study, the autophagy levels were higher in the patients with coronary collateral than healthy controls. Also, serum autophagy levels showed a significant positive correlation with reentrop score and collateral way. An increased autophagy level may be considered as an important activator and marker of the atherosclerotic inflammatory process in CAD.

**Conclusion:** The present study shows that level of autophagy was increased in subjects with coronary artery collateral, which may suggest positive remodeling.

*Keywords: Autophagy, Coronary artery disease (CAD), Collateral*



## ORAL PRESENTATION – 45 ETS PROTEIN Elk-1 IN BRAIN TUMOR PROLIFERATION

Melis Savaşan Söğüt<sup>2,3</sup>, Oya Arı Uyar<sup>2,3</sup>, Işıl Aksan Kurnaz<sup>1,3</sup>

<sup>1</sup>Molecular Neurobiology Laboratory (AxanLab), Department of Molecular Biology and Genetics, Gebze Technical University, Gebze Kocaeli

<sup>2</sup>Yeditepe University, Biotechnology Graduate Program, Kayisdagi Istanbul

<sup>3</sup>Institute of Biotechnology, Gebze Technical University, Gebze Kocaeli

E t w e n t y s i x (ETS) protein superfamily consists of a wide range of transcription factors with a highly consensus DNA binding domain, the ETS domain. Ternary Complex Factors (TCFs) comprise a subfamily, which bind DNA in complex with Serum Response Factor (SRF) protein, and are largely known for their mitogen-induced activation followed by upregulation of immediate-early genes such as c-fos. Elk-1, a member of the TCF subfamily, is a ubiquitously expressed protein, however Elk-1 knockout mice were found to display mild mental retardation, Elk-1 was found to be overphosphorylated during learning paradigms such as fear-conditioning, and was found to be in complex with a-synuclein aggregates in Parkinson disease models, which highly complicates the interpretation of the neuronal function of Elk-1. With respect to brain tumors, our laboratory and others have shown that Elk-1 is overexpressed and overphosphorylated in brain tumors through MAPK, PKC and PI3K signaling pathways. Recently, our laboratory has also discovered a mitosis-specific phosphorylation pattern of Elk-1 through mitotic kinases such as Aurora-A, Polo-like kinases and cyclin dependent kinases, Cdks. We are currently trying to decipher the dynamic phosphorylation code for Elk-1, and to identify the interaction domains with mitotic kinases. We have also identified novel stemness gene targets for Elk-1, in relation to its role in brain tumor initiating cell proliferation. Our results indicate that an imbalance in Elk-1 phosphorylation or expression levels results in mitotic problems, one outcome being hyperphosphorylation. Our future aims include identification of novel interaction inhibitors for Elk-1 and mitotic kinases, and to target its regulation of specific stemness genes.

*Note to the scientific committee: This work has been funded through TUBITAK project grants 211T167, 115Z344 and 115Z804.*

## ORAL PRESENTATION – 46

### THE EFFECTS OF RADIOFREQUENCY FIELDS ON CASPASE-DEPENDENT APOPTOSIS IN HUMAN COLORECTAL CARCINOMA CELLS

Arin Tomruk<sup>1</sup>, Yunus K. Terzi<sup>2</sup>, Göknur Güler Öztürk<sup>1</sup>

<sup>1</sup>Biophysics Department, Faculty of Medicine, Gazi University, Ankara, Türkiye

<sup>2</sup>Medical Genetics Departments, Faculty of Medicine, Baskent University, Ankara, Türkiye

**Background / Aim:** Although exposition to radiofrequency (RF) and microwave (MW) radiation for short and long periods of time has not been clarified yet in terms of its positive/ negative effects on environmental health and community health and its biological effects or in terms of risks it can have; and therefore, the issue is still controversial; World Health Organisation (WHO) and International Agency for Research on Cancer (IARC) included exposition to RF fields in Group 2B which can cause cancer in 2011. Tumour suppressing function, DNA repair and apoptosis have critical importance in the developmental period of cancer. In this process, cancer cells develop resistance to programmed cell death. Therefore, when it comes to researching the cancer making or curing effects of radio frequency fields, an approach to be adopted should be to research first the probable effects of EM fields on apoptosis mechanism.

**Materials and Methods:** This study uses HT-29 cells- which is a human colorectal adenocarcinoma cell line. HT-29 cells were analysed in different frequencies [1800 MHz; 2100 MHz; 2600 MHz] and by exposing the respondents to RF fields in different duration of exposure (3 hours continuously, 6 hours intermittently [RF field exposure system is on for 3 hours/ it is off for 1 hour/it is on for 3 hours], 6 hours continuously) and by using SYBR Green I dye with 4 caspases (caspase-8; caspase-9, caspase-3 and caspase-12) which play active roles in cell death pathway and in survival mechanisms through real time PCR method.

**Results:** It was found on analysing the caspases-dependent apoptosis process that initiator caspases (caspases-8 and caspases-9) gene expression levels significantly increased when 2100 MHz RF radiation was applied for 3 hours continuously and 6 hours intermittently ( $p < 0.05$ ). Caspase-3 gene expression levels were, however, found to increase significantly only during 6 hour intermittent exposure ( $p < 0.05$ ). There were no changes in the caspase gene expression levels under both 1800 MHz and 2600 MHz for all three exposure durations.

**Discussion:** Accordingly, it can be said that 2100 MHz RF radiation can activate both caspase-8 - death receptor pathway initiator and caspases-9 – internal mitochondrial pathway initiator caspase, and that the initiator caspases can active caspase-3 after 3 hours of exposure. Yet, the fact that there was no change in gene expression levels of caspase-12 according to its own negative control and sham groups indicated that caspase-9 and caspase-3 activation was not an apoptosis developing due to endoplasmic reticulum stress.

**Conclusion:** Apoptosis plays active roles in many pathological and physiological actions. Therefore, interfering in the apoptotic process and re-arranging it can bring new methods of treatment into discussion.

*Keywords: Radiofrequency Fields; HT-29; Caspases; Apoptosis, qRT-PCR*

## ORAL PRESENTATION – 47

### **SILENCING OF ERG TRANSCRIPTION FACTOR IN H596 LUNG CANCER CELL LINE INHIBITED THE EPITHELIAL-MESENCHYMAL TRANSITION MARKERS**

Abdulmecit Gökçe<sup>1</sup>, Gülay Bulut<sup>1</sup>

<sup>1</sup> Bahcesehir University, Faculty of Engineering and Natural Sciences, Molecular Biology and Genetics Department, Istanbul, Turkey.

**Background / Aim:** Epithelial-mesenchymal transition is an essential biological event which promotes metastatic abilities of cancer cells, and it has a direct relation with poor prognosis and drug resistance during chemotherapy. The studies attempting to understand the mechanisms related to epithelial-mesenchymal transition revealed a transcription factor called ETS-related gene (ERG) which is promoting the epithelial-mesenchymal transition in prostate cancer, and in other cancer types. In this study, to understand the effect of ERG expression on mesenchymal transition in lung cancer, ERG-expressing H596 cell line was treated with siRNA designed against ERG to silence ERG expression, and the expression levels of EMT markers were determined.

**Materials and Methods:** ERG gene expression was silenced in H596 cell line with 5nM and 50 nM concentrations of siERG (D-003886-01, Dharmacon), and scrambled siRNA (D-001206-13, Dharmacon) was used as negative control. siRNA molecules were transfected with Lipofectamine 2000 (Invitrogen) according to manufacturer's procedure. Following the transfection, ERG and EMT marker gene expressions were determined at mRNA level with qRT-PCR (BIORAD), and at the protein level with western blotting (BIORAD).

**Results:** Gene expression profiles of ERG silenced H596 cell lines showed that the expression of ERG was downregulated only in the 50mM application of siERG. The level of downregulation in ERG silenced samples (50mM treatment) was 54%, and the expression values of EMT marker genes were also changed. Following the confirmation of ERG downregulation in H596 cells, expression levels of epithelial-mesenchymal transition marker genes including E-cadherin, Vimentin, ZEB1, Snail and Slug were analyzed. ERG silencing resulted in the upregulation of the mesenchymal marker, E. cadherin (25%) and Slug (37%), and the downregulation of the transcription factors, Snail (55%) and ZEB1 (12%) at mRNA level. The upregulation of E.cadherin and Slug were also correlated with western blotting.

**Discussion:** The data gathered from silenced H596 lung cancer cell line showed that silencing of ERG transcription factor is resulting into downregulation of EMT markers whose function are to promote epithelial to mesenchymal transition such as Snail and ZEB1. On the other hand, EMT marker E.cadherin overexpression comprised that the cells are expressing more epithelial character rather than mesenchymal profile.

**Conclusion:** The results proposed the ERG transcription factor as a target gene for drug design to create novel treatments for the inhibition of epithelial to mesenchymal transition in lung cancer cases.

*Keywords:* Non-small cell lung cancer (NSCLC), H596 cells, epithelial-mesenchymal transition (EMT), the ETS-related gene (ERG).

*Note to the Scientific Committee:* This work was supported by the Scientific and Technological Research Council of Turkey (TUBITAK) [grant number 114S428 (PI: G. Bulut)]

## ORAL PRESENTATION – 48

### POTENTIAL EFFECTS OF METFORMIN IN DNA BER SYSTEM BASED ON OXIDATIVE STATUS IN TYPE 2 DIABETES

Irem Dogan Turacli<sup>1</sup>, Tuba Candar<sup>2</sup>, Emine Berrin Yuksel<sup>3</sup>, Sebnem Kalay<sup>4</sup>, Ali Kemal Oğuz<sup>4</sup>, Selda Demirtaş<sup>2</sup>

<sup>1</sup>Medical Biology Department, Ufuk University, Ankara

<sup>2</sup>Medical Biochemistry Department, Ufuk University, Ankara

<sup>3</sup>Medical Genetics Department, Ufuk University, Ankara

<sup>4</sup>Internal Medicine Department, Ufuk University, Ankara

**Background/Aim:** Metformin is a widely used agent in type 2 diabetes mellitus (T2D) for reducing hyperglycemia that induces energetic stress and leads to reduction in gluconeogenesis. Also, metformin inhibits complex I in oxidative phosphorylation, thereby decreasing cellular ATP levels. Inhibition of reactive oxygen species (ROS) production and activation of p53-mediated DNA repair can be induced by the activation of AMP-activated protein kinase (AMPK) which is caused by the reduced ATP levels. Base excision repair (BER) mechanism is a well-known DNA repair system for correctly repairing oxidation caused DNA damage. DNA polymerase- $\beta$  and XRCC1 function to repair DNA damages in the BER system. In T2D patients, metformin can enhance AMPK activation therefore suppress oxidative stress. p53's function may be altered by the changes on oxidative stress level. This change on oxidative stress level can also effect many cellular pathways such as; DNA repair. In our project the aim was to understand the effects of metformin on p53 activity and DNA-BER system based on the oxidative stress status in T2D patients.

**Materials and Methods:** Patients diagnosed with T2D using metformin or not and healthy controls matching age and gender proportions were analyzed based on oxidative and antioxidative status, antioxidant enzyme activities, p53 activity and DNA BER enzyme activities.

**Results:** Although the enhanced total oxidative stress was not significant, total antioxidant capacity was significantly decreased in the T2D patients, compared with the control group. Metformin enhanced SOD and GPx activities in T2D patients but the reflection of this increase to the total antioxidant capacity was not significant. XRCC1 and p53 activities were significantly upregulated with metformin treatment in T2D patients. However, the increase in DNA pol beta activity was not significant. Based on these findings, metformin induces DNA-BER system and activates cellular survival as specified with p53's antioxidant role. Furthermore, p53 activity is decreased with increased oxidative conditions but metformin reverses this reduction and enhances p53 activity in metformin using patients.

**Discussion:** Along with other efforts in the literature, we contribute not only to elucidation of molecular events underlying the conditions of T2D but also how metformin works in terms of antioxidative activity, change DNA repair activities thereby alter the disease progression or treatment as a multi-functional agent.

**Conclusion:** Our study reiterates the potential benefit of metformin in antioxidative capacity to protect cells from diabetic oxidative stress and in regulation of DNA BER system.

*Keywords:* Type 2 diabetes mellitus, metformin, p53, oxidative stress, DNA repair

*Note to the Scientific Committee:* This study was supported by the Turkish Research and Technology Council (TUBITAK) (Grant no: 115S015).

## ORAL PRESENTATION – 49

### **PTPN22 DEFICIENCY INFLUENCES B1 AND MARGINAL ZONE B CELL RESPONSES AND ACCELERATES LEUKEMIA DEVELOPMENT IN THE E $\mu$ -TCL1 TRANSGENIC MOUSE MODEL OF CHRONIC LYMPHOCYTIC LEUKEMIA**

Ozlem O. Ibrahimoglu<sup>1</sup>, Stefania Gobessi<sup>1</sup>, Francesca Belfiore<sup>1</sup>, Daniel Bilbao<sup>2</sup>, Brendan Doe<sup>3</sup>, Dimitar G. Efremov<sup>1</sup>

<sup>1</sup>Molecular Hematology, International Center for Genetic Engineering and Biotechnology, Trieste, Italy

<sup>2</sup>European Molecular Biology Laboratory (EMBL)-Mouse Biology Unit, Campus A. Buzzati-Traverso, Monterotondo-Scalo, Rome, Italy

<sup>3</sup>EMMA-INFRAFRONTIER-IMPC, Institute of Cell Biology and Neurology, CNR (National Research Council), Campus A. Buzzati-Traverso, Monterotondo-Scalo, Rome, Italy.

PTPN22 is a protein tyrosine phosphatase that functions as a negative regulator of antigen-receptor signaling in T cells. It is overexpressed in chronic lymphocytic leukemia (CLL) B cells and has been implicated in the pathogenesis of multiple autoimmune diseases. The function of PTPN22 in B cells has been studied to a lesser extent, but studies with PTPN22 knockout mice have failed to detect any significant effect on B cell development or function. In contrast, a study that we conducted in the past suggested that PTPN22 functions as a dual regulator of B cell receptor (BCR) signaling in human CLL B cells (Negro R et al, Blood. 2012;119:6278). In particular, we observed that siRNA-mediated knockdown of PTPN22 in primary CLL cells results in greater activation of LYN, SYK and other downstream molecules, while simultaneously leading to reduced activation of AKT and its immediate substrates. To reconcile the differences between the human and murine studies, we investigated PTPN22 expression in various murine B cell subsets. We detected high levels of PTPN22 in B1 B cells and to a lesser extent in marginal zone (MZ) B cells. In contrast, expression of PTPN22 in other mature B cell subsets, including follicular B cells that were primarily used for the functional experiments in the previous murine studies, was extremely low or negligible. Since PTPN22 was expressed primarily in B1 and MZ B cells, we next investigated the impact of PTPN22 deficiency on these two subsets. A significant reduction in the percentage of MZ B cells and an increase in the percentage of B1 B cells was detected in old PTPN22-deficient mice, which was accompanied by parallel changes in serum levels of antibodies typically produced by MZ and B1 B cells. PTPN22 deficiency also resulted in accelerated CLL development in E $\mu$ -TCL1 transgenic mice and affected BCR signaling in the leukemic B1 B cells in the same manner as in human CLL cells. Altogether, this study shows that PTPN22 has a highly restricted pattern of expression, which could explain the inability of earlier studies to detect a B cell-specific phenotype in PTPN22-deficient mice. In addition, these data validate our previous finding that PTPN22 plays a dual role in regulating the BCR pathway, which is likely a consequence of its capacity to directly dephosphorylate and inactivate LYN, a well established positive and negative regulator of the BCR pathway.

PTPN22, CLL, BCR signaling, B1 B cells

## ORAL PRESENTATION – 50

### COMPARISON OF THE EFFECTS OF ALBUMIN BOUND PACLITAXEL (Abi-007) ON TRIPLE NEGATIVE BREAST CANCER cII LINE MDA-MB-231 AND LUMINAL A BREAST CANCER CELL LINE MCF-7

İdil Çetin<sup>1</sup>, Mehmet Topçul<sup>1</sup>

<sup>1</sup>Istanbul University, Faculty of Science, Department of Biology, Istanbul/Turkey

**Background / Aim:** Conventional anticancer drugs display significant shortcomings which limit their use in cancer therapy. For this reason, important progress has been achieved in the field of nanotechnology to solve these problems and offer a promising and effective alternative for cancer treatment. Nab-paclitaxel has several practical advantages over classical paclitaxel, including a shorter infusion time (30 min) and no need for premedications for hypersensitivity reactions.

**Materials and Methods:** In this study, in vitro cytotoxic effect of nanotechnological drug albumin bound paclitaxel (ABI-007) was evaluated on triple negative breast cancer cell line MDA-MB-231 and luminal A breast cancer cell line MCF-7. For this purpose cell viability, cell index values obtained from xCELLigence RTCA (Real-Time Cell Analysis) DP instrument, mitotic index, apoptotic index and labelling index analysis among cell kinetic parameters were used. 25 µg/ml, 50 µg/ml ve 75 µg/ml doses of ABI-007 for MDA-MB-231 cell line and 5 µg/ml, 10 µg/ml and 25 µg/ml doses of ABI-007 for MCF-7 cell line were applied for 0-72 hours.

**Results (quantitative and / or statistical data):** It was seen from the results there was a significant decrease in cell viability, cell index values for both cell lines. While the mitotic index and labelling index values of both of cell lines increased at 24 h, decreased at 72 h significantly. Also there was a significant increase in apoptotic index values. The differences between control and all experimental groups were statistically significant ( $p < 0.01$ ).

**Discussion:** Our results showed that there was a significant decrease in cell viability, cell index values for both MDA-MB-231 and MCF-7 cell lines. While the mitotic index and labelling index values of both of cell lines increased at 24 h, decreased at 72 h significantly. Also there was a significant increase in apoptotic index values. These results are consistent with the studies in literature.

**Conclusion:** Replacing paclitaxel with nab-paclitaxel in different types of breast cancer adds the advantage of lower toxicities as already shown in the current conventional therapy.

*Keywords: Albumin bound paclitaxel, MDA-MB-231, MCF-7, xCelligence, Mitotic index, Labelling index*

*“Note to the Scientific Committee”: This work was supported by Scientific Research Projects Coordination Unit of Istanbul University. Project no: 37531 and 41832.*

## ORAL PRESENTATION – 51

### DIFFERENTIAL EXPRESSION OF PIWIL2 IN PAPILLARY THYROID CANCER

Ibrahim Halil Erdogdu<sup>1,2</sup>, Onder Yumrutas<sup>3</sup>, M. Ozgur Cevik<sup>4</sup>, Ibrahim Bozgeyik<sup>3</sup>, Miyase Erdogdu<sup>1</sup>, Hacı Mehmet Inan<sup>5</sup>, Haydar Bagis<sup>4</sup>

<sup>1</sup>Adnan Menderes University, Faculty of Medicine, Department of Pathology, Aydin, Turkey

<sup>2</sup>Adiyaman University, Faculty of Medicine, Department of Pathology, Adiyaman, Turkey

<sup>3</sup>Adiyaman University, Faculty of Medicine, Department of Medical Biology, Adiyaman, Turkey

<sup>4</sup>Adiyaman University, Faculty of Medicine, Department of Medical Genetics, Adiyaman, Turkey

<sup>5</sup>Atatürk Education and Training Hospital, Pathology Clinic, Ankara, Turkey

**Background and Aim:** Thyroid cancer is one of the most common endocrine malignancies and is a leading cause of death among endocrine organ-related cancers. Similar to other types of cancers, early diagnosis of thyroid cancer is important to improve the survival and treatment of the disease. Several immunohistochemical markers are used in the differential diagnosis of thyroid papillary carcinoma. Also, increasing evidence indicate that piwi like RNA-mediated gene silencing 2 (PIWIL2) involved in the development and progression of several types of malignancies such as breast, lung, colon, prostate and cervix cancers. However, the role of PIWIL2 was poorly investigated in thyroid cancers. Accordingly, the aim of the present study was to elucidate the relationship between PIWIL2 and thyroid cancers.

**Materials and Methods:** The expression level of PIWIL2 was determined at both mRNA and protein levels in papillary and micropapillary carcinoma tissues by using real-time PCR and immunohistochemistry methods. Immunohistochemical analysis of HBME-1, galectin-3 and CK19 was also performed.

**Results:** Similar to other immune markers of HBME-1, galectin-3 and CK19, protein expression levels of PIWIL2 was significantly up-regulated in both papillary and micropapillary thyroid cancers ( $p < 0.01$ ). Moreover, consistent with protein expression levels, mRNA expression levels of PIWIL2 was found to be elevated in both papillary and micropapillary thyroid cancer tissues. Yet, mRNA expression changes were found to be statistically insignificant.

**Discussion:** Consistent with the previous studies, in our study, protein expression levels of PIWIL2 is found to be significantly elevated in tissues of thyroid cancer patients as compared to adjacent healthy thyroid tissues.

**Conclusions:** Results of the current study suggest that PIWIL2 might be involved in the development and progression of thyroid cancers and can be novel predictive biomarker and/or therapeutic target for thyroid cancers.

*Keywords: Gene Expression, Immunohistochemistry, PIWIL2, Thyroid Cancer*

*Acknowledgements: This study was funded by the Scientific Research Projects Coordination Unit of Adiyaman University with the project number TIPFBAP-2013-0005.*

## ORAL PRESENTATION – 52

### NUCLEAR RETENTION OF p33<sup>ING1b</sup> THROUGH INHIBITION OF EXPORTIN-1 DEPENDENT NUCLEAR EXPORT IN HEAD AND NECK CANCER CELLS

Sibel Özdaş<sup>1</sup>, Talih Özdaş<sup>2</sup>

<sup>1</sup>Adana Science and Technology University, Faculty of Engineering and Natural Sciences, Department of Bioengineering, Adana, Turkey

<sup>2</sup>Adana Education and Research Hospital, Otolaryngology Clinic, Adana, Turkey

**Background / Aim :** Despite many technological advances there has been no significant change in head and neck cancer survival rates and it continues to constitute a serious threat to human life. The deviation of the expression level in many genes and intracellular mislocalization in some proteins may be responsible for the development of head and neck cancer.

The expression level of *p33ING1b* gene is either decreased or vanished and the regular nuclear localization of the p33<sup>ING1b</sup> protein is reported to be lost in head and neck carcinogenesis. The p33<sup>ING1b</sup> protein is transferred from the cytoplasm to the nucleus by the importins from the karyopherin family; however, it is unknown how to transferred from the nucleus to the cytoplasm.

Exportin-1 protein is a member of the karyopherin family of receptor proteins (including importins and exportins) which are involved in the transport of various macromolecules in the cell nucleus to the cytoplasm. The Exportin-1 protein, which is responsible for the transfer of many tumor-suppressing proteins, may also be responsible of the export of the p33<sup>ING1b</sup> protein from the nucleus. In this study we evaluated the effects of p33<sup>ING1b</sup> on nuclear localization in head and neck cancer.

**Materials and Methods:** Our study was conducted using the head and neck cancer cell lines UT-SCC-74A and its metastasis UT-SCC-74B. The exportin-1-dependent nuclear export was blocked by the Exportin-1-specific inhibitor, leptomycin B (LMB) in cell lines. The expression levels of *Exportin-1* and *P33ING1b* gene were analyzed by q-RT-PCR and Western blot analysis. The location p33<sup>ING1b</sup> protein in these cell lines is shown using immunofluorescence staining. The effect on proliferation capacity of Exportin-1 inhibition in the cell lines was studied using xCELLigence real-time cell analysis system and XTT and on cell migration capability was also examined by scratch assay.

**Results:** We show *Exportin-1* gene was highly expressed in UT-SCC-74A and UT-SCC-74B cell lines but *p33ING1b* gene was very lowly. Inhibition of nuclear export by LMB also results in retention of the p33<sup>ING1b</sup> in the nucleus, due to efficient export of nuclear p33<sup>ING1b</sup>. The nuclear retention of p33<sup>ING1b</sup> through inhibition of exportin-1 dependent nuclear export, in head and neck cells resulted in significant growth inhibition, migration reduction and apoptosis induction.

**Discussion:** The current therapies of the head and neck cancer are related to high rates of relapse and metastasis, highlighting the urgent need for alternative therapeutic modalities. Like most cancers, head and neck cancer is basically a genetic disease. Thus, there is a great need for the identification of some proteins, their intracellular localization, the expression level of some genes in head and neck cancer, as well as subsequent investigation of their roles in its pathogenesis and potential use in its treatment. Our results showed that Exportin-1 dependent nuclear export, in head and neck is highly expressed and is involved in regulating growth and survival mechanisms through the critical p33<sup>ING1b</sup> overexported from nuclear survival pathway. However, it needs to lighted with further functional studies role of the association between the p33<sup>ING1b</sup> and exportin-1 proteins in cancer pathogenesis



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**Conclusion:** Our work revealed a dramatic shift in p33<sup>ING1b</sup> subcellular localization from nuclear in primary cell line to cytoplasmic in metastatic head and neck carcinoma, suggesting that loss of nuclear p33<sup>ING1b</sup> may play a role in head and neck cancer development.

*Keywords:* Head and neck cancer, Exportin-1, p33<sup>ING1b</sup>, Nuclear Export, Leptomycin B

*Acknowledgments:* This study was financially supported by The Scientific and Technological Research Council of Turkey (TÜBİTAK) (Project No. 215S087) and the Adana Science and Technology University Scientific Research Projects Coordination Unit (Project No: 16103018).

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# POSTER PRESENTATION

## POSTER PRESENTATION – 01

### ANALYSIS OF TLR-9 GENE POLYMORPHISMS AND SERUM LEVELS IN SEPSIS

Nazan Atalan <sup>1</sup>, Leyla Acar <sup>2</sup>, Hande Karagedik <sup>2</sup>, Gonca Candan <sup>2</sup>, Arzu Ergen <sup>2</sup>

<sup>1</sup>Programme of Anesthesiology, Marmara University Vocational School of Health Services, Istanbul, Turkey

<sup>2</sup>Department of Molecular Medicine, Aziz Sancar Institute of Experimental Medicine, Istanbul University, Istanbul, Turkey.

**Background/Aim:** Sepsis, which is described as the systemic inflammatory response appearing in the host against infection, is a syndrome which can cause a serious sepsis and septic shock as well as such symptoms leading function disorder and organ failure in one or multiple organs through a progressing systemic inflammatory response. TLRs are transmembrane proteins which have a vital role which both creates a natural immune responses against lots of pathogens and activates the obtained immune response through the production of interleukin (IL)-1, IL-6, tumor necrosis factor (TNF)- $\alpha$  and other pro-inflammatory cytokines in toll-like receptors (TLR) in the defense of immune system against infections.

**Material and Methods:** In our study, we analyzed TLR-9 serum level and TLR-9 (-1486 T>C) and TLR-9 (C>T) gene polymorphisms by aiming at analyzing both the effect of these polymorphisms on TLR-9 levels and their effects together with their sepsis clinical and biochemical parameters. In this regard, PCR-RFLP technique was used in order to detect TLR-9 gene polymorphisms and ELISA technique was used in order to analyze TLR-9 serum levels in the control group of 80 sepsis patients and 100 healthy individuals.

**Results:** There was no substantial difference observed between sepsis and control groups in terms of TLR-9 genotype and allele distribution, there was a statistically substantial decrease in TLR-9 serum levels of both TLR-9 (-1486 T>C) TT and TLR-9 (C>T) TT genotypes individuals in sepsis group.

**Discussion:** Our findings as a result of our experimental studies put forward that there is no relation between sepsis and both TLR-9 (C>T) and TLR-9(-1486 T>C) polymorphisms; however there is a relation between serious sepsis and decreased serum and increased serum TLR-9 levels, in the cases of lactate which has tissue hypo-perfusion based on sepsis is >5 mmol/L.

**Conclusion:** We demonstrated that serum TLR-9 levels were statistically low in sepsis group compared to controls. We believe that low serum TLR-9 levels detected in our study, are due to serious sepsis and septic shock cases.

*Istanbul University Scientific Research Projects Unit supported this study. Project No: 38207*

## POSTER PRESENTATION – 02

### EVALUATION OF GUT-BRAIN AXIS THEORY IN DEPRESSION: THE LIGHT AND BLIND SIDE

Demet Sinem Guden<sup>1</sup>, Seyhan Sahan-Firat<sup>1</sup>

<sup>1</sup>Mersin University, Faculty of Pharmacy, Department of Pharmacology, Mersin, TURKEY.

**Background/Aim:** Major depression is a chronic disorder caused by multifactors which leads to low mood, low self-esteem, and loss of interest in normally enjoyable activities. Unfortunately, the delayed onset time and the low remission rate of antidepressant drugs are still major challenges. This report presents a broad range of reviews to evaluate the data from literature about the effect of gut-brain axis on depression.

**Materials and Methods:** Articles were chosen from PubMed database between September 2013 and January 2017. We have used the Keywords including “gut-brain axis” in combination “depression”, and “depressive disorder”. Studies about the depression, depressive behaviour, gut microbiota and gut-brain were evaluated as a criteria for inclusion.

**Results:** Initially screening of Keywords identified 74 records. Those were relevant references refer to the importance of gut-brain communication in central nervous system (CNS) diseases as well as, reports were about that gut-brain axis play a role in behaviour, stress, brain development. Therefore, of the 74 records, 16 articles are selected and summarized. Recently, *in vivo* and *in vitro* studies demonstrate that the gut-brain axis and depression are linked with each other and understanding the mechanism of this relationship has become an area of interest in neuroscience. General mechanisms related to this hypothesis are inflammation, hypothalamic–pituitary–adrenal axis (HPA), or disturbance of neurotransmitter signaling.

**Discussion:** Recently, it has been demonstrated in the preclinical studies that, the modulatory effects of gut-brain axis may contribute neuropsychiatric diseases. However, how preclinical observations translate into human clinical studies is required to determine.

**Conclusion:** This axis is a bidirectional complex communication network and modulates immune, gut and CNS functions. Activation of the HPA axis and the immune system are susceptible to gut microbiota alteration. Interventions such as diet modifications, enhanced consumption of probiotics and antibiotics should be monitored closely in depressive patients induced by disrupted gut-brain axis.

*Keywords:* gut, microbiota, brain, depression

## POSTER PRESENTATION – 03 IN VITRO EFFECTS OF CAPSAICIN ON CHONDROSARCOMA : PRELIMINARY DATA

Nagihan HELVACI<sup>1</sup>, Sabahattin CÖMERTPAY<sup>1</sup>

<sup>1</sup>Kahramanmaraş Sutcu Imam University, BioEngineering and Science Department, 46040, Kahramanmaraş, TURKEY

Chondrosarcoma is a malignant tumor of bones, characterized by the production of cartilage matrix. Chondrosarcoma affects bones of the legs, shoulder blades, upper arms, rib cage or pelvis. Capsaicin is a bioactive phytochemical abundant in red and chili peppers. While the preponderance of the data strongly indicates significant anticancer benefits of capsaicin, more information to highlight molecular mechanisms of its action is required to improve our knowledge to be able to propose a potential therapeutic strategy for use of capsaicin against cancer. In recent years, the role of capsaicin in cancer prevention and treatment has gained people's attention. However, how chondrosarcoma cells are affected by capsaicin in vitro has not been elucidated. In this study, 5000 normal and malignant cartilage cells were grown in vitro in each well of a 96 well plate. Subsequently, capsaicin was applied to the cells at ten different concentrations (0-1000  $\mu\text{M}$ ) for 24 hours and their viability was determined by the absorbances measured after an four-hour-enzymatic reaction with MTS reagent (Methylthiazole Tetrazolium Assay). With the absorbances obtained,  $\text{IC}_{50}$  values were calculated and evaluated by GraphPad Prism 6.0. As a result, we found that capsaicin was killing the cancerous cells with the  $\text{IC}_{50}$  value of as 254  $\mu\text{M}$ . Later, when we performed wound healing assay with chondrosarcoma cells grown in the media with or without capsaicin at  $\text{IC}_{50}$  for 48 hours, we observed that capsaicin treated cells were significantly slower than the only ethanol treated ( $p=0.0001$ ) and none-treated cells ( $p<0.0001$ ) in covering the wounded area. This observation implied that capsaicin might also have a role in preventing chondrosarcoma cells from invasion and/or metastasis.

*Keywords: Capsaicin, chondrosarcoma, wound healing, MTS*

## POSTER PRESENTATION – 04

### **DETERMINATION OF BAP1 MUTATION IN CANCEROUS, IMMORTALIZED OF MESOTHELIUM**

Bahaaddin A. Saber<sup>1</sup>, Sabahattin Comertpay<sup>1</sup>

<sup>1</sup>Kahramanmaraş Sutcu Imam University Bioengineering and science, Institute of Science, Kahramanmaraş/ Turkey

BAP1 is a deubiquitylase related to multi macromolecule complexes that regulate key cellular pathways, such as cell cycle, cellular differentiation, cell death, and gluconeogenesis. BAP1 is encoded by the BAP1 gene settled on the short arm of chromosome three (3p21.31-p21.2). BAP1 gene has been discovered to be mutated in various types of cancers including unveal carcinoma, prostatic adenocarcinoma, uveal melanoma and mesothelioma. According to the body site from which the tumor develops, there are three different types of mesothelioma; peritoneal mesothelioma (stomach), pericardial mesothelioma (heart), and pleural mesothelioma (lung). This malignancy is caused primarily by the exposure to microscopic asbestos fibers and erionite. Once these fibers are inhaled, they can become lodged in the lining around the lungs (or other organs mentioned above). The fibers become precipitated in the body, and cause cellular and genetic distractions that can ultimately lead to cancer. Global incidence of malignant pleura mesothelioma (MPM) has risen steadily over the past decade, and is predicted to continue to an estimated peak in 2020. Besides, an estimate based on 2008 data suggested an average of 14200 cases worldwide each year. Germline BAP1 mutations have been recently related with a higher risk of MPM, atypical melanocytic tumors and other neoplasms. The mutations found in mesothelioma tumors caused a change in the protein, whose most common trait was the loss of nuclear localization signal. Although BAP1 mutations have been detected in many mesothelial tumors, the number of the studies investigating the mutations in the cell lines used in vitro research is rare. Therefore, our purpose in this study is to sequence BAP1 gene in cancerous and immortalized cell lines of mesothelium which we regularly use in our laboratory, in order to reveal their mutation patterns. Cancerous cells were purchased from ATCC (Cat.No.5946) while immortalized cells were obtained from Coriell Institute (AG07086). Cells were cultured and grown in their regular media until they reached to %80 confluence. At that point, the cells were collected and DNA was isolated from them by using a DNA Isolation Kit (Vivantis, Malaysia). PCR was run with five different primer pairs which amplify the exons 1-2-3,4,6-7,9 and 13. Following the quality check of the amplicons through gel electrophoresis, they were sequenced and the sequences were compared to the reference gene.

*Keywords : BAP1 gene , Mesothelioma , DNA Sequencing .*

POSTER PRESENTATION – 05  
**IN VITRO EFFECT OF CAPSAICIN ON CANCEROUS AND IMMORTALIZED  
CELLS OF MESOTHELIUM: PRELIMINARY DATA**

Gizem Ceylan<sup>1</sup>, Sabahattin Cömertpay<sup>1</sup>

<sup>1</sup> Kahramanmaraş Sütçü İmam Üniversitesi, Ziraat Fakültesi, Tarımsal Biyoteknoloji Anabilim Dalı, Kahramanmaraş

Mesothelioma is a rare but fatal form of cancer developing from the membrane of the lung (pleura), stomach (peritonium) and heart (pericardium) and whose median survival after diagnosis is determined as approximately one year. The World Cancer Report showed that cancer rates would increase at an alarming rate in the global scope. Mesothelioma has a low response rate towards the conventional cancer treatment methods. The main risk factor of Malignant Mesothelioma is exposure to erionit. Besides simian virus 40 (SV40), a virüs, could have a role. Capsaicin, a homovanillic acid derivative, is an active component of Capsicum annuum. It has been shown that capsaicin may lead certain cancer cells (prostate cancer, acute T-Cell lymphoblastic leukemia) examined to apoptosis. There has not yet been found any study which investigates the effect of capsaicin on mesothelioma in vitro. In this project, a malignant mesothelioma cell line (5946) and immortalized cells of mesothelium (AG07086) were treated with capsaicin in vitro and how capsaicin effected the cell survival and the metastatic ability of mesothelioma was observed through MTS (Methylthiazole Tetrazolium Assay) and Wound Healing Assay, respectively, MTS, a technique based on the enzymatic reaction of living cells, was performed on both cancerous and immortalized cells which were treated with various amounts of capsaicin for 12 hours, and the IC<sub>50</sub> values were calculated accordingly. At the end of this process, IC<sub>50</sub> values were determined as 300.6 uM and 334.1 uM for 5946 cells and AG07086 cells, respectively. Later, 5946 cells, treated with capsaicin at its IC<sub>50</sub> value, were tested by Wound Healing for 72 hours. As a result of this study, it was observed that applying capsaicin caused a statistically significant limitation for cell movement compared to no treated (p<0.0001) and only EtOH applied cells (p<0.0001). In the light of these findings, it is thought that capsaicin might have potential to eliminate or slow down the growth of mesothelial tumors if used in proper concentrations.

*Keywords: Mesothelioma, capsaicin, immortalized mesothelial cells, in vitro.*

## POSTER PRESENTATION – 06

### PROTEOMICS ANALYSIS OF HIPPOCAMPAL EXTRACELLULAR MATRIX DURING EARLY, PROGRESSION AND LATE STAGE OF ALZHEIMER'S DISEASE

Busra Gurel<sup>1,5</sup>, Mehmet Cansev<sup>2</sup>, Cansu Sevinc<sup>2</sup>, Sami Aydın<sup>2</sup>, Busra Ocalan<sup>3</sup>, Aysen Cakir<sup>3</sup>, Nevzat Kahveci<sup>3</sup>, Mehmet Ozansoy<sup>1,4</sup>, Ozlem Taskapilioglu<sup>5</sup>, Ismail Hakki Ulus<sup>6</sup>, Ahmet Tarik Baykal<sup>7</sup>

<sup>1</sup> Regenerative and Restorative Medical Research Center, Istanbul Medipol University, Istanbul, Turkey;

<sup>2</sup> Department of Pharmacology, Faculty of Medicine, Uludag University, Bursa, Turkey;

<sup>3</sup> Department of Physiology, Faculty of Medicine, Uludag University, Bursa, Turkey;

<sup>4</sup> Department of Physiology, Faculty of Medicine, Medipol University, Istanbul, Turkey;

<sup>5</sup> Department of Neurology, Faculty of Medicine, Uludag University, Bursa, Turkey.

<sup>6</sup> Department of Pharmacology, Faculty of Medicine, Acibadem University, Istanbul, Turkey

<sup>7</sup> Department of Medical Biochemistry, Faculty of Medicine, Acibadem University, Istanbul, Turkey.

**Background / Aim:** Recent studies revealed that the brain extracellular matrix (ECM) molecules have several roles on the synaptic response and the stabilization of synaptic connectivity in Alzheimer's Disease (AD). In order to investigate the role of ECM in the genesis and progression of the disease, we analyzed the proteome alterations in the hippocampal extracellular matrix obtained in vivo from an AD mouse model.

**Materials and Methods:** 5XFAD transgenic mice were used as the experimental group (n=6) and their non-transgenic littermates were used as the control group (n=6). The hippocampal ECM samples from each mice were collected by in-vivo intracerebral push-pull method at month 3, 6 and 12. To analyze the expression differences between the groups, label-free shotgun proteomics analysis method was used. The tryptic peptides were separated and analyzed with ultra-performance liquid chromatography and electrospray ionization quadrupole time-of-flight mass spectrometry (UPLC-ESI-qTOF-MS). For the identification of the proteins and the statistical analysis, Progenesis QIP software was used.

**Results:** 204, 146 and 225 proteins were identified in the ECM samples obtained at month 3, 6 and 12. For the three time points, 35, 34 and 35 proteins showed statistically meaningful expression difference between non-transgenic littermates and 5XFAD ECM samples ( $p < 0,05$  and min. fold change  $> 1.4$ ) respectively. Unique and common pathways based on these proteins were evaluated by Reactome pathway analysis.

**Discussion/Conclusion:** The expression of some proteins were altered just in indicated times while the others change commonly in two or all groups. According to pathway analysis, we determined that certain pathways are dysregulated during early, progression and pathological stage of the AD.

*Keywords: Alzheimer's disease, ECM, 5XFAD, proteomics*

*Note to the Scientific Committee:*

*-This project(112S414) was supported financially by TÜBİTAK-ARRS Bilateral Cooperation Program.*

*- All animal procedures have been approved by the Ethics Committee of the Animal Care and Use Committee of Uludag University, Bursa, Turkey (Approval ID: 2012-10/06) and Istanbul Medipol University, Istanbul, Turkey (Approval ID: 38328770-54).*



## POSTER PRESENTATION – 07

### DETERMINATION OF P53 MUTATION IN CANCEROUS AND IMMORTALIZED MESOTHELIUM

Twana Z. Azzat<sup>1</sup>, Sabahattin Comertpay<sup>1</sup>

<sup>1</sup> Kahramanmaraş Sutcu Imam University, Bioengineering and science, Institute of science, Kahramanmaraş/ Turkey

TP53 (also known as protein 53 or tumor protein 53), is a tumor suppressor protein that in humans is encoded by TP53 gene located on the short arm of chromosome 17 (17p13.1). P53 is critical in multicellular organisms, where it regulates of S phase in cell cycle. As such, p53 has been described as “the guardian of the genome” because of the role in conserving stability by preventing genome mutation. TP53 gene has been linked with some types of cancers such as: mesothelioma, breast cancer, colorectal cancer and ovarian cancer. Malignant mesothelioma (MM) is a devastating and lethal cancer associated with exposure to mineral fibers. It arises from the mesothelial cells of the pleura (80–90%), peritoneum (10–15%) and more rarely pericardium (<5%). MM is rare: annually ~1–2 cases are diagnosed per million inhabitants in countries without significant use of asbestos. In the Turkey especially in Eskisehir city cohort consisted of 1,886 villagers. During the observation time, 377 deaths occurred and 24 MPM cases were diagnosed. Average annual mesothelioma incidence rates were 114.8/100,000 for men and 159.8/100,000 for women. Although MM incidence was predicted to decrease following the ban of asbestos, it is still increasing worldwide. Although p53 mutations have been found in many cases of mesothelioma, all cell lines that are commercially available and are used for in vitro studies globally have not carefully investigated. Our purpose in this study is to sequence TP53 gene in cancerous and immortalized cells of mesothelium in order to reveal their mutation patterns. Cancerous cells were purchased from ATCC (cat.No.5946) while immortalized cells were obtained from Coriell Institute (AG07086). Cells were cultured and grown in their regular media until they reached to %80 confluence. At this point, the cells were collected and DNA was isolated from them by using DNA isolation kit (Vivantis, Malaysia). PCR was run with five different primer pairs which amplify the exons 1,2,5-6,8-9, and 11. Following the quality check of the amplicon through gel electrophoresis, they were sequenced and the sequences were compared to the reference gene.

*Keywords; TP53 gene, Mesothelioma, DNA Sequencing.*

## POSTER PRESENTATION – 08 ANALYSIS OF CONNEXIN 43 GENE EXPRESSION IN PTERYGIUM TISSUE

Saime SEZER SONDAS,<sup>1</sup> Omer ATES<sup>1</sup>

<sup>1</sup>Department of Medical Biology, Faculty of Medicine, Gaziosmanpaşa University, Tokat, Turkey.

**Background /Aim :** Pterygium which is an abnormal wing-shaped growth of the conjunctiva across the limbus onto the cornea, impairs vision, and causes inflammation. This disease is similar to cancer with features such as cell proliferation, invasion, local angiogenesis and recurrence after resection. A fully developed pterygium formed than “apex”, “body” and “neck”. The exact pathogenesis and etiology of pterygium remains unclear, although it is generally considered to be caused by ultraviolet (UV) radiation, epithelial-mesenchymal transition (EMT), immunologic and anti-apoptotic mechanisms, angiogenic and lymphangiogenic stimulation, deregulation of extracellular matrix modulators and growth factors. EMT is critical in both developmental processes, wound healing and tissue remodeling, and tumor metastasis. E-cadherin is epithelial-mesenchymal transition (EMT)-related molecules. Ecadherin and  $\beta$ -catenin localised with at the sites of cell-to-cell contact. Connexins oligomerise into hexameric channels that form gap junctions and connect the cytoplasm of adjacent cells. Many connexin that have been identified, appear in different cells and tissues. One of them is connexin 43 (CX43). Connexin 43 have been shown that, it play an important role in carcinogenesis and tumor metastasis. In this context, we intend to find that, whether there is a function of CX43 gene expression, in the development of the pterygium disease.

**Materials and Methods :** This study, the 11 pterygium and normal conjunctive tissues received surgical excisions. The CX43 gene expression were examined with reverse-transcription polymerase chain reaction (RT-PCR) method. SPSS16.0 program was performed using for statistical analysis. The CX43 gene was normalized to the actin gene and the  $2^{-\Delta\Delta Ct}$  formula was calculated.

**Results (quantitative and / or statistical data) :** CX43 gene expression was higher than in the compared to actin in the  $2^{-\Delta\Delta Ct}$  method. But, statistical evaluation of the data results showed that, expression levels of CX43 gene were not significantly different between pterygium tissue and normal conjunctiva ( $p > 0.05$ ).

**Conclusions:** According to our data, CX43 gene expression don't play a role in determining susceptibility to pterygium tissue.

This work was accepted by Gaziosmanpaşa University the Ethics Committee for Clinical Investigations. Project numbers: 14-KAEK-229.

*Keywords: Connexin 43, Gene Expression, Pterygium*

*Note to Science Committee :This work was supported by Gaziosmanpaşa University Scientific Research Projects Fund. Project numbers: 2015/26.*

## POSTER PRESENTATION – 09

### EXPRESSION PROFILES OF SPERMATOZA SURFACE PROTEINS THOUGHT TO BE RESPONSIBLE FOR FERTILITY

Gül İpek GÜNDOĞAN<sup>1</sup> , Abit AKTAŞ<sup>2</sup> , M. Başak Ulkay<sup>2</sup>

<sup>1</sup>Istanbul Yeni Yüzyıl University, Faculty of Medicine, Department of Histology and Embryology, Zeytinburnu, Istanbul - TURKEY

<sup>2</sup>Istanbul University, Faculty of Veterinary Medicine, Department of Histology and Embryology, TR-34320 Avcılar, Istanbul – TURKEY

Spermatozoas at developing stages obtained from testis and 3 different regions of epididymis. Determination of existence and localisation of Fertilin- $\beta$ , Calmegin, Izumo-1, P34H, ACE and Fibronectin were analyzed quantitatively via their protein expression profiles by western blotting technique and indirect immunofluorescence technique. Localisation changes of ram spermatozoa during development and maturation have been determined and also ejaculate and structural features of freeze-thawed ram spermatozoas with and without in vitro capacitation/acrosome reaction also been evaluated.

Fertilin- $\beta$ , Calmegin, P34H proteins in caput, corpus, cauda and mature spermatozoas showed marking in different density and distribution with. Freeze-thawed samples had lower density and marking than both ejaculate and cauda samples.

Marking was not obtained except Izumo-1 protein from the samples undergo in vitro capacitation/acrosome reaction. Marking of Izumo-1 protein was seen as increasing band formation through equatorial region on acrosome, after in vitro capacitation, however after acrosome reaction, the band formation was only equatorial region. In contrast to expected marking on spermatozoa head, non specific marking was obtained on different localization changing with the region in fibronectin antibody and samples. ACE antibody did not mark the samples. Region specific differences of proteins at kDa level were obtained with western blotting and possible isoforms specific to ram spermatozoa or proteins with similar epitops were marked.

*Keywords: Surface protein, Spermatozoa, Ram*

*Istanbul University Animal Experiments Local Ethics Committee's approval number: 2015/43*

*Note to the Scientific Committee:*

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## POSTER PRESENTATION – 10 DEVELOPMENT OF THERANOSTIC PNIPAM/SPION NANOPARTICLES FOR CANCER TREATMENT

Yunus Akkoc<sup>1</sup>, Yasemin Yar<sup>2</sup>, Rouhollah Khodadust<sup>2</sup>, Devrim Gozuacik<sup>1,3</sup>, H. Yagci Acar<sup>2,3,\*</sup>

<sup>1</sup> Department of Molecular Biology Genetics and Bioengineering, Faculty of Engineering and Natural Science, Sabancı University, İstanbul, Turkey

<sup>2</sup> Koc University, Graduate School of Materials Science and Engineering, Rumelifeneri Yolu, Sariyer, Istanbul, Turkey

<sup>3</sup> Sabancı University, Center of Excellence for Functional Surfaces and Interfaces for Nano Diagnostics (EFSUN), Istanbul 34956, Turkey

\*Corresponding author.

**Background/Aim:** Stimuli-responsive nanoparticles are being investigated for controlled delivery of toxic drugs to the disease site, especially in cancer. Tumors are known as more acidic and hyperthermic in comparison with healthy body parts. Thus, pH and/or temperature-responsive drug delivery vehicles have a tremendous importance in achieving secure delivery and secretion of the cargo chemotherapeutic drug only to the tumor site to enhance the efficacy and reduce side effects.

**Materials & Methods:** In this study, Poly (N-isopropylacrylamide) (PNIPAM) bound Fe<sub>3</sub>O<sub>4</sub> nanoparticles (SPION-PNIPAM) were synthesized via surface initiated ATRP (atom transfer radical polymerization) and loaded with chemotherapeutic drug Doxorubicin (Dox). We performed MTT and Trypan Blue Exclusion Assay to evaluate dose and temperature dependent cell viability exposed to Dox, nanoparticles and Dox loaded nanoparticles. Confocal analysis was carried out to observe cellular uptake and intracellular trafficking of NPs. Gamma-H<sub>2</sub>AX phosphorylation, p53 and Caspase activation were examined through Immunoblotting to identify the NP and drug dependent DNA damage *in vitro*.

**Results:** Release studies performed at different temperatures (25 °C, 37 °C, 42 °C) and pH (7.4, 5.6) revealed both pH and temperature dependent release which is minimal at physiological pH and temperature and maximum at low pH-high temperature combination. For the toxicity studies, we have used HeLa cervical cancer cells. Administration of the PNIPAM/SPION alone did not show toxic effect event at high doses, proving safety of the delivery vehicle.. However, Dox loaded NPs (0.3 µg/ml and 1.3 µg/ml drug content) showed dose and time dependent toxicity. Based on the confocal microscopy studies, internalization of NPs increases with the NP dose, incubation time and temperature. We have also observed that NPs were internalized through endosomal pathway using the endosomal markers Rab5 and Rab9. In addition, cells incubated with Dox loaded NPs exhibited higher levels of gamma-H<sub>2</sub>AX phosphorylation, p53 and Caspase activation in comparison to free Doxorubicin.

**Conclusion:** According to our findings, dually responsive controlled drug release behavior makes these SPION-PNIPAM nanoparticles valuable stimuli responsive theranostic candidates.

*Keywords: Cancer, PNIPAM, Targeted Drug Delivery, Controlled Release, Magnetic Nanoparticles*

*\* This work was supported by The Scientific and Technological Research Council of Turkey (TUBITAK) 1001-110T116 Grant*

## POSTER PRESENTATION – 11

### NEUTROPHIL/LYMPHOCYTE RATIO HAD BETTER DIAGNOSTIC CAPABILITY THAN PLATELET/LYMPHOCYTE RATIO IN BREAST CANCER

Atakan Koro<sup>1</sup>, Hale Aral<sup>1</sup>, Didem Can Trabulus<sup>2</sup>, Mehmet Ali Nazlı<sup>3</sup>, Rıza Umar Gürsu<sup>4</sup>, Çiğdem Usul Afşar<sup>4</sup>, Didem Karaçetin<sup>5</sup>, Murat Usta<sup>6</sup>

<sup>1</sup>University of Health Sciences, Istanbul Research and Training Hospital, Department of Medical Biochemistry, Istanbul, Turkey

<sup>2</sup>University of Health Sciences, Istanbul Research and Training Hospital, Department of General Surgery, Istanbul, Turkey

<sup>3</sup>University of Health Sciences, Istanbul Research and Training Hospital, Department of Radiology, Istanbul, Turkey

<sup>4</sup>University of Health Sciences, Istanbul Research and Training Hospital, Department of Internal Medicine, Istanbul, Turkey

<sup>5</sup>University of Health Sciences, Istanbul Research and Training Hospital, Department of Radiation Oncology, Istanbul, Turkey

<sup>6</sup>Giresun University, Faculty of Medicine, Department of Medical Biochemistry, Giresun, Turkey

**Background:** Platelet (PLT) activation and the coagulation system have been demonstrated to have a critical role in cancer progression. High platelet counts were reported to be associated with tumor progression and poor prognosis in numerous types of cancer. We aimed to examine the relation between some blood count indexes and other laboratory parameters in women diagnosed early stage (stage I/II/III) breast cancer, in our population.

**Materials and Methods:** Using data retrieved from the medical records through six months' time, from May to October 2016, 53 women having early stage breast cancer met our study inclusion criteria as they had no any anti-cancer therapy before. Thirty women with benign neoplasm or healthy individuals followed up in the out-patient clinics and confirmed sonographically made up our controls. Exclusion criteria included patients having white blood cells (WBC) count  $>10.5 \times 10^9/L$ , fasting glucose  $>126$  mg/dL or defined diabetics. Differential leukocyte counts were determined by means of XE5000 (Sysmex Corp., Japan).

**Results:** There was no difference in PLT, and platelet/white blood cell ratio (PLT/WBC), mean platelet volume (MPV), erythrocyte sedimentation rate (ESR), glucose, albumin, alanine aminotransferase (ALT), gamma-glutamyltransferase (GGT), activated partial thromboplastin time (APTT) between the groups. Area Under the Curve (AUC) value obtained by ROC analysis was greater in neutrophil/lymphocyte ratio (NLR AUC: 0.775,  $p < 0.0001$ ) than platelet/lymphocyte ratio (PLR AUC: 0.694,  $p = 0.004$ ). PLT counts, PLT/WBC did not differ in cancer patients, but PLR was found significantly higher. There was a weak-moderate correlation between PLT counts and APTT ( $r = -0.338$ ,  $p = 0.014$ ) in the group of patients diagnosed breast cancer.

**Discussion:** NLR showed better diagnostic capability than PLR, as shown in our previous study by means of BC6800 (Mindray Medical International Ltd., China) in another population of patients diagnosed breast cancer and having no anti-cancer therapy. Despite different instrumentation, NLR has been found significantly higher in breast cancer.

**Conclusion:** At a level of 1.80, diagnostic sensitivity was 75.5% and diagnostic specificity was 66.7%; at a level of 1.92, sensitivity was 71.7% and specificity was 70% for NLR. We need more reliable cut-off values of these indicators related to chronic inflammation for diagnostic and/or prognostic value in breast cancer.

*Keywords: breast cancer; platelet/lymphocyte ratio (PLR); neutrophil/lymphocyte ratio (NLR); chronic inflammation; differential leukocyte counts*

## POSTER PRESENTATION – 12

### INVESTIGATIONS OF ANTIMICROBIAL ACTIVITIES AND DNA INTERACTIONS OF NN AND NO DONOR TYPED (2-PYRIDYL) SPIRO-CYCLOTRIPHOSPHAZENES

Pelin Ozbeden<sup>1</sup>, Leyla Acik<sup>1</sup>, Gamze Elmas<sup>2</sup>, Zeynel Kilic<sup>2</sup>

<sup>1</sup>Department of Biology, Gazi University, Ankara, Turkey

<sup>2</sup>Department of Chemistry, Ankara University, Ankara, Turkey

**Background/Aim:** The most important property of the cyclophosphazenes is that they can give replacement reactions with different side groups and cyclophosphazenes can acquire very different properties according to these side groups. These features have led to the expansion of the use areas of phosphazenes. For example, some aziridine substituted phosphazenes have anticarcinogenic and antibacterial properties and have low toxicity, thus providing advantages in chemotherapeutic applications. This study focused on the investigations of the antimicrobial activity and DNA interaction, NN and NO donor typed (2-pyridyl)Spiro-Cyclotriphosphazenes with plasmid DNA.

**Materials and Methods:** The antimicrobial activities of (2-pyridyl)spiro-cyclotriphosphazenes and their interactions with DNA were investigated. An agar well diffusion method and MIC analysis were performed using human pathogenic bacteria and yeast to determine the antimicrobial effects of the compounds. In this study, the interactions of the compounds with plasmid DNA was evaluated by agarose gel electrophoresis technique.

**Results and Discussion:** The result of antimicrobial activity show that NN-(2-pyridyl)spiro compound is active against *P.vulgaris*, NO-(2-pyridyl)spiro- product to *P.vulgaris*, *S.typhimirium*, *B.subtilis*, *K.pneumonia*, *B.cereus*, morpholino-NN-(2-pyridyl)spiro-cyclotriphosphazene is efficient against *B.subtilis*, *B.cereus* and morpholino-NO-(2-pyridyl)spiro derivative is active against *P.vulgaris*, *S.typhimirium*, *B.subtilis*, *K.pneumonia*, *B.cereus* and *C.albicans*, *C.kruzei*. The most effective compound, is found to be morpholino-NO-(2-pyridyl)spiro-cyclotriphosphazene with the zone diameter of 15 centimeters. The MIC values of the compounds range from 125-2000  $\mu$ M. MBC/MFC values were also changed from 125 to 2000  $\mu$ M. The results of the compounds and DNA interactions show that fully substituted compounds cause conformational changes on the DNA double helix.

**Conclusions:** According to these results, further studies need to prove anticancerogenic activities

*Keywords:* NN-(2-pyridyl)spirocyclotriphosphazenes, NO-(2-pyridyl)spirocyclotriphosphazenes, antimicrobial activity, DNA.

\*This study was supported by the "Scientific and Technical Research Council of Turkey" (Grant No. 216Z105).

POSTER PRESENTATION – 13  
**INVESTIGATIONS OF ANTIMICROBIAL ACTIVITIES AND DNA  
INTERACTIONS OF BISFERROCENYL-2-TRANS-6-DISPIRO-  
CYCLOTETRAPHOSPHAZENES**

Suheyla Pinar Celik<sup>1</sup>, Leyla Acik<sup>1</sup>, Gamze Elmas<sup>2</sup>, Zeynel Kilic<sup>2</sup>

<sup>1</sup>Department of Biology, Gazi University, Ankara, Turkey

<sup>2</sup>Department of Chemistry, Ankara University, Ankara, Turkey

**Background/Aim:** The most important feature of the cyclophosphazenes is that they can give substitution reactions with a large number of different organic substituents. Phosphazene derivatives exhibit various properties such as antimicrobial, anticarcinogenic and antituberculosis activities depending on the binding groups. These properties have led to the expansion of the use of phosphazenes. It is found that cyclophosphazenes known as alkylating agents cause cleavage in DNA cross-links. This study focused on the investigations of the antimicrobial activity and DNA interaction bisferrocenyl-2-*trans*-6-dispiro-cyclotetraphosphazenes, with plasmid DNA.

**Materials and Methods:** Agar Well-diffusion and micro dilution methods were used to examine the antimicrobial activity and minimal inhibitor concentration (MIC) values of the bis-ferrocenyl-cyclotetraphosphazenes. In the DNA interaction, studies the electrophoretic image was observed by treating with the plasmid DNA compounds in the supercoiled structure. Restriction enzyme digestion of the compound-DNA mixture was used to determine compound binds to which nucleotides. The data obtained from control and treatment groups were evaluated and compared.

**Results and Discussion:** According to the results of this study two cyclotetraphosphazene derivatives, DASD and N-methylethane-1,2-diamine substituted compounds, have strong antimicrobial activity against *S. typhimurium*. In addition, three cyclotetraphosphazene derivatives also exhibited very strong activity against *C. albicans*. MIC values of the compounds ranged from 15.63  $\mu$ M to 2000  $\mu$ M. Moreover, MBC/MFC values were also changed from <15.63 to >2000  $\mu$ M. The compounds inhibited DNA restriction indicating the compounds binds to A/A and G/G nucleotides.

**Conclusions:** It has been understood that some of the compounds used as a result of the studies carried out have antimicrobial activity. It is also understood that the compounds used have an effect on DNA. Findings obtained as a result of these studies are the first research findings about tetrameric phosphazenes.

*Keywords: Bisferrocenyl-cyclotetraphosphazenes, DNA interactions, antimicrobial activity*

*\*This study was supported by the "Ankara University, Scientific Research Unit" Grant No. 15H0430006.*

## POSTER PRESENTATION – 14

### **IDENTIFICATION OF PIK3CA MUTATION AND EXPRESSION BY BIOINFORMATIC ANALYSIS IN BREAST CANCER**

Ebubekir Dirican<sup>1</sup>

<sup>1</sup>Marmara University, School of Medicine Department of Medical Biology, Istanbul, Turkey

PIK3CA gene encodes the p110  $\alpha$  catalytic subunit of the oncoprotein phosphatidylinositol 3-kinase (PI3K) which regulates many biological processes such as cell proliferation, differentiation, migration and survival. PIK3CA gene mutations are common in breast cancer (BCa) and its frequency is about 25-40%. Describing the mutations, interaction networks and the expression profiles of PIK3CA may provide ideas for dissemination the mechanism of its ultimately leading to the breast carcinogenesis. The aim of this study was evaluated PIK3CA gene mutation and expression levels by bioinformatic analysis. We assessed Kaplan-Meier Plotter to identify the prognostic roles of PIK3CA. And then, COSMIC and cBioportal analysis were used to research the PIK3CA mutations. Finally, we used FIREHOSE and Oncomine analysis to evaluated PIK3CA mRNA levels. According to our findings PIK3CA mRNA expression levels decreased 1.268 fold. But, PIK3CA mRNA expression levels were statistically insignificant BCa ( $p=0.784$ ). CDH1, PTEN, PIK3R1 and NF1 were forecast to include in interaction network of PIK3CA in BCa. PIK3CA mutations localized in exon 9 and 20. Findings of the COSMIC that E542K, E545K, H1047R and H1047L are the highest frequency of PIK3CA mutations types. Kaplan-Meier Plotter analysis revealed that high PIK3CA expression level correlated with a poor survival rate in BCa ( $p=2E-07$ ). As a results PIK3CA gene mutations and expression or other genes interaction network of PIK3CA that may have common roles in BCa. These interactions or alterations in PIK3CA gene may be important for BCa treatment or diagnosis. Taken together, our findings shed new light on the PIKCA gene in BCa and add new insight regarding the carcinogenesis of BCa.

*Keywords: PIK3CA, COSMIC, FIREHOSE, Oncomine, Kaplan-Meier Plotter, cBioportal*



## POSTER PRESENTATION – 15

### **EVALUATION OF HISTONE DEACETYLASE SIRT6 EXPRESSION AND OXIDATIVE DNA DAMAGE IN PATIENTS WITH PREDIABETES AND TYPE 2 DIABETES**

Zeynep Caliskan<sup>1,2</sup>, Tuba Mutlu<sup>3</sup>, Matem Tuncdemir<sup>3</sup>, Mehmet Guven<sup>3</sup>, Mutlu Niyazioğlu<sup>4</sup>, Yalcin Hacıoğlu<sup>4</sup>, Yildiz Dincer<sup>1</sup>

<sup>1</sup>Department of Medical Biochemistry, Istanbul University Cerrahpasa Medical Faculty, Istanbul, Turkey.

<sup>2</sup>Department of Medical Biochemistry, Istanbul Yeni Yuzyil University, Istanbul, Turkey.

<sup>3</sup>Department of Medical Biology, Istanbul University Cerrahpasa Medical Faculty, Istanbul, Turkey.

<sup>4</sup>Department of Internal Medicine, Istanbul Education and Research Hospital, Istanbul, Turkey.

Type 2 diabetes (T2DM) is a multifactorial disorder characterized by insulin resistance and hyperglycemia. Oxidative stress is an important factor in the development of T2DM. As a closed circuit, hyperglycemia seen in diabetes also increases oxidative stress. 8-hydroxydeoxyguanosine (8-OHdG) is the most frequently formed oxidative DNA damage. Upon DNA repair, 8-OHdG appears in urine and is considered a good marker for oxidative DNA damage. SIRT6 is a deacetylase and mono-(ADP)-ribosyl transferase associated with glucose metabolism as well as DNA repair. In the present study, it was aimed to investigate SIRT6 expression at mRNA and protein levels in peripheral leukocytes of patients with T2DM and prediabetes (preDM), and to examine relationship between SIRT6 expression and urinary 8-OHDG level.

A total of 70 patients with T2DM, 50 patients with preDM and 40 healthy subjects were included in the study. SIRT6 mRNA and SIRT6 protein levels were determined by qRT-PCR and immunocytochemical staining, respectively. Urinary 8-OHDG levels were measured by ELISA.

No statistically significant difference was found between the groups for SIRT6 mRNA level. Immunocytochemical analysis showed a statistically significant reduction in the number of SIRT6 (+) cells in T2DM and preDM groups in comparison to the control group ( $P < 0,01$ ). The number of SIRT6 (+) cells in the T2DM group was found to be lower than that of in the preDM group ( $P < 0,05$ ). Urinary 8-OHDG levels were significantly higher in the T2DM group than that of in the preDM group ( $P < 0,05$ ). No significant correlation was determined between urinary 8-OHDG levels and the number of SIRT6 (+) cells.

The relation between SIRT6 expression and oxidative DNA damage in diabetes has not been investigated to date. According to our findings, SIRT6 protein level is diminished in both patients with T2DM and preDM. A lack of a significant correlation between urinary 8-OHDG levels and the number of SIRT6 (+) cells gives rise to thought that SIRT6 may regulate glucose metabolism by altering expression of genes involved in glucose metabolism through histone modification rather than its role in DNA repair.

It was concluded that decreased SIRT6 protein level in peripheral leukocytes may be associated with development of T2DM.

*Keywords: Type 2 diabetes, prediabetes, oxidative stress, 8-OHDG, SIRT6 expression*

*Istanbul University Cerrahpasa Medical Faculty Clinical Research Ethics Committee's approval number: 83045809/604.01/02-145635 Date of decision: 14 May 2015*

*Note to Scientific Committee: The present work was supported by the Research Fund of Istanbul University. Project No. 53685*

## POSTER PRESENTATION – 16

### EXPRESSION LEVELS OF microRNA 126-3p, *Spred1* and *Pik3r2* IN HUMAN CAROTID ARTERY PLAQUES

Ciğdem Sezer Zhmurov<sup>1</sup>, Özlem Timirci Kahraman<sup>2</sup>, Ümit Zeybek<sup>2</sup>, Osman Fazlıoğulları<sup>3</sup>, Cem Başaran<sup>4</sup>, Hakan Bermek<sup>5</sup>

<sup>1</sup> Department of Genetics and Bioengineering, Istanbul Bilgi University, Istanbul, Turkey

<sup>2</sup> Department of Molecular Medicine, Institute of Experimental Medicine, Istanbul University, Istanbul, Turkey

<sup>3</sup> Department of Cardiovascular Surgery, Medical Park Hospital, Gebze, Kocaeli, Turkey

<sup>4</sup> Department of Cardiovascular Surgery, Medicana Bahcelievler Hospital, Bahcelievler, Istanbul, Turkey

<sup>5</sup> Department of Molecular Biology and Genetics, Istanbul Technical University, Istanbul, Turkey

According to World Health Organization Global Status Report on Noncommunicable Diseases of 2014, 17.5 million people die of cardiovascular diseases, such as coronary artery disease or stroke, annually. The underlying pathological condition is known as atherosclerosis, occurring in the medium and large sized arteries. It is a chronic and immune-inflammatory complex disease that progresses slowly. Initiated by potential sources of injury, such as hyperlipidemia, hypertension, metabolites, infections and mechanical factors such as shear stress, atherosclerosis results in thickening of the inner layer of arteries with lipid rich material (atheroma) and connective tissue (sclerosis).

Angiogenesis, formation of new vessels from existing ones, is mainly controlled by vascular endothelial growth factor (VEGF) and Notch signaling pathways. Angiogenesis inside atherosclerotic plaques has been associated with disease progression, as well as plaque rupture. The molecular pathways that contribute to angiogenesis are potential targets for therapies aiming to prevent intraplaque neoangiogenesis. In this study, we aimed to investigate the role of angiogenic mechanisms related to vascular endothelial growth factor pathway and the regulators that interact with this pathway, such as microRNAs, the small, non-coding RNAs that post-transcriptionally control many cellular processes, including angiogenesis. For this purpose, we investigated the expression profile of miRNA-126 signalling pathway molecules involved in atherosclerosis, including miR 126-3p and its target genes, *Pik3r2* and *Spred1* in human carotid atherosclerotic plaques.

14 plaque samples from carotid arteries were obtained from patients undergoing carotid endarterectomy in Istanbul Medicana Bahcelievler Hospital. The region immediately adjacent to the plaque area was used as control. The expression levels of miR 126-3p, *Pik3r2* and *Spred1* were assessed with quantitative real-time PCR in plaque and control samples. Using relative quantification strategy, target gene and miRNA expression levels in plaques were compared to those of controls and normalized to the levels of the 18S ribosomal RNA and U6 small nuclear RNA.

We found overall 2.14 fold ( $p < 0.05$ ) up-regulation in miR-126-3p in plaques compared to controls. Up-regulation was observed in 11 samples. *Spred* and *Pik3r2* were down-regulated in 8 and 9 samples compared to controls.

This is the first evidence on miR 126-3p expression in deep intraplaque regions. To our knowledge, the expression analyses on miR 126-3p, *Spred1* and *Pik3r2* levels, was done for the first time in human carotid artery disease. This work demonstrates the contribution of miR-126 signalling and neoangiogenesis driven by these signaling molecules to plaque progression in advanced atherosclerosis.

**Keywords:** Angiogenesis, Atherosclerosis, Plaque, microRNA

**Note to the Scientific Committee:** This work was supported by Istanbul Technical University Scientific Research Projects Unit (ITU/ BAP) (Grant no. 36999).

POSTER PRESENTATION – 17  
**ERYTHROCYTE MEMBRANE CHOLESTEROL CONTENT AND  
POSTPRANDIAL LIPEMIA IN SUBJECTS WITH METABOLIC SYNDROME**

Tuğba MAZLUM ŞEN, Birgül KURAL, Asım ÖREM, Cihan ÖREM\*, Serap ÖZER YAMAN, Sevil KÖR

Departments of Medical Biochemistry and \*Cardiology, Faculty of Medicine, Karadeniz Technical University, Trabzon, Turkey

A series of the metabolic events that occur following the digestion and absorption of lipids after a fatty meal has been defined as postprandial lipemia which is important in development of cardiovascular diseases (CVD) such as metabolic syndrome. Free cholesterol in the erythrocyte membrane is thought to affect atherosclerotic plaque development and stability. This study was aimed to investigate the relationship between total cholesterol content in erythrocyte membranes (EMC) and postprandial lipemia in patients with metabolic syndrome (MetS).

30 non-MetS and 48 MetS subjects (male age range of 25-65 years) were included. Oral triglyceride tolerance test (OTTT) were applied them and area under curves (AUC) were calculated by using triglyceride levels at the fasting state and at 4th hours after the high fat diet. EMC were determined enzymatic colorimetric methods after isolation of erythrocyte membranes by high speed centrifugation.

EMC of subjects with MetS were significantly higher than of subjects with non-MetS ( $p < 0.001$ ). In MetS group, positive correlation was found between EMC and total cholesterol levels ( $r = 0.399$ ,  $p = 0.005$ ). EMCs did not show statistically significant difference between postprandial lipemia subgroups of non-MetS and MetS groups ( $p > 0.05$ ). In conclusion, although EMC was found increased in MetS, EMC did not change according to postprandial lipemia.

*Keywords: Cholesterol, Erythrocyte Membrane, Metabolic Syndrome, Postprandial Lipemia*

*Note to the Scientific Committee : This abstract is a part of a supported Karadeniz Technical University BAP Project and it's project number: TDK-2015-147. Ethics Committee's approval number: 2014/33.*

## POSTER PRESENTATION – 18 **OVEREXPRESSION OF ERG TRANSCRIPTION FACTOR IN H358 LUNG CANCER CELL LINE ACTIVATED THE EPITHELIAL-MESENCHYMAL TRANSITION MARKERS**

Abdulmecit Gökçe<sup>1</sup>, Gülay Bulut<sup>1</sup>

<sup>1</sup> Bahçeşehir University, Faculty of Engineering and Natural Sciences, Molecular Biology and Genetics Department, 34353 Beşiktaş, Istanbul, Turkey.

**Background / Aim:** Epithelial-mesenchymal transition is a biological process which allows the epithelial cells to undergo several changes that enable epithelial cells to become more invasive, drug-resistant during chemotherapy, and lowers prognosis rate in cancer. The studies attempting to understand the mechanisms of epithelial-mesenchymal transition revealed a transcription factor called ETS-related gene (ERG) which is positively regulating the epithelial-mesenchymal transition in prostate cancer and in other cancer types. In this study, to understand the effect of ERG gene expression on mesenchymal transition in lung cancer, H358 human lung cancer cell line, which has very low ERG expression was transfected with ERG gene bearing plasmid, and the expression levels of EMT markers were determined.

**Materials and Methods:** ERG gene overexpression in H358 cell line was achieved through the transient transfection of H358 cell line with pERG vector plasmid (originated from pCMV-AC-GFP (Origene) on which ERG gene was cloned) with FreeStyle Max (Invitrogen) transfection reagent according to manufacturer's procedure. For the control, pCMV-AC-GFP vector (pEV) which is not bearing ERG gene was transfected with the same reagent to H358 cell line. Following the transfections, total RNA was isolated from transiently transfected H358 cells with Invitrogen total RNA isolation kit. ERG and EMT marker gene expressions were determined at mRNA level with qRT-PCR (BIORAD).

**Results:** The H358 cells transfected with pERG plasmid expressed ERG gene 14.000 times more compared to the cells which were transfected with pEV after 48 hours from the transfection. Following the confirmation of ERG upregulation in H358 cells, expression levels of epithelial-mesenchymal transition marker genes including E-cadherin, Vimentin, ZEB1, Snail and Slug were analyzed. ERG overexpression resulted in the upregulation of the mesenchymal marker, Vimentin (1.2 folds) and the transcription factors, Snail (1.7 folds) and ZEB1 (1.6 folds) at mRNA level.

**Discussion:** The data gathered from ERG overexpressing H358 lung cancer cell line showed that expression of ERG transcription factor is resulting in the upregulation of EMT markers whose functions are to promote epithelial to mesenchymal transition such as Snail and ZEB1.

**Conclusion:** The results proposed the ERG transcription factor as a target gene for drug design to create novel treatments for the inhibition of epithelial to mesenchymal transition in lung cancer cases.

*Keywords:* Non-small cell lung cancer (NSCLC), H358 cell line, epithelial-mesenchymal transition (EMT), the ETS-related gene (ERG).

*Note to the Scientific Committee:* This work was supported by the Scientific and Technological Research Council of Turkey (TUBITAK) [grant number 114S428 (PI: G. Bulut)].

## POSTER PRESENTATION – 19 THE INVESTIGATION OF MDR1 GENE C1236T AND C3435T POLYMORPHISMS ON THE EPILEPSY PATIENTS

Kubra Sahin<sup>1</sup>, Akin Tekcan<sup>2</sup>, Betul Cevik, Aydın Rustemoglu<sup>3</sup>, Serbulent Yigit<sup>1</sup>, Azize Ipekbayrak<sup>3</sup>

<sup>1</sup>Department of Medical Biology, Medical Faculty, Gaziosmanpaşa University, Tokat, Turkey

<sup>2</sup>Department of Medical Biology, Medical Faculty, Ahi Evran University, Kirsehir, Turkey

<sup>3</sup>Department of Neurology, Medical Faculty, Gaziosmanpaşa University, Tokat, Turkey

Epilepsy is a debilitating and neurological disease characterized by uncontrolled seizures impacting millions of people worldwide. The role of genetic factors in the development of epilepsy is still under investigation.

MDR1 (ABCB1) is a drug transporter protein expressed on the endothelial cells of the blood–brain barrier as well as the epithelial cells of the intestine. MDR1 gene, localized in chromosome 7q21. MDR1, which encodes p-glycoprotein and functions as an efflux transporter in different cells, is widely found in many tissues such as the kidney, brain and is used for the absorption and distribution of various drugs. Therefore, MDR1 gene variants have been proposed as potential susceptibility factors for diseases and as determinants of treatment for various drugs.

In this study, the possible association between epilepsy and MDR1 gene rs 1045642 (C3435T), and rs1128503 (C1236T) gene polymorphisms were investigated.

The present study researched the genotype distribution and allele frequency for C3435T and C1236T polymorphisms using the polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) technique in 64 patients with epilepsy and 100 healthy individuals. The results were analyzed with SPSS 16.0 software.

Our results showed that C1236T polymorphism may be associated with epilepsy. There was a significant difference between the patient and control group in terms of general genotype distribution ( $p = 0.044$ ). Especially TT genotype was found significantly higher in patients ( $p=0.032$ ,  $OR=2.00$ ,  $95\%CI=1.03-3.90$ ). At the same time, the T allele was found significantly higher in the patients ( $p=0.031$ ), and this allele may predispose to the epilepsy ( $OR=1.65$ ,  $95\%CI=1.05-2.58$ ).

But, the genotype and allele distribution of MDR1 C3435T polymorphism have not been found associated with epilepsy ( $p=0.721$  and  $p=0.734$ , respectively).

In our study, we obtained significant results with a relatively low number of samples. Future work with larger sampling is important for confirming our observations.

*Keywords: Epilepsy, MDR1 gene, rs 1045642, rs1128503, Polymorphisms*

*Note to the Scientific Committee:*

*The study protocol was approved by the Local Ethics Committee of Gaziosmanpasa University Faculty of Medicine (Ethical Approve Number: 14-KAEK-253) .*

*This study was supported by Ahi Evran University Scientific Research Projects Fund (Project Number:SYO.A3.16.001)*

## POSTER PRESENTATION – 20 LOW DOSE GENISTEIN UNLIKELY INDUCES PROLIFERATION OF PC3 CELLS

Sule Terzioglu-Usak<sup>1</sup> and Nur Ozten Kandas<sup>2</sup>

<sup>1</sup>Bezmalem Vakif University, Faculty of Medicine, Department of Medical Biology, Istanbul-Turkey.

<sup>2</sup>Bezmalem Vakif University, Faculty of Pharmacy, Department of Toxicology, Istanbul-Turkey.

**Background:** Many epidemiological studies have revealed inverse correlations between soy consumption and incidence rate of prostate cancer, suggesting soy has chemopreventive effects. Genistein, a main active compound of soy, is an isoflavone that has a capability to bind estrogen receptor and to activate estrogen-regulated gene transcription in target organs. Besides, it is widely studied *in vitro* anticancer and antioxidant properties of genistein. However, there are controversial results in *in vivo* experiments. For example, in TRAMP and PC3 rodent model of animals, genistein increased carcinogenesis and metastasis whereas it decreased induction of breast cancer formation in genistein exposed perinatal mice.

**Objectives:** Therefore, we aimed to investigate effects of genistein at physiological concentrations on human prostate cancer cell line in terms of proliferation and migration.

**Methods:** Human prostate cancer cell line, PC3 cells were cultured in RPMI 1640 supplemented with 10% FBS in a humidified atmosphere of 5% CO<sub>2</sub> and 95% air at 37°C. Subconfluent cells were treated with genistein (50, 25, 10, 5, 2.5, 1 and 0.5 µmol/L; dissolved in DMSO) diluted in culture media and treated cells for 48 hours. Cytotoxic effects of genistein on PC3 cell proliferation were determined by colorimetric WST-1 cell viability assay. Metastatic effect of genistein on PC3 cells were analysed by wound healing assay under light microscopy.

**Results:** We found that genistein has a biphasic effect. Low dose of genistein (<10 µM) which are physiological concentrations stimulated proliferation of PC3 cells whereas high dose (>10 µM) inhibited cell growth and migration which is most probably toxic to cells.

**Conclusion:** We sought to explore *in vitro* effect of genistein on PC3 cell viability and migration. Contrary to earlier reports, we found that genistein at physiological concentrations (0.5-10 µM) have proliferative effects on PC3 cells that higher consumers of soy should reconsider while taking soy supplements in order to avoid prostate or breast cancer risks.

*Keywords: Genistein, Prostate Cancer and PC3 cells.*

## POSTER PRESENTATION – 21

### REGULATION OF ARTERIAL CONTRACTION BY PERIVASCULAR ADIPOSE TISSUE DERIVED MEDIATORS IN HEALTH AND DIABETES

Radoslava Emilova<sup>1</sup>, Daniela Dimitrova<sup>2</sup>, Teodora Daneva<sup>3</sup>, Mitko Mladenov<sup>4</sup>, Nikola Hadzi-Petrushev<sup>4</sup>, Rudolf Schubert<sup>5</sup>, Hristo Gagov<sup>6</sup>

<sup>1</sup> Department of Immunology, National Centre of Infectious and Parasitic Diseases, Sofia, Bulgaria

<sup>2</sup> Institute of Biophysics and Biomedical Engineering, Bulgarian Academy of Sciences, Sofia, Bulgaria

<sup>3</sup> Institute of Biology and Immunology of Reproduction, Bulgarian Academy of Sciences, Sofia, Bulgaria

<sup>4</sup> Institute of Biology, Faculty of Natural Sciences and Mathematics, Sts. Cyril and Methodius, University of Skopje, Skopje, Macedonia

<sup>5</sup> Ruprecht-Karls-University Heidelberg, Medical Faculty Mannheim, Mannheim, Germany

<sup>6</sup> Department of Animal and Human Physiology, Faculty of Biology, Sofia University St. Kliment Ohridski, Sofia, Bulgaria

**The aim** of our research is to study the regulatory role of PVAT mediators H<sub>2</sub>S and H<sub>2</sub>O<sub>2</sub> on the 5-hydroxytryptamine (5-HT) induced contractions of rat skeletal muscle arteries isolated from healthy and diabetic rats.

**Introduction:** Perivascular adipose tissue (PVAT) surrounds many blood vessels including small arteries and arterioles. PVAT is a thin sheet, which consists of several cell types – mainly adipocytes, but also endothelial cells, leukocytes, and fibroblasts. PVAT either increase, or decrease the amplitudes of force of contraction of smooth muscle layer.

**Materials and Methods:** We studied the influence of an inhibitor of H<sub>2</sub>S producing enzyme cystathionine gamma lyase and of a reactive oxygen species trapping agent on the force of contraction of rat artery gracilis isolated from healthy and diabetic rats. Diabetes was induced by a single intraperitoneal injection of streptozotocin. Endothelium-denuded artery rings without or with intact PVAT were used for isometric measurements of the force of contraction induced by increasing concentrations of 5-HT

**Results:** Different agents were applied as pharmacological tools for investigation of the H<sub>2</sub>S and H<sub>2</sub>O<sub>2</sub> release from PVAT. In *a. gracilis* preparations from healthy rats, PVAT produces H<sub>2</sub>S that antagonizes the 5-HT contractions, while in diabetic animals higher concentrations of 5-HT increases the PVAT production of H<sub>2</sub>O<sub>2</sub>.

**Discussion:** H<sub>2</sub>O<sub>2</sub> as mediator sensitizes the 5-HT-induced contraction of the studied diabetic skeletal muscle arteries.

**Conclusion:** In health dominates H<sub>2</sub>S-dependent vasorelaxation. In diabetes when pro-inflammatory PVAT phenotype dominates the common effect is vasoconstriction. It, at least partly, depends on increased H<sub>2</sub>O<sub>2</sub> production.

## POSTER PRESENTATION – 22

### A CANDIDATE NOVEL MARKER FOR CAROTID ARTERY DISEASE: VISFATIN

Ozlem Timirci Kahraman<sup>1</sup>, Umit Zeybek<sup>1</sup>, Servet Tunoglu<sup>1</sup>, Arzu Ergen<sup>1</sup>, Mehmet Kurtoglu<sup>2</sup>

<sup>1</sup>Istanbul University, Aziz Sancar Institute of Experimental Medicine, Department of Molecular Medicine, Istanbul, Turkey

<sup>2</sup>Istanbul University, Istanbul Faculty of Medicine, Department of Surgery, Istanbul, Turkey

**Background:** Visfatin, which plays a role in nicotinamide adenine dinucleotide (NAD) biosynthesis, has been implicated in inflammatory states. Visfatin is highly expressed in adipose tissue, but it is also ubiquitously present in most tissues. The role played by visfatin in atherosclerosis is still confused, but some studies recognize the involvement of this adipokine in atherosclerotic processes. The purpose of this study was to investigate the gene expression levels of visfatin as novel marker according to differences between carotid plaque regions and to correlate it with clinical features of plaque destabilization.

**Materials and Methods:** The study included 15 endarterectomy specimens available from operated symptomatic carotid artery stenoses. The specimens were separated according to anatomic location: internal carotid artery (ICA) and common carotid artery (CCA) as control region, and then stored in liquid nitrogen. The amounts of cDNA for visfatin was determined by Quantitative real-time PCR (Q-RT-PCR). Target gene copy numbers were normalized using GAPDH gene. The fold change between carotid artery plaque tissue and control tissue was calculated using  $2^{-\Delta\Delta CT}$  method.

**Results:** In our study, visfatin was appeared to be upregulated in 11 samples. Q-RT-PCR data showed that relative visfatin gene expression was increased in ICA plaque regions when compared to CCA regions ( $p < 0.05$ ).

**Conclusion:** Other studies suggest that visfatin develops certain actions in the progression of atherosclerosis, probably related to the fact that visfatin acts as an inflammatory mediator. In the present study, the clinical significance is the differences between the proximal and distal regions of the lesion, associated with the ICA and CCA respectively, with increased visfatin in the ICA region.

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## POSTER PRESENTATION – 23

### **TUMOR NECROSIS FACTOR RELATED APOPTOSIS INDUCING LIGAND LEVELS WERE HIGHER IN NEWLY DIAGNOSED STAGEIV NON-SMALL CELL LUNG CANCER**

Saadet Gumuslu<sup>1</sup>, Aysegül Kargı<sup>2</sup>, Atıl Bisgin<sup>3</sup>, Arzu Didem Yalcın<sup>4</sup>, Bulent Kargı<sup>5</sup>, Emel Sahin<sup>1</sup>

<sup>1</sup>Department of Biochemistry, Faculty of Medicine, Akdeniz University, Antalya, Turkey.

<sup>2</sup>Medical Oncology Clinic, Medstar Hospital, Antalya, Turkey.

<sup>3</sup>Department of Medical Genetics, Faculty of Medicine, Cukurova University, Adana, Turkey,

<sup>4</sup>Allergy and Clinical Immunology Unit, Training and Research Hospital, Antalya, Turkey.

<sup>5</sup>Department of Thoracic Surgery, Medical Park Hospital, Antalya, Turkey.

**Background:** Tumor necrosis factor (TNF)-related apoptosis-inducing ligand (TRAIL), has a complex physiological role beyond that of merely activating the apoptotic pathway in cancer cells. Vitamin D is converted to its active form locally in the lung, and is also thought to play an important role in lung health. The aim of this study is to investigate the possible clinical significance of serum soluble TRAIL (sTRAIL) and 1,25-dihydroxyvitamin D<sub>3</sub> levels in patients with non-small cell lung cancer (NSCLC).

**Materials and Methods:** Totals of 18 consecutive adenocarcinoma and 22 squamous cell carcinoma patients with stage-IV non-small cell lung cancer were included in this study. 21 healthy individuals served as a control group. Serum levels of sTRAIL and 1,25-dihydroxyvitamin D<sub>3</sub> were measured in all samples.

**Results:** Both adenocarcinoma (1660±41.70 pg/ml) and squamous cell carcinoma (1520±38.70 pg/ml) patients had significantly higher serum levels of sTRAIL than the healthy controls (634±18.00 pg/ml). 1,25-dihydroxyvitamin D<sub>3</sub> levels were 15.90±2.10 ng/ml (adenocarcinoma patients); 16.90±1.30 ng/ml (squamous cell carcinoma patients); and 20.00±2.00 ng/ml (healthy individuals). We found a correlation between sTRAIL and 1,25-dihydroxyvitamin D<sub>3</sub> levels in healthy individuals, although no such correlation was seen in NSCLC patients.

**Discussion:** One advantage to our study is that patients were newly diagnosed stage-IV NSCLC and none had undergone any treatment, so that sTRAIL levels were not influenced by previous drug treatment. However, the small size of the study population may in itself have been a contributing factor to our failure to establish a link between sTRAIL levels and disease outcome. Many studies have demonstrated a relationship between vitamin D and cancer, including malignancies of the breast, prostate and lung. Vitamin D or its analogs, alone or in combination with cytotoxic drugs, may have some efficacy in the treatment of lung cancer.

**Conclusion:** This is the first study to assess sTRAIL levels in NSCLC patients. This study shows that sTRAIL levels were higher in newly diagnosed stage-IV NSCLC than in healthy controls.

*Keywords: sTRAIL, lung cancer, adenocarcinoma, squamous cell carcinoma.*

## POSTER PRESENTATION – 24 ANALYSIS OF WWOX GENE EXPRESSION IN PTERYGIUM TISSUE

Nihan BOZKURT<sup>1</sup>, Ömer ATEŞ<sup>1</sup>

<sup>1</sup>Department of Medical Biology, Faculty of Medicine, Gaziosmanpaşa University, Tokat, Turkey.

**Background :** Pterygium is an abnormal wing-shaped growth of epithelial and fibrovascular tissue from the corneoscleral limbus. It is characterized by an altered basal epithelial cell proliferation, vascularization, and invasion of the adjacent corneal epithelium. The pathogenesis of this disease is unclear. Pathogenic factors has been proposed, including viral infections, epigenetic aberrations, epithelialmesenchymal transition,immunologic and anti-apoptotic mechanisms, angiogenic and lymphangiogenic stimulation, deregulation of extracellular matrix modulators and growth factors. However, after abnormal expression of the p53 was found in the epithelium of pterygia, the condition is considered to be an uncontrolled cell proliferation, like a tumour. WWOX gene is a candidate tumor suppressor gene. Abnormal expression level of WWOX have been reported in numerous neoplasia such as breast, ovarian, lung, stomach, liver, pancreas, and hematological malignancies. In this study, we investigated the WWOX gene expression in pterygium.

**Materials and Methods :** In this study, the 11 pterygium specimens and 11 normal conjunctive tissues received surgical excisions. Quantative RT-PCR was performed to detect the mRNA expression of WWOX. SPSS16.0 program was performed using for statistical analysis. The actin gen was used as an internal control and relative mRNA levels were calculated using the  $2^{-\Delta\Delta CT}$  method.

**Results :** The mRNA expression of WWOX was lower in the pytergium samples compared with the normal conjunctiva. 2.2 fold-decreased in WWOX expression was observed in pytergium samples.

**Conclusions:** According to our data, inactivation of WWOX gene may contribute to the progression of pytergium.

*Keywords: Gene Expression, Pterygium, WWOX*

*This work was acceptanced by Gaziosmanpaşa University the Ethics Committee for Clinical Investigations. Project numbers: 14-KAEK-228.*

*Note to Science Committee :This work was supported by Gaziosmanpaşa University Scien-tific Research Projects Fund. Project numbers: 2015/26.*

POSTER PRESENTATION – 25  
**EVALUATION OF HULC AND 7SL LONG NON-CODING RNA  
EXPRESSION LEVELS IN PATIENTS WITH CRIMEAN CONGO  
HEMORRHAGIC FEVER**

Burcu BAYYURT<sup>1</sup>, Serdal ARSLAN<sup>1</sup>, Aynur ENGİN<sup>2</sup>, Mehmet BAKIR<sup>2</sup>

<sup>1</sup>Cumhuriyet University Medical Faculty Medical Biology Department, Sivas

<sup>2</sup>Cumhuriyet University Medical Faculty Infectious Diseases Department, Sivas

Crimean Congo hemorrhagic fever (CCHF) is a tick-borne disease caused by the arbovirus Crimean Congo hemorrhagic fever virus (CCHFV). Long non-coding RNAs (lncRNAs) are generally classified as transcripts longer than 200 nucleotides. Viral infections induce strong modifications in the cell transcriptome including lncRNA. Several lncRNAs expressed in the infected cells are used to regulate the expression of viral and host genes. In recent years, it is thought that some lncRNAs can be used as therapeutic targets and prognostic markers for disease progression. In this study, HULC and 7SL RNA expression levels were examined in CCHF patients for the first time. For this purpose, blood samples of 100 individuals, including 60 experimentals (CCHF patients) and 40 controls (healthy), were used. Blood was collected into the RNA blood tube (paxgene) containing the specific detection fluid. First, total RNA, including lncRNAs, was isolated from all samples. After the isolation step, RNA concentrations were measured and complementary DNA (cDNA) synthesis was performed. The quantitative real time polymerase chain reaction (qRT-PCR) phase was followed to determine the expression levels of the lncRNAs (HULC and 7SL RNA) and housekeeping gene (SF3A1) in patient and control blood using SYBR Green method. All the qRT-PCR results were uploaded to the PCR Array Data Analysis software and analyzed according to the  $\Delta\Delta Cq$  method. According to the data analysis results, experimental and control group (patient vs. healthy and ex vs. healthy) were compared, it was found that expression level of HULC was increased 1,1049 times ( $p = 0,05$ ) and expression level of 7SL RNA was decreased 1,8828 times ( $p = 0,93$ ) in patients. The fact that CCHF disease results in liver damage in many patients and HULC is a lncRNA that is upregulated especially in liver defects supports our findings. Since 7SL RNA plays a role in antiviral response, it was decreased in patients as we expect. It is believed that our findings will contribute to understanding the pathogenesis of CCHF disease. (Ethics Committee Decision No: 2016-03/10 - This study was supported by the Scientific Research Council of Cumhuriyet University Sivas, Turkey, project no: T-683).

*Keywords: Crimean Congo hemorrhagic fever, long non-coding RNAs, gene expression*

## POSTER PRESENTATION – 26

### **SYNTHESIS AND CHARACTERIZATION OF SILVER NANOPARTICLES USING *JUGLANS REGIA* LEAF EXTRACT IN THE 'GREEN SYNTHESIS' METHOD AND THEIR BIOLOGICAL EFFECTS**

Ahmet Şimşek<sup>1</sup>, Burak Küçük<sup>1</sup>, Ali Aydın<sup>1</sup>, Ali Destegül<sup>2</sup>, Hüseyin Akbaş<sup>2</sup>, Necati Özpınar<sup>3</sup>, Feyzanur Çaldıran<sup>1</sup>, Ahmet Karadağ<sup>2</sup>, Saban Tekin<sup>1</sup>

<sup>1</sup> Gaziosmanpaşa University, Science and Art Faculty, Department of Molecular Biology

<sup>2</sup> Department of Chemistry Tokat, Turkey

<sup>3</sup> Cumhuriyet University, Faculty of Medicine, Department of Parasitology, Sivas, Turkey

**Background:** Nanomaterials like silver nanoparticles (AgNPs) have anticancer, antibacterial, antiparasitic and disinfectant agents potential because of their strong inreaction with biomolecules on target cells. The aim of our study was to evaluate the biological effects of the AgNPs formed using various AgNO<sub>3</sub> concentrations with *Juglans regia* leaf extracts as a reducing agent against two cancer cells and some microbial flora such as bacteria, fungi, and protozoans.

**Materials and Methods:** We used 'Green Synthesis' method for the AgNPs by stirring silver ions with hot aqueous extract of the *Juglans regia* leaf. Characterization of the synthesized AgNPs was conducted by UV-Vis absorption spectroscopy, FT-IR, TGA, and scanning electron microscopy. DNA/BSA binding properties and binding constant (K<sub>b</sub>) will be determined using a UV-Vis spectrophotometer. The antiproliferative and cytotoxic activities of the AgNPs on cancer cells were determined using MTT and LDH assay, respectively. Disc diffusion, minimum inhibitory concentrations (MIC) and minimum bactericidal concentration (MBC) assay were used to determine whether AgNPs induces microbial flora death. Moreover, the morphological analysis of the protozoans was evaluated using a Giemsa stain procedure.

**Results and Discussion:** The silver nanoparticles obtained with *Juglans regia* leaf extract reduction method were spherical, cubic or rod types and uniform size distribution patterns with particle size between 70 to 100 nm. According to the MTT and LDH assay test results, AgNPs were inhibited the cell viability of cancer cells compared to positive control anticancer drug, 5-FU. Remarkably, the LDH test results disclosed that AgNPs were as low cytotoxic as 5-FU, suggesting that this compound may affect by lose membrane integrity of cell as a result of apoptosis. Moreover, the AgNPs induced death of *Leishmania major* ATCC30012 and *Trichomonas vaginalis* ATCC50148, indicating that it may act antiprotozoal agents. The AgNPs were also showed high antibacterial and antifungal activity against Gram positive and Gram negative bacteria including resistant types, and *Candida albicans*, respectively. Based on our results, it is suggested that AgNPs may be potential and valuable pharmacological agents.

**Conclusion:** The AgNPs exhibited strong antiproliferative effects with low cytotoxic feature for cancer cells and displayed considerable antiprotozoal, antibacterial and antifungal activity for microbial flora. The present preliminary findings suggest that AgNPs may enter to medical field as valuable pharmacological agents.

*Keywords:* Silver nanoparticles, *Juglans regia*, HeLa, C6, *Leishmania major*, *Trichomonas vaginalis*, Microbial flora  
This study has supported by TUBITAK 2209A University Student Research Project Support Program in the second half of 2015

## POSTER PRESENTATION – 27

### **SYNTHESIS AND CHARACTERIZATION OF COPPER NANOPARTICLES USING L-ASCORBIC ACID IN THE 'GREEN SYNTHESIS' METHOD AND THEIR PHARMACOLOGICAL EFFECTS**

Beyza Duran<sup>1</sup>, Eda Perçin<sup>1</sup>, Ali Aydın<sup>1</sup>, Ali Destegül<sup>2</sup>, Hüseyin Akbaş<sup>2</sup>, Necati Özpınar<sup>3</sup>, Feyzanur Çaldıran<sup>1</sup>, Ahmet Karadağ<sup>2</sup>, Saban Tekin<sup>1</sup>

<sup>1</sup> Gaziosmanpaşa University, Science and Art Faculty, Department of Molecular Biology

<sup>2</sup> Department of Chemistry Tokat, Turkey

<sup>3</sup> Cumhuriyet University, Faculty of Medicine, Department of Parasitology, Sivas, Turkey

**Background:** Pharmacological agents which inhibit proliferation of cancer cells or kill microbial flora like bacteria, fungi, and parasites, not cytotoxic to normal cells and have fewer side effects are preferred to treat various disease. Thus, development of copper nanoparticles (CuNPs) with better pharmacological properties and fewer side effects are intensely investigated. According to literature, we believe that this study is the first work that demonstrates potential pharmacological activities of the CuNPs formed using various copper (II) chloride concentrations with L-ascorbic acid as a reducing agent against two cancer cells and some microbial flora such as bacteria, fungi, and protozoans.

**Materials and Methods:** The new CuNPs were prepared with 'Green Synthesis' method by reduction of copper (II) chloride in the presence of L-ascorbic acid as a reducing agent. Characterization and particle size of CuNPs were demonstrated by scanning electron microscopy (SEM), UV-Vis absorption spectroscopy, FT-IR and thermal gravimetric analysis (TGA) analysis. DNA/BSA binding properties and binding constant (K<sub>b</sub>) will be determined using a UV-Vis spectrophotometer. Pharmacological activity of CuNPs were assessed by determination of their IC<sub>50</sub>, GI<sub>50</sub>, TGI and LC<sub>50</sub> for cancer cells, and by obtain of their minimum inhibitory concentrations (MIC), minimum bactericidal concentration (MBC), and disc diffusion method as well as Giemsa stain against some microbial flora such as bacteria, fungi, and protozoans.

**Results and Discussion:** The CuNPs with various shapes like spherical, cubic or rod were successfully synthesized and particles size distribution patterns measured between 70 to 100 nm. Analysis of the binding experiment results showed that the CuNPs may interaction DNA/BSA. According to BCPA and LDH test results, CuNPs was significantly antiproliferative and low cytotoxic on tumor cell lines compared to control anticancer drug, 5-fluorouracil (5-FU). The CuNPs displayed high antibacterial activity against Gram positive and Gram negative bacteria and caused killing of *Leishmania major* ATCC30012 and *Trichomonas vaginalis* ATCC50148 protozoans, indicating that it may act antimicrobial and antiprotozoal agents.

**Conclusion:** This work is an original project, for CuNPs used were newly synthesized and their *in vitro* pharmacological potential and mechanism of action are uncovered for the first time.

*Keywords:* Copper nanoparticles, L-ascorbic acid, HeLa, C6, *Leishmania major*, *Trichomonas vaginalis*, Microbial flora  
This study has supported by TUBITAK 2209A University Student Research Project Support Program in the second half of 2015

## POSTER PRESENTATION – 28

### EFFECTS OF RESVERATROL ON GLUTATHIONE LEVELS AND ANTIOXIDANT ENZYME ACTIVITIES IN HEART TISSUE OF HYPERCHOLESTEROLEMIC RATS

Gizem Esra Genc<sup>1</sup>, Saadet Gumuslu<sup>1</sup>, Ayse Yesim Gocmen<sup>2</sup>

<sup>1</sup>Department of Medical Biochemistry, Faculty of Medicine, Akdeniz University, Antalya, Turkey

<sup>2</sup>Department of Medical Biochemistry, Faculty of Medicine, Bozok University, Yozgat, Turkey

**Background:** Resveratrol, a natural polyphenol, exerts a beneficial effect on health and disease. The aim of this study was to investigate the effects of resveratrol on some antioxidants (reduced glutathione (GSH), oxidized glutathione (GSSG), *glucose-6-phosphate dehydrogenase (G-6-PD)*, *glutathione peroxidase (GSH-PX)*, *catalase (Cat)* and *glutathione-S-transferase (GST)*) and lipid peroxidation (thiobarbituric acid reactive substances (TBARS)) in heart of hypercholesterolemic rats.

**Materials and methods:** Fifty male Wistar rats were divided randomly into five groups: control (C), ethanol (E), resveratrol (R), hypercholesterolemia (HC), and hypercholesterolemia plus resveratrol (HCR). Rats in the C, E, and R groups were fed a normal diet for 80 days. For 20 days before sacrifice, we intraperitoneally (i.p) administered 0.1 ml ethanol (50% v/v) to the E group, and 0.1 ml resveratrol (20 mg/kg/day) to the R group. Rats in the HC and HCR groups were fed a 5% cholesterol diet for 80 days. Rats in the HCR group were administered i.p. 0.1 ml resveratrol (20 mg/kg/day) for 20 days before sacrifice. The animals were sacrificed and the heart tissues were used for antioxidants and TBARS determinations.

**Results:** Our findings show that TBARS levels were increased in HC ( $p < 0.01$ ) group. The administration of resveratrol in R and HCR groups decreased the TBARS levels compared to HC group ( $p < 0.01$ ). Cat and GST activities were higher in R group than HCR group ( $p < 0.01$ ). GSH-PX activity was higher in HCR group than in HC group ( $p < 0.01$ ).

**Discussion:** Hypercholesterolemia is accepted as one of the most important risk factors in the development of heart diseases. In the hypercholesterolemia group TBARS, GSH and GSSG levels, and GST, Cat and G-6-PD activities decreased after resveratrol administration may be due to the antioxidant effect of resveratrol in heart tissue. The finding of decreased activities of antioxidant enzymes in the heart tissues treated with resveratrol alone suggest that resveratrol exhibits a direct scavenging effect on free radicals.

**Conclusion:** Results of the present study suggest that resveratrol could have protective effect against heart tissue damage induced by lipid peroxidation in hypercholesterolemia.

**Keywords:** Resveratrol, hypercholesterolemia, glutathione, glucose-6-phosphate dehydrogenase, glutathione peroxidase, catalase, glutathione-S-transferase, thiobarbituric acid reactive substances.

POSTER PRESENTATION – 29  
**THE EFFECT OF ORAL GLUCOSE CHALLENGE TEST (OGTT) INDUCED  
HYPERGLYCEMIC PEAK ON ERYTHROCYTE OXIDANT STATUS**

Ayşe Yeşim GÖCMEN<sup>1</sup>, Tuğba Özdemir<sup>2</sup>, Elif TURAN<sup>2</sup>, Tekin YILDIRIM<sup>2</sup>, Elif BÖREKÇİ<sup>2</sup>, Hilmi ATASEVEN<sup>2</sup>, Muhammet Fevzi POLAT<sup>1</sup>

Bozok University, Faculty of Medicine, Departments of Biochemistry<sup>1</sup> and Internal Medicine<sup>2</sup>

**Objective:** Supplementation with high glucose consumption during oral glucose challenge test (OGTT) is speculated to trigger insulin resistance and some patients hesitate to perform the test as they have suspicion that it may enhance the damaging effects

**Aim:** We aimed to examine the effect of hyperglycemic peak induced by OGTT on erythrocyte oxidative stress, by exploring the erythrocyte asymmetric dimethylarginine (ADMA) and malondialdehyde (MDA) level and GPX activity differences

**Material and Methods:** 80 patients for suspicious of diabetes who applied to our laboratory for OGTT was included in the study GPX activity and Glucose, insulin, ADMA and MDA levels were determined in zero, 30 min, first and second hours during OGTT test in each samples.

**Results:** Patients were categorized according to their serum glucose values; normal tolerance, impaired tolerance and diabetic. Within the normal tolerance group, GPX activity and Glucose, insulin, ADMA and MDA levels were not different compared to 2nd hour.

**Conclusion:** It is observed that the hyperglycemic peak induced by OGTT might cause some change on the GPX activity and ADMA and MDA levels, yet the basal cellular antioxidant defense in normal tolerance group brings these changes to basal level after 2 hours.

*Keywords: OGTT, Hyperglycemia, erythrocyte, oxidative stress.*

## POSTER PRESENTATION – 30

### THE EFFECTS OF THE EXTRACTS OF GARLIC (*ALLIUM SATIVUM*) AND MUSHROOM (*LAETIPORUS SULPHUROUS*) ON BREAST CANCER CELLS

Fevziye E. Akman<sup>1</sup>, Pınar Alper<sup>2</sup>, Didem Karakaş<sup>2</sup>, Engin Ulukaya<sup>3</sup>, Keriman Günaydın<sup>1</sup>

<sup>1</sup> Istanbul University, Faculty of Science, Department of Molecular Biology and Genetics, Istanbul

<sup>2</sup> Uludağ University, Faculty of Science, Department of Biology, Bursa

<sup>3</sup> Istinye University, Faculty of Medicine, Department of Biochemistry, Istanbul

**Abstract Aim:** To investigate the effect of methanol extract obtained by maceration and soxhlet extraction of *Laetiporus sulphureus* and *Allium sativum* on apoptosis in human mammary cancer cell line.

**Methods:** Cytotoxicity was analyzed by sulforhodamine B (SRB) assays. The mode of cell death was evaluated morphologically using the fluorescence microscopy (Hoechst 33342 and Propidium iodide (PI) staining, flow cytometry (quantitative analysis of live, early/late apoptotic, dead cells and caspase 3/7 activity), biochemically using M30 ELISA assay and the RT-PCR. The genes analyzed with RT-PCR were BCL-2L10, BIK, BAX, BCL-2, FASLG, HRK, TNFRSF10B, and TNFRSF10A.

**Results:** *Laetiporus sulphureus* extract from Muğla region (100µg/mL) obtained by maceration method (LSMM) demonstrated anti-growth effect at 48 h in both human breast cancer cell lines MCF-7 and MDA-MB-231. The mode of cell death in cancer cells was shown to be apoptosis-like death cells due to the presence of early pyknotic nuclei, and PI positivity, increments in M30 and over expression of proapoptotic genes of HRK. The use of garlic extract of 100µg/mL and 200µg/mL was not established anti-growth effect.

**Conclusion:** These results suggest that LSMM both inhibits the proliferation of MCF-7 cells and induces apoptosis-like death of MCF-7 cells. This should be taken into account in its use for therapeutic purposes.

*Keywords: Allium sativum, Laetiporus sulphureus, breast cancer cells.*



## POSTER PRESENTATION – 31

### IRAK-4 rs4251481 GENE VARIANT IN INFLAMMATORY BOWEL DISEASE

Gonca Candan<sup>1</sup>, Resul Kahraman<sup>2</sup>, Ayhan Demir<sup>1</sup>, Arzu Ergen<sup>1</sup>

<sup>1</sup>Department of Molecular Medicine, Aziz Sancar Institute of Experimental Medicine, Istanbul University, Istanbul, Turkey.

<sup>2</sup>Umraniye Training and Research Hospital, Department of Gastroenterology, Istanbul, Turkey

**Background/Aim:** Crohn's disease and ulcerative colitis are inflammatory bowel diseases (IBD) that cause chronic inflammation and damage in the gastrointestinal tract. This abnormal immune response occurs in individuals have alleles associated with innate and adaptive immune mechanisms that predispose to IBD. IRAK-4 is involved in the pathway produces cytokines that initiate and maintain inflammation through Toll-like receptors and interleukin-1 receptors on the membranes of innate immune cells are stimulated with antigens. In this study it is aimed to investigate whether IRAK-4 rs4251481 polymorphism predispose to IBD and the possible effects of these polymorphisms by examining this gene polymorphism with clinic and prognostic parameters of IBD.

**Material and Methods:** Real-time PCR technique was used to detect IRAK-4 polymorphisms in 107 patients with IBD including 63 ulcerative colitis and 44 Crohn's disease and also 103 healthy controls.

**Results:** In the patient group, the frequency of occurrence of rs4251481 polymorphism related AG genotype ( $p=0,029$ ) and G allele ( $p=0,005$ ) was found to increase statistically compared with the control group. In the control group, the rs4251481 AA genotype rate of incidence increased compared with the patient group ( $p = 0.005$ ).

**Discussion:** These results suggest that the AG genotype and the G allele related with rs4251481 polymorphism are associated with increased IBD risk in patients. We did not find any correlation between rs4251481 and clinical parameters.

**Conclusion:** This is the first study in terms of both polymorphisms on IBD in our country.

Istanbul University Scientific Research Projects Unit supported this study. Project No: 59062

## POSTER PRESENTATION – 32

### **MICROTUBULE ASSOCIATED SCAFFOLD PROTEIN 1 (MTUS1) IS A CANDIDATE TUMOR SUPPRESSOR IN BREAST CANCER**

Ibrahim BOZGEYİK<sup>\*1,2</sup>, Ecir Ali Çakmak<sup>2</sup>, Abu Shameem Md Saadat Khandakar<sup>2</sup>, Mehri IGCİ<sup>2</sup>

<sup>1</sup>Adiyaman University, Faculty of Medicine, Department of Medical Biology, Adiyaman, Turkey

<sup>2</sup>University of Gaziantep, Faculty of Medicine, Department of Medical Biology and Genetics, Gaziantep, Turkey

**Background and Aim:** Growing mass of evidence indicates that *MTUS1* is highly down-regulated in a various types of cancer including breast, ovarian, pancreas, and colon cancers. Especially the *ATIP3a* and *ATIP1* transcript variants were shown to have important tumor suppressor functions in cells. On the other hand, expression levels of *MTUS1* were also reported to be up-regulated in some types of cancers such as prostate and lung cancers. Yet, these studies were limited in terms of the number of studies and cancer types included in these studies. Therefore, the current knowledge about the function of *MTUS1* in various cancers is very limited and some findings are conflicting with the tumor suppressor function of this gene. Accordingly, in this particular study, our aim was to show differential expression of *MTUS1* mRNA in various cancerous and normal cell lines.

**Materials and Methods:** Cell lines of MCF7, CRL-2329, MDA-MB-231, CRL4010 (American Type Culture Collection, VA, USA) were included in the study. To assess the expression levels of *MTUS1* gene both RT-PCR and qPCR methods were used.

**Results:** As a result of the RT-PCR and qPCR experiments, *MTUS1* gene was found to be differentially expressed. In particular, *MTUS1* was found to be down-regulated in breast cancer cells as compared to control cells. In fold change analysis, expression levels of *MTUS1* were found to be significantly down-regulated in MDA-MB-231 as compared to CRL-4010 normal breast epithelial cells. Also, *MTUS1* levels were significantly reduced in breast cancer cells (CRL-2329 and MDA-MB-231) as compared to CRL-4010 cells.

**Discussion:** In consistent with the previous findings, *MTUS1* expression levels were found to be down-regulated in breast cancer cells of MCF7, CRL-2329, and MDA-MB-231.

**Conclusions:** The findings of the current study strongly suggest that *MTUS1* may be involved in the development and progression of breast cancers.

*Keywords: ATIP, Cancer, Dual functions, MTUS1, MTSG1, Tumor Suppressor*

POSTER PRESENTATION – 33  
**THE EFFECT OF SHIKONIN ON A $\beta$ <sub>25-35</sub> INDUCED CELL CYTOTOXICITY AND  
OXIDATIVE INJURY IN PC12 CELL LINE**

Neslihan ÖZTAS<sup>1</sup>, Seyithan TAYSI<sup>1</sup>, Mehmet TARAKCIOGLU<sup>1</sup>

<sup>1</sup>Gaziantep University, Health Sciences Institute, Department of Medical Biochemistry Gaziantep

**Aim:** Alzheimer's Disease (AD) is a chronic neurodegenerative disorder characterized by progressive loss of memory. Although its etiology has not been fully explained, basic features seen in AD include the accumulation of extracellular amyloid plaques (AP) and formation of intracellular neurofibrillary tangles. Studies carried out on the human brain and in animals (*In vivo* and *in vitro*) show that oxidative stress plays an important role in the neurodegeneration observed in AD. Shikonin has been shown to have many positive effects such as anti-oxidant, anti-inflammatory, antithrombotic, antimicrobial, anticancer and wound healing properties. In this study, using the AD model induced with A $\beta$ <sub>25-35</sub> in the PC12 cell line, we aimed to investigate the potential protective effect of Shikonin against A $\beta$  toxicity and its resulting oxidative damage.

**Method:** The effects of A $\beta$ <sub>25-35</sub> and shikonin on PC12 cell viability were determined by MTT assay. To examine the effects of A $\beta$ <sub>25-35</sub> and Shikonin on oxidative stress, we analyzed the levels of superoxide dismutase (SOD), glutathione peroxidase (GSH Px), catalase and lipid peroxidation product, malondialdehyde (MDA) using Enzyme Linked Immunosorbent Assay (ELISA) method. Nitric oxide (NO) was colorimetrically analyzed by Griess method.

**Results:** On addition of 20 $\mu$ M shikonin, reduced cell viability noted with 5 $\mu$ M A $\beta$ <sub>25-35</sub> was significantly increased ( $p < 0.01$ ). Increased concentration of nitrite and MDA was observed with A $\beta$ <sub>25-35</sub>, decreased with addition of shikonin ( $p < 0.001$ ). Reduced level of SOD and GSH Px observed with A $\beta$ <sub>25-35</sub> increased on addition of shikonin ( $p < 0.05$ ). Similarly, reduced levels of catalase enzyme noted with A $\beta$ <sub>25-35</sub> increased on addition of shikonin ( $p < 0.001$ ).

**Conclusion:** Results obtained from this study reveal the positive effects of shikonin on neurotoxicity and oxidative damage in A $\beta$ <sub>25-35</sub>-induced AD model created *in vitro* in the PC12 cells. We therefore are of the opinion that shikonin may be a potential agent in preventing the cytotoxicity and oxidative damage induced by A $\beta$  (an important pathophysiologic mechanism in AD).

*Keywords: Alzheimer's Disease, Amyloid  $\beta$ , Oxidative stress, Shikonin.*

## POSTER PRESENTATION – 34

### EVALUATION OF microRNA-221/222 EXPRESSION LEVELS IN PATIENTS WITH CORONARY ARTERY IN ATHEROSCLEROTIC PLAQUE AND CIRCULATION

Aslıhan Esra Bildirici<sup>1</sup>, Serdal Arslan<sup>1</sup>, Nil Özbilum Şahin<sup>2</sup>, Sebahattin Göksel<sup>3</sup>, Mehmet Birhan Yılmaz<sup>4</sup>, Öcal Berkan<sup>3</sup>

<sup>1</sup>Department of Medical Biology, Cumhuriyet University, School of Medicine, 58140 Sivas, Turkey,

<sup>2</sup>Department of Molecular Biology and Genetic, Cumhuriyet University, Faculty of Science, 58140 Sivas, Turkey,

<sup>3</sup>Department of Cardiovascular Surgery, Cumhuriyet University, School of Medicine, 58140 Sivas, Turkey,

<sup>4</sup>Department of Cardiology, Cumhuriyet University, School of Medicine, 58140 Sivas, Turkey

Atherosclerosis is a kind of arteriosclerosis that affecting arteries and commonly referred to as “hardening of vein”. MicroRNAs (miRNAs) (19-25 nt) are a class of non-coding RNAs that regulates target gene sequence in posttranscriptional level and have a critical role in pathological and physiological processes such as cell proliferation, differentiation and apoptosis. MiR-221/222 are found in high levels in vascular smooth muscle cells and endothelial cells and are responsible for roles of cells in pathology of the disease. In this study, we aimed to investigate of the levels of microRNA-221/222 in coronary arter plaques and circulating during the atherosclerosis. In this study use of coronary artery plaques that obtained by coronary artery by-pass surgery for the first time and internal mammarian artery (IMA) tissue samples and the blood samples that are classified as the patient and control groups according to the result of angiography. Total RNA was isolated from samples and then expression levels of these miRNAs was measured using RT-PCR (Real Time Polymerase Chain Reaction). According to the results of expression analysis and statistical evaluation, expression of miR-221 has a statistically significant increase in coronary artery plaques compared IMA tissue (p=0,015). The fold change was found 8,94. It was observed that the expression of miR-222 increased 14,91 times in coronary artery plaques compared with IMA tissues, but no statistical significant could be determined (p=0,117). In contrast this, in analysis of blood samples both of the miRNAs were not found statistical significant (miR-221 p=0,139 and miR-222 p=0,080) but miR-221 is 6,22 times less expressed in patients group compared with control group and miR-222 is 5,19 times. Our results are consistent with studies on different tissues. The expression levels of these miRNAs are increased with the development of disease and thus, it is thought that miR-221/222 are involved in the progression of pathological processes. In our study, it has been found to reduce levels of miR-221/222 in the patient group compared to the control group, as in similar studies. Thought that increased expression levels of miR-221/222 can be an important factor in formation of coronary artery plaque and pathological process of disease. (Ethics Committee Decision No: 2015-03/62 - This study was supported by Cumhuriyet University Scientific Research Projects Commission, project number: T-641 and TÜBİTAK, project number: 214S031).

*Keywords: Atherosclerosis, Coronary Artery, miR-221, miR-222*

*Bilim kuruluna not: bu çalışma Cumhuriyet Üniversitesi Bilimsel Araştırma Projeleri Koordinasyon Birimi (proje no: T-641) ve TÜBİTAK (proje no: 214S031) tarafından desteklenmiştir.*

## POSTER PRESENTATION – 35

### INHIBITION OF TELOMERASE ENHANCES ENZALUTAMIDE THERAPY IN ANDROGEN-SENSITIVE PROSTATE CANCER CELLS

Karaca Kaan Geçgel<sup>2</sup>, Mustafa Müdüroğlu<sup>2</sup>, Suat Erdogan<sup>1</sup>

<sup>1</sup>Department of Medical Biology, School of Medicine, Trakya University, Balkan Campus, Edirne, Turkey

<sup>2</sup>Undergraduate students, School of Medicine, Trakya University, Balkan Campus, Edirne, Turkey

**Background/Aim:** Prostate cancer (PCa) is a leading cause of cancer related death in males, and androgen receptor (AR) antagonists such as enzalutamide are mainstay treatments for castration-resistant prostate cancer. PCa cells express high telomerase activity, and there is a direct correlation between the total amount of telomerase and the Gleason score. Therefore, we hypothesized that the combination of enzalutamide plus telomerase inhibitor is more effective than enzalutamide alone in inhibiting cancer cell survival.

**Materials and Methods:** In this study, androgen-sensitive human prostate cancer cell line LNCaP was used. The cell viability and IC<sub>50</sub> values of the agents were determined by MTT test. mRNA expressions associated with apoptosis, AR, prostate specific antigen (PSA) and telomerase were analyzed by RT-qPCR. Cell cycle progression and image based apoptosis evaluations were determined by an image-based cytometer. The cells were treated with 5  $\mu$ M enzalutamide and 40  $\mu$ M telomerase inhibitor BIBR1532 for 72 h.

**Results:** Enzalutamide and BIBR1532 alone inhibit cell proliferation in a dose-dependent manner, and enzalutamide in combination with the telomerase inhibitor significantly increased the cytotoxic effects at IC<sub>50</sub> values. Combination therapy induced cell death and apoptosis to a significantly greater extent than treatment with either agent alone. Enzalutamide and BIBR1532 significantly inhibited cell growth by blocking transition at the G1 phase, though combining the two drugs did not enhance the cell cycle arrest activity of the individual agents. Combine therapy decrease androgen receptor and PSA expressions in the cells.

**Discussion:** It has been demonstrated that BIBR1532 induced a direct cytotoxic effects in leukemia and breast cancer cells. Our results showed for the first time that telomerase inhibition therapy may contribute to the efficacy of enzalutamide in the CRPC model.

**Conclusion:** These results suggest combination of BIBR1532 and enzalutamide could be a novel therapeutic strategy for AR-sensitive prostate cancer that may be clinically accessible in the near future.

*Keywords:* BIBR1532, enzalutamide, prostate cancer, telomerase, LNCaP cells

*Acknowledgments:* This study was supported by a grant from The Scientific and Technological Research Council of Turkey (project no: 2209/A-2015 to KKG and MM).

## POSTER PRESENTATION – 36

### INVESTIGATION OF CIRCULATING EXPRESSION LEVELS miR31 and miR204 IN CORONARY ARTERY DISEASE

<sup>1</sup>Nil ÖZBİLÜM ŞAHİN, <sup>2</sup>Serdal ARSLAN, <sup>3</sup>Eylem İtr AYDEMİR, <sup>4</sup>Osman BETON, <sup>1</sup>Ali Fazıl YENİDÜNYA

<sup>1</sup>Department of Molecular Biology and Genetics, Faculty of Science, Cumhuriyet University, Sivas, Turkey

<sup>2</sup>Department of Medical Biology, Faculty of Medicine, Sivas, Turkey

<sup>3</sup>Department of Statistic, Faculty of Science, Cumhuriyet University, Sivas, Turkey

<sup>4</sup>Department of Cardiology, Faculty of Medicine, Cumhuriyet University, Sivas, Turkey

Coronary artery disease is an inflammatory disease, that leading to cause of cardiovascular morbidity and death worldwide. The most common cause of CAD is atherosclerosis of coronary arteries. MicroRNAs (miRNAs) are a class of noncoding RNAs that regulate target gene expression at the posttranscriptional level. miRNAs are an small non-coding RNAs, and play a crucial role in several physiological and pathological processes, including cell proliferation, differentiation, and apoptosis. Several miRNAs are involved in the modulation of endothelial dysfunction, which inhibits a number of pro-inflammatory genes in ECs such as VCAM-1, E-selectin. Circulating miRNAs have enormous potential as novel disease biomarkers, since differential plasma miRNA profiles have been described for atherosclerosis. The aim of this study was to investigate miR-31 and miR-204 expression levels in circulation of patient with atherosclerosis first study comparing these circulating microRNAs in the world. Blood samples were obtained after all participants provided informed written consent. Collected tissue samples were immediately transferred into Qiagen PAXGene Tube. Total RNA was isolated from 88 blood samples from patient and controls. The expression levels of miR31 and mir204 RNAs that suspected to be associated with cardiac pathology were measured using qRT-PCR. Analysis of data was performed using  $\Delta\Delta C_T$  methods. Although we have not any statistical significant difference miR31 and miR204 expression level ( $p=0.12$  and  $p=0.37$ , respectively), mir31 expression level was decreased approximately 4-times (Fold change=3.74) and miR204 expression level was decreased approximately 1.5-times (Fold change=1.37). miR31 is important in regulation of vascular cell adhesion molecules. miR31 has an important role in inflammatory disease and is downregulated especially inflammatory disease. miR204 have important role in STAT-3 signaling pathway and this micro RNA have found downregulated, as we found, especially arterial disease, like pulmonary arterial hypertension. In conclusion, these results showed that miR204 and miR31 have important role pathogenesis of coronary artery disease. This project supported by Research Council of Cumhuriyet University (Project No:F-456) (Ethical committee file number: 2015-05/07)

*Keywords: Atherosclerosis, miR-31, miR-204, microRNA expression*

*Bilim kuruluna not: Proje Cumhuriyet Üniversitesi Bilimsel Araştırma Proje Başkanlığı tarafından desteklenmektedir. Proje No: F-456*

## POSTER PRESENTATION – 37

### AN EFFECTIVE DIETARY SUPPLEMENT AGAINST IMAZALIL INDUCED GENOTOXIC DAMAGE IN HUMAN LYMPHOCYTES: ALPHA-LIPOIC ACID

Hasan TÜRKEZ<sup>1</sup>, Özlem ÖZDEMİR<sup>1</sup>, Abdulgani TATAR<sup>2</sup>

<sup>1</sup>Department of Molecular Biology and Genetics, Faculty of Science, Erzurum Technical University, Erzurum, Turkey

<sup>2</sup>Department of Medical Genetics, Faculty of Medicine, Ataturk University, Erzurum, Turkey

**Background / Aim:** Alpha-lipoic acid (LA; 1,2-dithiolane-3-pentanoic acid), a naturally occurring compound, has great potential due to its significant biological functions. It has been used for improving many diseases including neurological, cardiovascular and diabetic disorders due to its antioxidant nature. On the other hand, the fungicide imazalil (IMA) is extensively used for protecting vegetable and fruit fields in agricultural and also for clinical purposes. In recent, IMA was shown to present both mutagenic and teratogenic potentials. Therefore, the objective of the present in vitro study was to assess the role of LA in preventing the genotoxic damage by IMA on human whole peripheral blood cell cultures (n=3)

**Materials and Methods:** For this aim, the cultures were treated with LA, IMA and their combinations (LA: 25, 50 and 100  $\mu$ M; IMA: 336) and incubated with them for 72 h. The micronucleus (MN) and chromosome aberration (CA) assays were performed for evaluating genotoxicity/anti-genotoxicity.

**Results:** IMA was shown to induce genotoxic damage in cultured human lymphocyte cells via causing the increased MN and CA frequencies. Moreover the present results showed that LA applications significantly reduced IMA-induced DNA damage in a clear dose dependent manner.

**Discussion:** Our results indicate that LA provides a significant protection against IMA-induced DNA damage in vitro

**Conclusion:** In a summary, we suggest that LA is considered as safe in genetically and it can be used as an effective supplement to protect human populations exposed to chemical or environmental hazards.

*Keywords: Anti-genotoxicity, Human lymphocytes, Imazalil, Protective agent, Natural antioxidants*

## POSTER PRESENTATION – 38

### **BRAIN BIOCHEMISTRY AND GUT MICROBIOTA (GM) INFLUENCED BY ANTIBIOTIC TREATMENT DURING ADOLESCENCE PERIOD OF MICE**

Taha Ceylani<sup>1,2</sup>, Rafiq Gurbanov<sup>3</sup>, Hikmet Taner Teker<sup>1</sup>, Ewa Jakubowska-Doğru<sup>1</sup> and Ayse Gul Gozen<sup>1</sup>

<sup>1</sup>Department of Biological Sciences, Middle East Technical University, 06800, Ankara, Turkey

<sup>2</sup>Department of Molecular Biology and Genetics, Muş Alparslan University, 49250, Muş, Turkey

<sup>3</sup>Department of Molecular Biology and Genetics, Bilecik Şeyh Edebalı University, 11230, Bilecik, Turkey

**Background:** Although microbiology and neuroscience have developed historically as separate fields, recent studies show that microbiota; especially within the gut have great influence on brain biochemistry in general. However, there are still few studies examining the cumulative effect of repeated antibiotic administration in childhood on the brain status and behavior at the adult age. Particularly, we tried to determine the impact of gut microbiota (GM) perturbed by antibiotics during childhood on brain biochemistry in adults.

**Material and Methods:** In this study 21 days old male Balb/C mice was used. For the disruption of gut microbiota two broad spectrum antibiotics have been treated (ampicillin and cefoperazone 1g/l) in place of drinking water for 6 weeks to perturb the GM. At the end of antibiotic treatment period brain derived neurotrophic factor (BDNF), N-methyl-D-aspartate receptor (NMDA) glutamate receptor subunits NR2B, serotonin receptor 5-HT1A and corticosterone concentrations were measured from mice blood serum using Enzyme-Linked Immune Sorbent Assay (ELISA) based assays. In addition, GM analysis was performed by using denaturing gradient gel electrophoresis system (DGGE).

**Results:** GM profile shift was observed between untreated and antibiotic-treated mice. GM composition mostly perturbed by ampicillin treatment. Serum level of BDNF was higher in cefoperazone treated group compared to other antibiotic regimes. NR2B levels did not changed between control and antibiotic treated groups, however its concentration in ampicillin treated group was significantly higher compared to cefoperazone treated group. There is no significant differences between control and antibiotic treated groups for serum levels of serotonin receptor (5-HT1A) and corticosterone.

**Discussion:** It is obviously can be realized that, the use of antibiotics during childhood and fluctuation of GM have role to determine the level of cognitive abilities and also affects brain biochemistry by taking role in the expression of related neurotransmitters.

**Conclusion:** The findings of our study indicated GM alteration and overuse of antibiotics during childhood have role on brain plasticity during its development. Other important neurotransmitters which are indicators for cognition are influenced. The effect of these biochemical changes show their effect on behaviour in adult. Interplay between neurotransmitter changes and GM profile requires further investigations.

*Keywords: Gut microbiota, DGGE, Brain biochemistry, BDNF, 5-HT1A, NR2B, Corticosterone*  
*Ethics Committee's approval number: 49783314-/32 (Ankara University)*



## POSTER PRESENTATION – 39

### INVESTIGATION OF ANTIBACTERIAL PROPERTIES BY ADSORPTION SILVER TO 4-VINYL PYRIDINE MONOMER GRAFTED POLY(ETHYLENE TEREPHTHALATE) FIBER

<sup>1</sup>Emine YAGCI, <sup>2</sup>Ogun BOZKAYA, <sup>3</sup>Mustafa YIGITOGU

<sup>1</sup>Eskisehir Osmangazi University Medical Faculty, Department of Medical Biology, Eskisehir

<sup>2</sup>Kırıkkale University, Scientific and Technological Research Laboratories, Kırıkkale

<sup>3</sup>Kırıkkale University, Faculty of Engineering, Department of Bioengineering, Kırıkkale

Silver known for its heavy metal properties has an important effect on the cellular pathways. Silver metal releases silver ions when it reacts with water. These ions destroy the metabolism of the bacterium, prevent cell proliferation and cause apoptosis by reacting with the sulfhydryl groups of the selective enzymes or with the nucleic acids in the cell. It can also cause cell death by reacting with dissolved oxygen in water and producing reactive oxygen. Therefore, investigation of the antibacterial activity of silver ions is located between current researches in biotechnology. We planned to investigate the efficacy of silver adsorbed fiber on bacterial proliferation in our study.

For this purpose, 4-vinyl-pyridine (4-VP) was grafted on poly (ethylene terephthalate) (PET) fibers and then adsorption of silver ions was performed. The antibacterial properties of the synthesized fibers were investigated by using optimal values for the adsorption of Ag (I) ion. *Staphylococcus aureus* ATCC-29213, *Pseudomonas aeruginosa* ATCC-27853 and *Escherichia coli* ATCC-25922 bacteria were used for antibacterial characterization studies. Bacteria were cultured on solid medium, and silver adsorbed fibers were placed on as a disk. It has been determined that the discs have antibacterial properties by looking at the zones formed around the discs placed in the medium. PET fiber, 4-VP grafted PET fiber, 4-VP grafted and silver adsorbed PET fiber discs were placed in a solid medium and their antibacterial properties were compared. In addition to the discs prepared in the media, antibiotic discs acting on bacteria were also placed and compared in terms of zone diameters.

When the zone diameters which formed of PET fibers on the solid medium were compared, it was determined that silver was most effective on *S. aureus* bacteria. *S. aureus* was cultured in the liquid medium and fibers which adsorbed Ag (I) at different concentrations were put in the liquid medium. It was found that silver has antibacterial activity and the antibacterial activity was increased as the silver concentration increased by looking growth curve in the liquid medium.

It is considered that 4-VP-grafted and silver-adsorbed PET fibers may be used as surgical threads in hospitals. This material, which has antibacterial properties, can be a tool to minimize the infections after surgery. The antibacterial effect of silver on *S. aureus*, which causes hospital infection in particular, is promising for use in hospital supplies and will enable the production of new biotechnological materials in the medical field.

*Keywords: Silver, Antibacterial activity, Bacterial proliferation.*

## POSTER PRESENTATION – 40 SYNERGISTIC EFFECT OF 4-AMINOPYRIDINE AND PACLITAXEL ON MDA-MB 231 BREAST CANCER CELL LINE

Esra M. Cüce Aydoğmuş<sup>1</sup>, Ayşe İnhan Garip<sup>1</sup>

<sup>1</sup>Marmara Uni. School of Medicine, Biophysics Dep. İstanbul, Turkey

Paclitaxel (PTX) is an antineoplastic agent that induces arrest at G2/ M phase and has been widely used in chemotherapy. However its use is limited due to its side effects at therapeutic doses. On the other hand it has been shown that pharmacological or genetic block of potassium Kv channels reduces proliferation. 4 aminopyridine (4-AP) is a K<sup>+</sup> blocking agents in use in neurological diseases and its use for cancer treatment is being considered.

This study aimed to determine whether 4-AP would enhance the antiproliferative effect of PTX on MDA –MB 231 breast cancer cell line.

MDA –MB 231 cells were grown in DMEM supplemented with 10% FBS, 2 mM L glutamine and 100 U penicillin/streptomycin in 5% CO<sub>2</sub> at 37 °C. Cells were seeded at 10<sup>5</sup> cells/ well into a 6 well plate and incubated overnight. Cells were incubated with 4- AP or PTX or both for 24 hours and cells were counted by trypan blue on hemocytometer. Beforehand a titration was made to determine IC 50 values for both agents and values lower than IC 50 values were chosen.

MDA- MB 231 cells were incubated with low concentration (5 nM, 10 nM) of PTX for 24 hours. A reduction by 5 nM 20% ±2, 10 nM 41%±3 in cell viability was detected. Incubation with 4 mM and 5 mM concentrations of 4- AP for 24 hours caused 4 mM 35 % ±3, 5 mM 45% ± 2 reduction in cell viability. Application of both agents caused a decrease in viability of about 80% ± 5 indicating the enhancement of paclitaxel activity.

PTX and 4-AP block the cell cycle at different stages at G2/M and G1/S respectively. The effect of both agents blocking the cell cycle at different stages caused a significant decrease in viability. Since 4- AP causes a change in membrane potential (depolarization) the results also show that membrane potential is an important factor that would probably enhance (or decrease) the effectiveness of chemotherapeutic agents.

There is a need for alternative methods to increase the effectiveness of paclitaxel to be able to reduce the side effects. This work showed that 4- AP can be used synergistically with PTX to decrease the viability of breast cancer cells.

*Keywords: 4- aminopyridine, paclitaxel, MDA- MB 231 breast cancer cell line.*

## POSTER PRESENTATION – 41

### LncRNA CCAT1 MAY HAVE A ROLE IN OSTEOSARCOMA AND LUNG CANCER

Meltem Koruk Ozer<sup>1</sup>, Yunus Sahin<sup>1</sup>, Zekiye Altan<sup>1</sup>, Kaiffee Arman<sup>1</sup>, Sibel Oguzkan Balci<sup>1</sup>

<sup>1</sup>Faculty of Medicine, Department of Medical Biology, University of Gaziantep, Gaziantep, Turkey

**Background/Aim:** Cancer is a major health problem and one of the leading causes of death in the world. Despite extensive researches about molecular mechanism of cancer, knowledge of cancer progression, prognosis and diagnosis is still insufficient. Recent studies have revealed that long non-coding RNAs (lncRNAs) are involved in various stages of cancer development. CCAT1 is a lncRNA which was first discovered in colorectal cancer. Recent studies have indicated that CCAT1 might play roles in the initiation and progression of breast, gastric, gall bladder and pancreatic cancer. In this study, determining gene expression of CCAT1 in normal tissues and different cell lines was aimed.

**Materials and Methods:** For the tissue expressions analysis, Human Total RNA Master Panel II (containing 18 different human tissue samples) was used. Total 10 cancer cell lines and 2 normal cell lines were included in this study. For the expression analysis, RT-PCR and qPCR methods were used.

**Results:** As a result, expression level of CCAT1 among the tissues was found highest in fetal liver tissue but low in liver tissue. CCAT1 was highly expressed in stomach tissue after fetal liver tissue. However, CCAT1 expression was not observed in heart, brain, fetal brain, placenta, skeletal muscle and spleen tissues. CCAT1 was also found to be differentially expressed in other cancer cell lines. It was highly expressed in U-2 OS, A549 and HCT-116 cell lines while its expression level was observed low in prostate and breast cancer cell lines.

**Discussion:** Overexpression of CCAT1 in fetal liver tissues showed that it might have a role in hematopoiesis during mammalian prenatal development while low expression of CCAT1 in liver tissue further confirmed its role to be only in fetus. CCAT1 was highly expressed in osteosarcoma cell line (U-2 OS) and lung cancer cell line (A549). However, its expression was lost in osteoblast cell line (hFOB 1.19) and low in normal lung tissue. These results show that CCAT1 might have a role in lung cancer and osteosarcoma.

**Conclusion:** Results of this study confirmed that CCAT1 acts as an oncogenic lncRNA. In conclusion, CCAT1 can be a regulator lncRNA in mammalian prenatal development and also initiation and progression of osteosarcoma and lung cancer.

*Keywords: CCAT1, lncRNA, osteosarcoma, lung cancer,*

## POSTER PRESENTATION – 42

### **DETERMINATION OF THE EFFECT OF IGF1 AND FBLN5 PROMOTER VARIANTS ON THE FORMATION OF URINARY INCONTINENCE IN POST-AND PREMENOPAUSAL WOMEN**

Hani Alsaadoni<sup>1</sup>, Burcu Çaykara<sup>1</sup>, SadrettinPençe<sup>2</sup>, Emin Özbek<sup>3</sup>, Alper Ötünçtemur<sup>4</sup>

<sup>1</sup> Istanbul University, Aziz Sancar Institute of Experimental Medicine (ASDETAE), Department of Molecular Medicine, Istanbul

<sup>2</sup> University of Health Sciences, Faculty of Medicine, Department of Physiology, Istanbul

<sup>3</sup> Istanbul Research and Education Hospital, Department of Urology

<sup>4</sup> Okmeydani Education and Research Hospital, Department of Urology

**Background:** Urinary Incontinence (UI) is defined by the International Continence Society (ICS) as a waste of power, exercise, sneezing or coughing. It is a social problem which are frequently seen especially middle age and older age group, reduces the quality of life of the patients can indirectly affect the environment. In studies carried out until today have determined that a variety of genetic factors have increased the susceptibility to the UI. Genetic variations that especially affect muscle and connective tissue structure have been shown to cause the susceptibility stress type urinary incontinence. We aimed to find out any possible relation between IGF1 and FBLN5 promoter variants and urinary incontinence

**Material-Method:** The study consisted of 4 groups: 43 premenopausal women with UI as a patient group and 30 premenopausal women without disease as a control group, 43 postmenopausal women with UI as a patient group and 30 postmenopausal women without disease as a control group. DNA was isolated from blood samples, purity determinations were made, and DNA quantities were calculated. Polymerase chain reaction was used to obtain the desired amplicon and Illumina®MiSeq was sequenced using the next generation platform and chemicals by following up the manufacturer's protocols. The results were analyzed as statistically by Fisher Exact Test.

**Results:** As a result of all the comparison tests, no significant difference ( $p < 0.05$ ) was found between the groups. The A>G variant of rs6214 was found 5.26% (2/38) in the patient group and 0% (0/30) in the control group ( $p = 0.308$ ) of the premenopausal group. The A>G variant of rs6214 was found 2.44% (1/41) in the patient group and 0% (0/30) in the control group ( $p = 0.308$ ) of the postmenopausal group. Compared with total urinary incontinence patient and total control; in the patient group rs6214 was found 3.79% (3/79), but this variant was not found in the control group ( $p = 0.197$ ). The FBLN5 rs929608 variant was not found in any group.

**Discussion:** We report here the first analysis of FBLN5 rs929608 and IGF1 rs6214 in urinary incontinence. We didn't find any relation between that genes and urinary incontinence. However, Cao Q and his colleagues found rs6214 significantly decreased in renal cell carcinoma findings (OR = 0.65, 95% CI = 0.45-0.86).

**Conclusion:** No significant difference ( $p < 0.05$ ) was found between urinary incontinence and variants.

*Keywords: Urinary incontinence, rs6214, IGF1, FBLN5*

*Note to the Scientific Committee: This work was supported by Istanbul University Scientific Research Projects Unit (BAP project number: 2181).*

*Ethics Committee's approval number: 2014/921*

## POSTER PRESENTATION – 43 ANALYSIS OF CLUSTERIN AND BACE1 GENE EXPRESSION LEVELS IN ALZHEIMER'S DISEASE

Hani Alsaadoni<sup>1</sup>, Burcu Çaykara<sup>1</sup>, Sadrettin Pençe<sup>2</sup>, Saffet Tüzgen<sup>3</sup>

<sup>1</sup> Istanbul University, Aziz Sancar Institute of Experimental Medicine (ASDETAE), Department of Molecular Medicine, Istanbul

<sup>2</sup> University of Health Sciences, Faculty of Medicine, Department of Physiology, Istanbul

<sup>3</sup> Istanbul University, Cerrahpasa Medical Faculty, Department of Neurosurgery, Istanbul

**Background:** Alzheimer's disease (AD) is a neurological disorder and is the most common pathology among age-related dementia. At the present time a differential AD diagnosis can only be performed with a postmortem histopathological analysis intandem with a clinical diagnosis. However actual neurodegenerative process begins 20-30 years prior to first clinical symptoms. Defining of a marker present in blood will facilitate to produce a therapeutic procedure at the onset of neurodegenerative process. Clusterin is chaperon protein, which is induced and released under cellular stress. It can be transported to cytoplasm and inhibit neuronal apoptosis by binding Bax protein. These features suggest a preventive effect for his protein. BACE1 is a dimerising aspartic-acid protease functioning in the formation of myelin sheath of peripheral neurons. We aimed to determine the association of BACE1 and Clusterin gene expression with Alzheimer's disease.

**Material and Methods:** In the study, total 68 samples, 34 Control and 34 Alzheimer patients, were included. Total RNA isolation from blood samples was performed with "QiagenRNeasy Mini Kit" and the RNA samples were measured with the "NanoDrop 2000c" spectrophotometer. cDNA synthesis was performed with the 'SensiFASTcDNA synthesis kit'. The qPCR reaction mix was prepared with the 'SensiFAST SYBR® No-ROX kit'. GAPDH was used as housekeeping gene.

**Results:** Gene expressions were calculated according to the  $\Delta\Delta C_t$  method. The Clusterinand BACE1 gene was found 10.37-fold and 5.9-fold expressed in the blood of AD group than controls, respectively.

**Discussion:** We found that CLusterin gene was more highly expressed in patients with Alzheimer's disease. In a study of post-mortem brain tissue, increased BACE1 gene expression was observed in Alzheimer's patients (Chen and et al., 2012). Additionally, we found that the BACE1 gene was more highly expressed in Alzheimer's patients blood.

**Conclusion:** Our study showed that the blood mRNA levels of the BACE1 gene and the Clusteringenewere associated with Alzheimer's disease. Many studies have emphasized the importance of plasma values of these proteins and their strategic importance for treatment has been addressed. Our findings are compatible with these studies, but more extensive investigations should be done for more reliable results.

*Keywords: Alzheimer's disease, BACE1, Clusterin, Gene expression*

*Note to the Scientific Committee: This work was supported by Istanbul University Scientific Research Projects Unit (BAP project number: 450).*

## POSTER PRESENTATION – 44 UNDERSTANDING THE HEME ENVIRONMENTS OF NITRIC OXIDE SENSING PROTEINS

Joana Efua Aggrey-Fynn<sup>1</sup>, Nur Başak Sürmeli<sup>2</sup>

<sup>1</sup>Moleküler Biyoloji ve Genetik Bölümü, İzmir Yüksek Teknoloji Enstitüsü, Gülbahçe Köyü, Urla 35430 İzmir, Türkiye

<sup>2</sup>Biyomühendislik Bölümü, İzmir Yüksek Teknoloji Enstitüsü, Gülbahçe Köyü, Urla 35430 İzmir, Türkiye

**Introduction / Aim:** Nitric oxide (NO) signalling pathway is involved in smooth muscle proliferation, vasodilation, neurotransmission, leukocyte recruitment, and platelet aggregation. Their function is mediated through the soluble guanylate cyclases (sGC) by the synthesis of cGMP. A dysfunction in this pathway contributes to the pathology of cardiovascular and pulmonary diseases such as atherosclerosis, pulmonary and arterial hypertension, heart failure, and peripheral vascular disease. Although, there have been extensive biochemical studies, their explicit molecular mechanisms remain elusive. With the aim of understanding their biochemistry, three mutations were made within the heme-containing sensor domain of the heme-nitric oxide/oxygen binding (H-NOX) from *Thermoanaerobacter tengcongensis*, a heme protein homologous to sGC.

**Materials and Methods:** The Q5 Site Directed Mutagenesis Kit was used to create the desired mutations in the wild type H-NOX DNA. Plasmids were transformed into DH5 $\alpha$  competent cells and grown on ampicillin plates for cloning. Plasmids were purified using commercial DNA purification kits and sequenced. Expressions were done in BL21 (DE3) *E. coli*. After large scale expression, protein extractions and purifications were performed using the Gravity-flow Column with HisPur Ni-NTA Resin. UV spectroscopic measurements, between 250 - 650 nm, were performed on all the purified proteins.

**Results:** Sequence analysis confirmed all mutations. The variants had different physical properties and yields. The proximal ligand variants: histidine-102 to cysteine and tyrosine (H102C and H102Y) experienced intense Soret band shifts from 415 nm for the wild type to 405 nm. This is interpreted to be due to changes in ligation and bond cleavage. The distal pocket variant; tyrosine-140 to alanine (Y140A), had a shift to 409 nm due to changes in oxidation state and stable complex formations.

**Discussion:** The morphological and spectroscopic differences of all the variants and wild type suggest a change in structure and function. These changes could provide further insights into the molecular and biological roles that these amino acids have on heme proteins. They also provide a better understanding on how the changes in ligation could be optimized and fine-tuned for the development of drugs and antidotes for medicine.

**Conclusion:** The cloning of the homologous sGC protein, H-NOX variants were successful with clear changes that could affect structure and function. Therefore, this study will help in understanding molecular details of nitric oxide signalling.

*Keywords:* Heme proteins, nitric oxide signalling, soluble guanylate cyclase, site directed mutagenesis

*Note to the Scientific Committee:* This project is supported by TUBITAK grant 115C134.

## POSTER PRESENTATION – 45

### ANALYSIS OF GCK-MODY (MODY2) GENE POLYMORPHISM ON Chr.7:44149424 IN CORONARY ARTERY DISEASE PATIENTS

Dilara Aydemir<sup>1</sup>, Ezgi Yalbir<sup>1</sup>, Tuğçe Gül<sup>1</sup>, Emre Murat Altıncılıç<sup>1</sup>, Seda Güleç Yılmaz<sup>1</sup>, Selim İsbir<sup>2</sup>, Atike Tekeli Kunt<sup>3</sup>, Orhan Fındık<sup>3</sup>, Turgay İsbir<sup>4</sup>

<sup>1</sup>Department of Molecular Medicine, Institute of Health Sciences, Yeditepe University, Istanbul, Turkey

<sup>2</sup>Department of Cardiovascular Surgery, Marmara University, Istanbul, Turkey

<sup>3</sup>Department of Cardiovascular Surgery, Kocaeli Derince Education and Research Hospital, Kocaeli, Turkey.

<sup>4</sup>Department of Medical Biology, Faculty of Medicine, Yeditepe University, Istanbul, Turkey

Diabetes mellitus results from production of inadequate insulin or damage of insulin producing cells of the pancreas. Because endothelial cell, vascular smooth muscle dysfunction, impaired platelet function and abnormal coagulation occurs in Diabetes mellitus, it shows high prevalence in patients with coronary artery disease which is one of the major reasons of death. MODY 2 is a form of Type 2 maturity onset diabetes of the young. It occurs because of mutation in the GCK gene on chromosome 7 encoding glucokinase enzyme. The effect of MODY2 (T>C) gene polymorphisms and HDL and LDL subfraction were investigated on coronary artery disease patients. Genotyping of MODY2 (rs2268576) polymorphism was performed using real-time polymerase chain for blood samples of patients who have coronary artery disease (n=25) and controls (n=25). Statistical analysis was performed by SPSS. The frequency of the CT heterozygote genotype was found to be significantly higher in patients and genotype had a ~4-fold increased risk (p= 0,011; Odds Ratio [OR]= 4,571; 95% Confidence Interval [CI]= 1,383 - 15,109). Small LDL was higher than in the control group (p= 0,013; 95% Confidence Interval [CI]= (-10,642)-(-1,294)), whereas small HDL was found to be higher in the control group (p=0.001; 95% Confidence Interval [CI]=1,592 - 5,368). According to recent studies, there has been found the relationship between MODY and coronary artery disease. In our study, CT heterozygote genotype significantly increases the risk. In addition, studies state that whereas small dense LDL has an atherogenic effect, small dense HDL reverses the oxidation effect of small dense LDL. The findings in our study show that small dense LDL increases the risk and small dense HDL decrease the risk. While there was no significantly relation between TT and CC genotypes and the disease, CT was seemed to be associated with higher risk of pathological stage.

*Keywords: Coronary artery disease; type II diabetes mellitus; MODY2; glucokinase (GCK); polymorphism.*

## POSTER PRESENTATION – 46

### EFFECTS OF GCK-MODY (MODY2) GENE POLYMORPHISM ON Chr.7:44163407 IN PATIENTS WITH CORONARY ARTERY DISEASE

Ezgi Yalbir<sup>1</sup>, Dilara Aydemir<sup>1</sup>, Tuğçe Gül<sup>1</sup>, Seda Güleç Yılmaz<sup>1</sup>, Selvi Duman<sup>1</sup>, Selim İsbir<sup>2</sup>, Atike Tekeli Kunt<sup>3</sup>, Orhan Fındık<sup>3</sup>, Turgay İsbir<sup>4</sup>

<sup>1</sup>Department of Molecular Medicine, Institute of Health Sciences, Yeditepe University, Istanbul, Turkey

<sup>2</sup>Department of Cardiovascular Surgery, Marmara University, Istanbul, Turkey

<sup>3</sup>Department of Cardiovascular Surgery, Kocaeli Derince Education and Research Hospital, Kocaeli, Turkey.

<sup>4</sup>Department of Medical Biology, Faculty of Medicine, Yeditepe University, Istanbul, Turkey

Coronary artery disease (CAD) is caused by atherosclerotic plaques formation on the walls of coronary arteries. Recent studies show the relation between diabetes and CAD. In this study, we investigated MODY2 (T>C) gene polymorphism in CAD patients and control group. MODY2, maturity-onset diabetes of the young type 2, is caused by mutation in the glucokinase (GCK) gene. In addition, the effects of LDL and HDL sub-fractions on CAD were investigated. Genotyping of MODY2 (rs758989) polymorphism were performed by using real time polymerase chain reaction (QPCR) for blood samples of coronary artery disease patients (n=25) and control group (n=25). There were significant differences for MODY2 (T>C) genotypes between CAD patients and controls. The frequency of TT homozygote genotype was found to be significantly lower (odds ratio (OR)=0.242, 95% Confidence Interval (CI)=0.056-1.040 ; p=0.047), whereas CT heterozygote genotype was found to be significantly higher in CAD patients compared to control group (odds ratio (OR)=3.160, 95% Confidence Interval (CI)=0.996-10.031; p=0.048). In addition, the MODY2 (rs758989) C allele was higher in CAD patients (odds ratio (OR)=4.125, 95% Confidence Interval (CI)=0.961-17.704; p=0.047). Also, according to the demographic characteristics of CAD and controls, CAD patients has significantly higher levels of small density LDL (p=0.013), and lower levels of small density HDL (p=0.001). Recent studies indicate that the coronary artery disease is correlated with diabetes. Our study shows that while wild type (TT homozygote genotype) has a protective role, CT heterozygote genotype is a risk factor in patients with coronary artery disease. Besides, according to reports, small dense LDL (sdLDL) increase the risk of coronary artery disease because of oxidation, small dense HDL (sdHDL) has potent antioxidative activity. sdLDL was found to be significantly higher in patients, whereas sdHDL was found to be significantly lower in patients. MODY2 (T>C) polymorphism, having heterozygote mutant genotype (CT), might increase the risk for coronary artery disease.

*Keywords: Coronary artery disease, diabetes, MODY2, glucokinase (GCK), polymorphism, small dense LDL, small dense HDL*



## POSTER PRESENTATION – 47

### THE POLYMORPHISM IN THE GLUCOKINASE GENE IS ASSOCIATED WITH OVARIAN CANCER

Selvi Duman<sup>1</sup>, Seda Güleç Yılmaz<sup>1</sup>, Rukset Attar<sup>2</sup>, Ahmet Büyükören<sup>3</sup>, Emre Murat Altıncılıç<sup>1</sup>, Hüseyin Ayhan<sup>1</sup>, Zerrin Barut<sup>1</sup> and Turgay İsbir<sup>4</sup>

<sup>1</sup>Department of Molecular Medicine, Institute of Health Sciences, Yeditepe University, Istanbul, Turkey;

<sup>2</sup>Department of Obstetrics and Gynecology, Faculty of Medicine, Yeditepe University, Istanbul, Turkey;

<sup>3</sup>Department of Obstetrics and Gynecology, Faculty of Medicine, Istanbul University, Istanbul, Turkey;

<sup>4</sup>Department of Medical Biology, Faculty of Medicine, Yeditepe University, Istanbul, Turkey

Ovarian cancer is the most common cause of cancer death from gynecologic cancers and most patients are diagnosed at advanced stage of ovarian cancer. Glucokinase plays a key role in glucose homeostasis. Glucokinase gene (c.47702T>C, intron 6) polymorphism is located in a putative splicing region and it may effect GCK activity. The aim of this study is to investigate the effects of GCK gene (c.47702T>C, intron 6) polymorphism on ovarian cancer. This case-control study was consisted 30 women with ovarian cancer and 30 healthy control group. Thirty histologically confirmed patients who have ovarian cancer were diagnosed and followed up in Yeditepe University Hospital and Istanbul University, Department of Obstetrics and Gynecology. Thirty healthy control subjects were carefully chosen not to have ovarian cancer. Blood specimens protected with EDTA were taken from all the study subjects. Genotyping of Glucokinase gene (c.47702T>C, intron 6) polymorphism was performed using real-time polymerase chain for blood samples of patients and controls. Statistical analysis was performed by SPSS Version 22 statistic software package. There was no statistical significance between the ages of patient and control groups, mean of age were  $49,80 \pm 8,79$  and  $49,13 \pm 8,39$ , respectively ( $p=0.765$ ). Body Mass Index, Fasting Blood Glucose level were significantly higher in ovarian cancer group compared to the control cases ( $p=0.001$ ,  $p=0.004$ ). In addition, postmenopausal status were noticeably higher ( $p<0,001$ ) in cancer group (76,7%) than control group (30%). There were no a significant difference for GCK (c.47702T>C, intron 6) genotypes between patient and control groups ( $\chi^2=3,571$ ;  $p=0.168$ ). GCK (c.47702T>C, intron 6). The frequency of G allele was significantly higher in the control group ( $p=0,020$ ,  $\chi^2= 5,455$ , OR=0,231, 95%CI=0,064-0,831) while A allele frequency was not statistically significant ( $p=0.448$ ,  $\chi^2= 0.577$ , OR=1,8, 95%CI= 0,389-8,323). Results of our study show that carrying G allele have a 4,3- fold protective effect against ovarian cancer. Importance of this study is being the first to assess the relationship of GCK (c.47702T>C, intron 6) polymorphism and ovarian cancer. New studies with large sample size and different population are essential to appreciate the associated of GCK (c.47702T>C, intron 6) polymorphism with ovarian cancer. In conclusion, the significant protective effect was shown for the carriers G allele *against* ovarian cancer. The study suggested that GCK (c.47702T>C, intron 6) polymorphism could be associated with ovarian cancer.

*Keywords: Ovarian cancer, glukokinase gene, single nucleotide polymorphism, genetic variability, case-control study.*

## POSTER PRESENTATION – 48

### INVESTIGATION OF MODY 2 (c.7: 44183880G>A) POLYMORPHISM IN PATIENTS WITH CORONER ARTERY DISEASE

Tugce GUL<sup>1</sup>, Dilara AYDEMİR<sup>1</sup>, Ezgi YALBIR<sup>1</sup>, Seda GULEC YILMAZ<sup>1</sup>, Huseyin AYHAN<sup>1</sup>, Selim ISBIR<sup>2</sup>, Atike TEKELI KUNT<sup>3</sup>, Orhan FINDIK<sup>3</sup>, Turgay ISBIR<sup>4</sup>

<sup>1</sup>Department of Molecular Medicine, Institute of Health Sciences, Yeditepe University, Istanbul, Turkey

<sup>2</sup>Department of Cardiovascular Surgery, Marmara University, Istanbul, Turkey

<sup>3</sup>Department of Cardiovascular Surgery, Kocaeli Derince Education and Research Hospital, Kocaeli, Turkey.

<sup>4</sup>Department of Medical Biology, Faculty of Medicine, Yeditepe University, Istanbul, Turkey

Coronary arteries have a critical role of blood flow. When the plaque builds up inside the coronary artery, the atherosclerosis is seen which cause to the formation of coronary artery disease (CAD). It is a chronic inflammatory disease leads cause of death worldwide. In monogenic forms of diabetes mellitus type 2, some mutations are seen in maturity onset diabetes of the young (MODY) genes are 6 different types. But only MODY2 is related to glucokinase which is the regulatory enzyme in glycolysis. In this study, our purpose is to investigate the relationship between CAD and MODY2 (G>A) polymorphism. Genotyping of the MODY2 (G>A) polymorphism was performed using real-time polymerase chain reaction for blood samples of CAD patients (n=25) and controls (n=30). SPSS was used for statistical analyses. There was statistically significant difference between patients with CAD and the control group in the frequency of small HDL (p=0.001) and small LDL (p=0.004). But there wasn't any significance between MODY2 (G>A) genotypes and small HDL, small LDL and between the groups in the frequency of MODY2 (G>A) genotypes ( $\chi^2=0.315$ ; p= 0.854). MODY2 (G>A) AA genotype was observed that in patients with CAD have family history ( $\chi^2=4.125$ ; p= 0.042; Confidence Interval [CI]= ((0.984) – (18.220)) have 4.235 times protection from the disease in comparison with the control group. There was statistically significant difference between coroner artery patients with MODY2 (G>A) G allele and family history ( $\chi^2=4.125$ ; p= 0.042 Odds Ratio [OR]= 0.236; [CI]= (0.055) – (1.106)). It is reviewed that CAD and diabetes are characterized with increased small dense LDL (sdLDL) and decreased small dense HDL (sdHDL) levels. In this study, we could observe the significant differences between sdHDL and sdLDL of patients with CAD but couldn't observe significant difference with the MODY2 (G>A) genotypes. In conclusion; we can't say there isn't any association between the genotypes of MODY (G>A) and CAD.

*Keywords: Coronar artery disease, diabetes, MODY2, glucokinase, polymorphism, sdHDL, sdLDL*

## POSTER PRESENTATION – 49

### RELATIONS OF SDF-1 AND CXCR-4 POLYMORPHISMS AND CD55 AND CD59 MARKERS WITH ETIOPATHOGENESIS AND PROGNOSIS IN TYPE 2 DIABETES

OZGUR B<sup>1</sup>, COŞKUNPINAR E<sup>2</sup>, GAZİOĞLU S<sup>1</sup>, AĞAÇHAN B<sup>2</sup>, MUSTERİ OLTULU YASEMİN<sup>2</sup>, DENİZ G<sup>1</sup>, YILMAZ MT<sup>1,3,4</sup>, GÜROL AO<sup>1,3</sup>

<sup>1</sup>Istanbul University, Institute of Experimental Medicine (DETAE), Department of Immunology, Istanbul

<sup>2</sup>Istanbul University, DETAE, Department of Molecular Medicine, Istanbul

<sup>3</sup>Istanbul University, Diabetes Application and Research Center (DİYAM), Istanbul

<sup>4</sup>Istanbul University, Istanbul Faculty of Medicine, Department of Internal Medicine, Division of Endocrinology and Metabolism Diseases, Istanbul, Turkey

Diabetes is a metabolic hyperglycemic disease resulting from impaired insulin production, secretion or insulin resistance. Complement regulators and chemokines are pivotal in pathogenesis. In the context of complications related to T2DM, CD55, CD59 expressions, and SDF-1, CXCR-4 polymorphisms were investigated in 75 patients and 73 healthy subjects. CD55 and CD59 expressions in patients with T2DM nephropathy, retinopathy and cardiovascular disease were significantly lower than healthy subjects. SDF-1 genotype and allele distributions between groups were not different. CXCR-4 genotype distribution wasn't different between groups, while a low significance was observed in allele distributions. CXCR-4 T allele was increased in patients, with 1.6-fold risk in terms of disease. Although SDF-1 genotypes in nephropathics did not show any difference, a significant difference was detected for CXCR-4 genotypes. CXCR-4 A allele carriers had decreased nephropathy, while 2-fold high nephropathy frequency was observed in the carriers of CXCR-4 T allele. The nephropathy risk increases 10-fold in CXCR-4 TT genotype carriers. A significant difference was observed in SDF-1 genotypes associated with retinopathy presence. Our results show that all SDF-1 CC genotype carriers have retinopathy, and CC genotype is effective in retinopathy development, however no significance was found for CXCR-4 genotypes. For the presence of cardiovascular disease, a significant difference was observed for SDF-1 genotypes. Increased cardiovascular risk of 5- and 1.9-fold in SDF-1 T and CXCR-4 T allele carriers, respectively was observed. In conclusion we suggest that CD55 and CD59 have a predictive importance in the process of the disease, and the polymorphism of CXCR-4 gene promoter site (rs2680880) plays a role in the susceptibility to T2DM.

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POSTER PRESENTATION – 50  
**INVESTIGATION OF NITROSATIVE STRESS AND OXIDATIVE DNA DAMAGE  
IN PATIENTS WITH CARBON MONOXIDE POISONING**

Fatma MIDİK ERTOSUN<sup>1</sup>, Seyithan TAYSI<sup>1</sup>, Suat ZENGİN<sup>2</sup>, Basrı CAN<sup>2</sup>, Hasan ULUSAL<sup>1</sup>

<sup>1</sup>Department of Medical Biochemistry, Gaziantep University,

<sup>2</sup>Department of Emergency medicine, Gaziantep University,

Carbon monoxide (CO) remains the most common cause of lethal poisoning around the world. Influence of brain, which is the most susceptible organ of hypoxia in patients with carbon monoxide poisoning (COP), is a determining factor of the severity of the clinical condition and mortality. In this study, we aimed to investigate the malondialdehyde (MDA), nitric oxide (NO<sup>•</sup>), peroxynitrite (ONOO<sup>-</sup>), 8-hydroxy-2'-deoxyguanosine (8-OHdG) levels and nitric oxide synthase (NOS) activity during admission and treatment processes in serum of patients with COP. The study was conducted prospectively on 36 patients who were admitted to Gaziantep University Medical Faculty Emergency Medicine Department between November 2015 and March 2016 due to COP. Serum were prepared for all the COP patients on admission. They were repeated at the 180th minute of treatment. The samples were taken once from the control group. Admission levels of MDA, NO<sup>•</sup>, ONOO<sup>-</sup>, 8-OHdG and NOS activity in patients with COP were higher than that observed at 90th minutes. These values were also higher in COP patients compared to control group. As a result, these findings showed that nitrosative stress should play a role in the pathophysiology of COP and increase DNA damage.

*Keywords: carbon monoxide poisoning, nitrosative stress, oxidative DNA damage*

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## POSTER PRESENTATION – 51

### ALTERNATING OXYGENATION CONDITIONS DON'T MODULATE Egr-1 EXPRESSION IN HUMAN BRAIN CANCER CELLS *IN VITRO*

Harun. M. Said<sup>1</sup>, Guler Gul<sup>1</sup>, Burcu Acikgoz<sup>1</sup>, Duygu Harmanci<sup>1</sup>, Ayse Kocak<sup>1</sup>,  
Cemre Ural<sup>1</sup>, Fatma Demet Ince<sup>1</sup>, Yasemin Soysal<sup>1</sup>

<sup>1</sup> Dept. of Molecular Medicine, Graduate Institute of Health Sciences, Dokuz Eylül University, Izmir, Turkey

**Background:** It has been shown in several publications (Ellen et al. 2007, Zhang et al. 2007) that the transcription factor Egr-1 is regulated via hypoxia, and the authors hypothesized that Egr-1 is responsible for hypoxia-induced NDRG1 gene regulation in human tumors cells. HIF-1a is the main the regulator of several hypoxia induced genes.

**Methods:** Egr-1 regulation level was examined in human Glioblastoma cells lines including U373, U251, GaMG and U87-MG under extreme hypoxic oxygenation conditions (0.1 O<sub>2</sub>), reoxygenation after hypoxia for 24 and 48 hours and oxygenated conditions (21% O<sub>2</sub> and 5% CO<sub>2</sub>) in vitro. Protein and mRNA level were detected via western blots and RT-PCR. Cells incubated for 24 hours with 100 μM DFO served positive control for hypoxia and b-tubulin and β-actin served as loading control, respectively.

**Results:** Egr-1 was not up-regulated via hypoxic development in different glioblastoma cells in vitro under extreme hypoxic conditions (0.1% O<sub>2</sub>) or reoxygenation after hypoxia, either at protein or mRNA level. Further, there was no association between Egr-1 expression and the expression of the hypoxia induced, HIF-1 a regulated genes in human glioblastoma tumor specimens examined, *in vitro*.

**Conclusions:** Egr-1 regulation as an answer to hypoxic development in glioblastoma, both on protein and mRNA level is not a general phenomenon: no hypoxic conditions influenced Egr-1 regulation. Therefore, at least in glioblastoma, HIF-1a still can be considered as a major regulator of NDRG1 under hypoxic conditions. In our opinion, Egr-1 regulation under hypoxia is a cell-specific post-translational event.

*Keywords: Egr-1, NDRG1, Hypoxia, Glioblastoma*

## POSTER PRESENTATION – 52 STANDARDIZATION OF ELISA METHOD FOR MILK SAMPLES

Hava Taslak<sup>1</sup>, Tuğba Tunalı-Akbay<sup>1</sup>

<sup>1</sup> Marmara University, Faculty of Dentistry, Department of Basic Medical Sciences, Biochemistry, Maltepe, Istanbul, Turkey

**Background/Aim:** Milk is an opaque fluid and its usage in the analytical methods may cause optical interferences and may disturb the sensitivity of the methods. As milk sample is discarded after the incubation in the ELISA method, optical interferences do not exist when milk is used as a sample. Despite this feature, milk does not usually recommended as a suitable sample in the ELISA kit manuals. In this case, standardization becomes necessary when using a sample that is not recommended in the test manual. Therefore, the aim of this study is to standardize the ELISA method for the milk samples.

**Material and Methods:** Bioo Scientific MaxSignal Fluoxetine ELISA procedure was used for the standardization of the method. For this purpose, two sets of standards were prepared. In the first set, blank and standard solutions were prepared either with milk samples or with phosphate buffer according to the standard preparation method that is recommended in the ELISA kit manual. Second set of standard solutions were prepared either with milk or with the phosphate buffer by considering the amount of fluoxetine excreted into the breastmilk. ELISA test results were calculated and standard graphics were plotted.

**Results:** It has been determined that phosphate buffer that contains fluoxetine in milk reference ranges was found to be suitable for calculating the concentration of fluoxetine in the milk samples.

**Discussion:** Usage of positive and negative control that is prepared with milk sample is recommended for the accuracy of the method. It should be noted that when working with a sample other than those specified in the ELISA kit manual, sample based standard and the kit standard preparation procedures should be considered.

**Conclusion:** In order to assure that the test method is suitable for its intended purpose, it is critical to assess the sensitivity of it.

*Keywords: Milk, ELISA, Fluoxetine*

## POSTER PRESENTATION – 53

### DO MCF7 CELLS COPE WITH METFORMIN TREATMENT UNDER ENERGETIC STRESS IN LOW GLUCOSE CONDITIONS?

Irem Dogan Turacli<sup>1</sup>, Haldun Umudum<sup>2</sup>, Arzu Pampal<sup>3</sup>, Tuba Candar<sup>4</sup>, Lara Kavasoglu<sup>5</sup>, Yaren Sari<sup>5</sup>

<sup>1</sup> Department of Medical Biology, Ufuk University, Ankara

<sup>2</sup> Department of Pathology, Ufuk University, Ankara

<sup>3</sup> Department of Pediatrics Surgery, Ufuk University, Ankara

<sup>4</sup> Department of Medical Biochemistry, Ufuk University, Ankara

<sup>5</sup> Faculty of Medicine, Ufuk University, Ankara

**Aim:** There is a growing body of evidence about metformin, a well-known antihyperglycemic agent, in the literature about being effective in cancer therapy. Despite controversies about the ways of its effectiveness, several ongoing clinical trials are evaluating the anticancer effects of drug when used as an adjuvant or a neo-adjuvant chemotherapeutic agent. The aim of the study is to investigate metformin's effects on cell viability, metastasis, and hormone receptor expressions in MCF7 breast cancer cell line incubated in high and low glucose conditions.

**Material and Methods:** MCF-7 cells were incubated in high or low glucose media and treated with consecutive metformin doses for 24 and 48 hour. The metabolic activity of living cells was studied using MTT test. The cells were harvested after 24 hour incubation with 5 or 10 mM metformin in high or low glucose media and stained for Ki67, estrogen and progesterone receptors and elevated for galectin-3 expression.

**Results:** The cell viability following consecutive doses of metformin in either glucose condition for 24 and 48 hours represented a significant decrease when compared to control groups. The cell viability detected in low glucose medium following metformin at doses less than 20 mM was found significantly decreased when compared to high glucose medium at 48 hour. The increase in galectin-3 levels in high glucose medium with metformin treatment was found statistically significant when compared to control group and the decrease in galectin-3 levels in low glucose medium was found statistically significant only with 10 mM of metformin treatment. Progesterone receptor staining demonstrated a significant prominent increase in low glucose medium.

**Discussion:** The overall findings of this study represent better outcomes for cancer lines incubated in low glucose media treated with metformin in terms of viability, receptor expression and metastatic activity independent of other factors.

**Conclusion:** Taken together, these results highlight the potential benefit of metformin as an adjuvant therapy especially in restraining the cell's ability to deal with energetic stress in low glucose conditions in breast cancer.

*Keywords: Metformin, cancer, low glucose, cell viability, galectin-3, estrogen receptor, progesterone receptor, Ki-67*

## POSTER PRESENTATION – 54

### CYTOTOXICITY OF *JUNIPERUS EXCELSA* AQUEOUS BERRY EXTRACT ON CASTRATION-RESISTANT PROSTATE CANCER CELLS

İşıl Ezgi Eryılmaz<sup>1</sup>, Ünal Egeli<sup>1</sup>, Hulusi Malyer<sup>2</sup>, Gülşah Çeçener<sup>1</sup>, Saliha Şahin<sup>3</sup>, Berrin Tunca<sup>1</sup>

<sup>1</sup>Uludag University, Faculty of Medicine, Department of Medical Biology

<sup>2</sup>Uludag University, Faculty of Science and Art, Department of Botany

<sup>3</sup>Uludag University, Faculty of Science and Art, Department of Analytical Chemistry

As a natural source of numerous pharmacological active molecules, plant kingdom has quite important anticancer potential. Since cancer treatment is still limited with the available agents, new therapy approaches need to be developed. This is also a requirement for castration-resistant prostate cancer (CRPC), the lethal form of prostate adenocarcinoma. Recently, it has been revealed by a few studies that *Juniperus L.* is an important plant due to its anticancer potential against some cancer cells. In the present study, we investigated cytotoxic and anticancer effects of *Juniperus excelsa* aqueous berry extract on two CRPC cell lines and HUVEC control cells. According to WST-1 results, cytotoxic effect of the extract on CRPC cells were time and concentration dependent and maximum effect was observed at 72h. 250µg/ml berry extract decreased cell viability to 47,68% ( $p<0.0001$ ) and 44,48% ( $p<0.001$ ) for DU145 and PC-3, respectively. At the same exposure time with this concentration, the inhibition of viability was lower in HUVEC cells. Based on morphological analysis, early apoptosis increased after 48h, late apoptotic and necrotic deaths were observed at 72h in DU145 cells. It was detected with annexin V analysis that 250µg/ml berry extract caused 36,05% apoptosis and 3,90% necrosis in DU145, 40,1% apoptosis and 7,25% necrosis in PC-3, 17,05% apoptosis and 6,15% necrosis in HUVEC cells. Based on RT-qPCR results, the extract significantly downregulated *MMP-2* and *MMP-9* expression levels. In addition the extract was determined to contain phenolic compounds including chlorogenic acid and ferulic acid by HPLC-DAD analysis. Cytotoxic effect of *Juniperus excelsa* aqueous berry extract on CRPC cells was investigated for the first time with this study. Thus, we suggest that *Juniperus excelsa* might be one of the important plant species in further investigations for CRPC treatment.

*Keywords: Juniperus excelsa, cytotoxicity, castration-resistant prostate cancer*



## POSTER PRESENTATION – 55

### INHIBITION OF GROWTH FACTOR MIDKINE by siRNA ENHANCES THE EFFECTS OF QUERCETIN ON CD133<sup>+</sup>/44<sup>+</sup> PROSTATE CANCER STEM CELLS

Suat Erdogan<sup>1</sup>, Kader Turkekul<sup>1</sup>, Rıza Serttas<sup>1</sup>, Oguzhan Doganlar<sup>1</sup>, Zeynep B. Doganlar<sup>1</sup>, Ilker Dibirdik<sup>2</sup>, Ayhan Bilir<sup>3</sup>

<sup>1</sup>Department of Medical Biology, <sup>2</sup>Department of Biochemistry School of Medicine, Trakya University, Balkan Campus, Edirne, Turkey

<sup>3</sup>Department of Histology and Embryology, School of Medicine, Istanbul Aydin University, Istanbul, Turkey

**Background/Aim:** Midkine (MK) is a heparin-binding growth factor which is undetectable in normal adult tissues but it is overexpressed in various types of cancer patients. Overexpression of the oncogene MK protein is associated with aggressive human prostate cancer (PCa). Cancer stem cells (CSCs) are often considered to be associated with chemo-resistance and radio-resistance that lead to the failure of traditional therapies. Therefore, the aims of this study were to: 1) evaluate the role of MK protein, 2) seek the effect of the flavonoid quercetin in prostate cancer CD133<sup>+</sup>/44<sup>+</sup> stem cells (PCSC).

**Materials and Methods:** CD133<sup>+</sup>/44<sup>+</sup> CSCs were isolated from PC3 human PCa cell lines using magnetic-activated cell sorting system. Knockdown of endogenous MK mRNA expression was performed by siRNA transfection. Cell survival was evaluated by MTT assay. Apoptosis was evaluated by RT-qPCR and image-based cytometry. Spheroid culture was used to measure growth diameter. PCSCs were treated with various concentrations of quercetin for 72 h. The cell migration rate was evaluated by wound healing assay.

**Results:** Downregulation of MK caused a significant amount of cell death via apoptosis. Quercetin dose- and time-dependently decreased the cell viability. Treatments of MK knock-downed PCSCs with 40 µM of quercetin significantly decreased the cell viability through apoptosis and necrosis compared cells treated with either agent alone. Quercetin therapy significantly reduces the cell migration and spheroid diameter of three-dimensional cell culture.

**Discussion:** Tumor growth and migration are the major challenge in cancer biology. MK has been shown to promote cell growth, survival and migration in various cancer cells. The flavonoids prevent the proliferation of cancer cells by disturbing cell survival and death balance by either enhancing apoptosis or decreasing the survival signaling.

**Conclusion:** MK plays an important role in stem cell survival and co-treatment with quercetin might provide a promising treatment for PCSC therapy as well as inhibit cancer cell migration.

*Keywords:* Cancer stem cells, CSC, midkine, quercetin, prostate cancer

*Acknowledgments:* This work was supported by The Scientific and Technological Research Council of Turkey (Grant no: 115S356).

## POSTER PRESENTATION – 56 RELATIONSHIP BETWEEN SERUM RESISTIN AND OXIDATIVE STRESS IN OBESE PATIENTS

Ramila HAJIYEVA<sup>1</sup>, Türkan YİĞİTBAŞI<sup>1</sup>, Maide Hacer ALAGOZ<sup>2</sup>, Gözde ÜLFER<sup>1</sup>, Nesrin EMEKLİ<sup>1</sup>

<sup>1</sup>Department of Biochemistry, Medical Faculty, MedipolUniversity, Istanbul, Turkey.

<sup>2</sup>Department of Clinical Biochemistry, Okmeydani Educational and Research Hospital, Istanbul, Turkey

Obesity, a pandemic disease, is caused by an excessive accumulation of fat that can have detrimental effects on health. Adipose tissue leading to a dysfunctional production of several factors, known as adipocytokines. Multiple mechanisms may contribute to obesity-related comorbidity development, including an abnormal production of adipocytokines, aberrant oxidative stress and dysregulated proinflammatory response in tissues. Resistin is an adipocyte- and monocyte-derived cytokine that represents a link between obesity, insulin resistance, and type 2 diabetes. The aim of this study is to investigate the relationship between serum resistin levels and oxidative stress in obese individuals.

**Materials and Method:** We evaluated clinical and biochemical data in 85 participants, 24 control with BMI <24.9 kg/m<sup>2</sup> and 61 overweight (25 ≤ BMI <30 ) and obese (30 ≤ BMI) patients. Biochemical parameters, including lipid profile (TG, total cholesterol, LDL-C, HDL-C), fasting glucose, Total Oxidation Status (TOS) and Total Anti-Oxidation Status (TAS) measured by photometric method. Total Oxidative Stress Index (OSI) is calculated by the ratio of TOS and TAS levels. Insulin, CRP and HbA1c levels measured by chemiluminescence immunoassay. Serum resistin measured by ELISA method. All statistics were calculated using the SPSS 17.0 software (Chicago, IL, USA). P values < 0.05 were considered statistically significant.

**Results:** Serum TAS levels are found to be low at statistically significant level (p < 0.001) in overweight-obese patient groups and a negative correlation observed in between TAS and BMI values (p < 0.05). Serum TOS levels in obese patient group don't show a significant difference (p > 0.05), whereas OSI values, HbA1C and glucose levels are significantly high (p < 0.001). Resistin values don't show a statistically significant difference in neither overweight-obese patient groups or healthy control groups (p > 0.05).

**Conclusions:** This results suggest that diminished levels of TAC and increased levels of OSI associated with obesity. It is thought that observed reduction of anti-oxidant defense system in obesity cases can't be related to resistin levels.

*Keywords: Obesity, Resistin, TAS, TOS, OSI*

*Acknowledgements: 200 / 16.04.2015*

## POSTER PRESENTATION – 57

### EXPRESSION ANALYSIS OF FOUR GENES FROM HEART-SPECIFIC SUBTRACTIVE HYBRIDIZATION cDNA LIBRARY IN MULTIPLE TISSUES AND EMBRYOS

Muhammed Abdulvahid KALKAN<sup>1</sup>, Gizem ÇELEBİ<sup>1</sup>, Bilge ÖZSAİT-SELÇUK<sup>1</sup>, Evrim KOMURCU-BAYRAK<sup>1</sup>, Nihan ERGINEL-UNALTUNA<sup>1</sup>

<sup>1</sup>Istanbul University, Aziz Sancar Institute for Experimental Medicine, Department of Genetics, Istanbul, Turkey

**Background/Aim:** Identification of differential gene expression and determination of co-expressed genes is important in the characterization of tissue specific molecular pathways. Many different techniques such as SHL (subtractive hybridization cDNA library), differential display, SAGE (serial analysis of gene expression) and microarrays are used to analyze differentially expressed genes. Although microarray-based transcription profiles can be obtained faster, low-throughput techniques such as SHL can provide isolation of many tissue-specific full-length transcripts as well as novel transcripts. In our previous studies, we constructed a heart-specific SHL and conducted several functional studies in order to analyze the role of the isolated transcripts in heart tissue. In this study, our aim was to investigate the expression patterns of four selected transcripts from SHL in multiple tissues and total embryos.

**Materials and Methods:** Total RNA isolation and cDNA synthesis were performed from 14 different tissues, 4 different stages of total embryos and neonatal heart and skeletal muscle (skm) of BALB/c mice. The expression profiles of SHL isolated four genes, mitofusin-2 (*Mfn2*), importin (*Kpnb1*), midnolin (*Midn*) and mt-*Atp6* (ATP synthase 6, mitochondrial) were analyzed by quantitative real time PCR (qRT-PCR). Additionally, Northern blot analysis of the four transcripts in adult tissues was performed.

**Results:** Gene expression levels of the four transcripts were higher in neonatal heart than in neonatal skm. Similar pattern was observed in adult heart and skm. However, *mt-Atp6* and *Mfn2* genes were over-expressed in heart tissue compared to all other tissues and embryonic stages.

**Discussion:** Differential expression of the transcripts among different tissues as well as in different embryonic stages suggests that these four genes have crucial roles in cellular physiology.

**Conclusion:** Demonstration of the gene expression levels of the transcripts in the subtractive hybridization cDNA library in healthy tissues and embryonic development will contribute to the identification of the function of the genes in related metabolic pathways.

*Keywords:* subtractive hybridization, qRT-PCR, mitofusin 2, importin, mt-atp6, midnolin

POSTER PRESENTATION – 58  
**TRIAPINE INDUCES APOPTOSIS OF DOCETAXEL-RESISTANT PROSTATE  
CANCER CELLS THROUGH ENDOPLASMIC RETICULUM STRESS**

Riza Serttas<sup>1</sup>, Suat Erdogan<sup>1</sup>

<sup>1</sup>Department of Medical Biology, School of Medicine, Trakya University, Balkan Campus, Edirne, Turkey

**Background:** Chemotherapy resistance is the major problem for prostate cancer (PCa) therapy in men. Cancer cells are exposed to various environmental factors that disrupt protein homeostasis, producing endoplasmic reticulum (ER) stress via unfolded protein response. Triapine (3-aminopyridine-2-carboxaldehyde thiosemicarbazone, 3-AP), a ribonucleotide reductase inhibitor, demonstrates potent anti-cancer activity in a range of cancers. However, its effect in drug-resistant PCa cells has never been investigated. The aim of this study was to investigate the effect of 3-AP in Docetaxel-resistant PCa (DR-PC3) cells.

**Materials and Methods:** Human castration-resistant PCa cell line PC3 was used in this study. Drug resistance was developed by treatment of the cells with docetaxel. The cell viability was determined by MTT test. Apoptosis and cell cycle progress were analyzed by image-based cytometer. The mRNA expression analyzes were conducted by RT-qPCR. Three-dimensional (3D) cell culture was established to estimate the effect of 3-AP treatment on tumor volume.

**Results:** DR-PC3 cells were treated with different concentrations of 3-AP for 72 h. 3-AP treatment significantly reduced cell survival at 72 h with an IC<sub>50</sub> of 7.5  $\mu$ M, and induced ER-stress. In order to reveal whether 3-AP decreased cell number through cell cycle arrest and/or induced apoptotic cell death, DR-PC3 cells were treated with 7.5  $\mu$ M of 3-AP for 72 h. The results indicated that 3-AP induced apoptosis pathway, and caused to G<sub>1</sub> phase arrest of the cells. Treatment of the cells with 3-AP for 10 days reduced the volume of spheroid diameter by 16 %.

**Discussion:** Previous studies have shown that 3-AP is a promising drug candidate for the systemic treatment of several hematological malignancies. Furthermore, 3-AP may safely be used in combination treatment with cisplatin in patients with advanced-stage solid tumor malignancies. On the other hand, 3-AP combination with gemcitabine is effectiveness in advanced non-small-cell lung cancer.

**Conclusion:** ER stress is a potential target in cancer treatment, so the ability of 3-AP to induce ER stress response and to activate apoptosis in DR-PC3 cells make this molecule become a promising anticancer agent for PCa treatment. However, further investigations are required to evaluate its in vivo efficacies.

*Keywords: Prostate cancer, ER stress, drug resistance, triapine*

*Acknowledgments: This work was supported by the Trakya University Research Project Foundation (Grant no: 2016-04).*

## POSTER PRESENTATION – 59

### THE *IL-1Ra* GENE VNTR VARIANT IS ASSOCIATED WITH SUSCEPTIBILITY TO TEMPOROMANDIBULAR DISORDERS IN TURKISH POPULATION

Serbulent Yigit<sup>1</sup>, Mehmet Kemal Tumer<sup>2</sup>, Ayse Feyda Nursal<sup>3</sup>, Akın Tekcan<sup>4</sup>

<sup>1</sup>Gaziosmanpasa University, Faculty of Medicine, Department of Medical Biology, Tokat, Turkey

<sup>2</sup>Gaziosmanpasa University, Faculty of Dentistry, Department of Oral Surgery, Tokat, Turkey

<sup>3</sup>Hitit University, Faculty of Medicine, Department of Medical Genetics, Corum, Turkey

<sup>4</sup>Ahi Evran University, Faculty of Medicine, Department of Medical Biology, Kirsehi,, Turkey

**Aims and Scopes:** Temporomandibular joint disorders (TMD) are a group of disorders involving temporomandibular joint and related structures. Interleukine-1 receptor antagonist (IL-1Ra) is an important antiinflammatory molecule that competes with other interleukin-1 molecules. The current study was designed to investigate the possible association of the IL-1Ra VNTR variant with the risk of TMD in the Turkish population.

**Methods:** Peripheral blood samples were collected from 100 patients with TMD (23 males, 77 females) and 110 healthy individuals (35 males, 75 females). Genotyping of IL-1Ra 86 bp VNTR variant was evaluated by gel electrophoresis after polymerase chain reaction (PCR).

**Results:** Our results show that there is a statistically significant difference between TMD patients and control group with respect to IL-1Ra genotype distribution and allele frequencies. 1.2, 1.4, and 4.4 genotypes were more common in patients, while 2.2 and 3.3 genotypes were rarer ( $p < 0.000$ ). Frequency of allele 1 and 4 was higher in patient groups ( $p < 0.000$ ), whereas allele 2 and 3 had a lower frequency in patients with TMD ( $p < 0.000$ ).

**Conclusions:** This is the first correlation study that evaluates the association between IL-1Ra gene VNTR variant and TMD. The VNTR variant related to IL-1Ra gene showed a strong pattern of association with TMD that may have a potential impact on disease counseling and management. Larger studies with various ethnicities are needed to establish the impact of IL-1Ra VNTR variant on risk of developing TMD. Further studies are needed to confirm this observation.

*Keywords: Temporomandibular joint disorders, Interleukine-1 receptor antagonist, VNTR variant.*

*This study was approved by the Gaziosmanpasa University Clinical Research Ethical Committee (Approval no: 15-KAEK-124).*

## POSTER PRESENTATION – 60 ANTI-MIGRATION EFFECTS OF BEVACIZUMAB ON THE BREAST CANCER CELL LINES

Guler Gul<sup>1</sup>, Yasemin Soysal<sup>1</sup>, Gul Guner Akdogan<sup>2</sup>, Harun Muayad Said<sup>1</sup>

<sup>1</sup>Department of Molecular Medicine, Institute of Health Sciences, Dokuz Eylul University, Izmir, Turkey

<sup>2</sup> Izmir Enconomy University, Medical Faculty, Izmir, Turkey

**Background/Aim:** Bevacizumab was the first approved therapeutic agent targeting blood vessels of tumors and plays a critical role in cancer disease development. Our study aimed to investigate the effect of different concentrations of Bevacizumab and durations on cell migration of human breast adenocarcinoma cell lines (MCF-7 and MDA-MB-231) and human normal breast cell line (MCF-10A).

**Materials and Methods:** Bevacizumab was diluted in culture medium at a concentration of 250 and 350 µg/mL, respectively. To detect the cell viability, MCF-7, MDA-MB-231 and MCF-10A cell lines were incubated at the defined concentrations for 24, 48 and 72 h, respectively for WST-1 analysis. Following WST-1 analysis, IC50 values of Bevacizumab were determined for each cell lines. Cell migration was measured by using the *in vitro* scratch assay. Cells were incubated with 250 µg/mL, 350 µg/mL of Bevacizumab and IC50 for up to 48h. Recorded images of scratch assay measured was realized using Image J software at the same location after 48h of incubation.

**Results:** According to our WST-1 results, Bevacizumab significantly decreased the cell viability in MCF-7 and MDA-MB-231 cells depending on the time and the concentration. For MCF-7, MDA-MB-231 and MCF-10A cells respectively, the IC50 values of Bevacizumab were 232.8 µg/mL, 335.7 µg/mL, 380.5 µg/mL at 72h. In migration assay, spaces of the cultured and treated MCF-7 and MDA-MB-231 groups closed less as against control group while MCF-10A cells closed completely within 12 hours.

**Conclusion:** It can be suggested that Bevacizumab may decrease cell migration in breast cancer cell line. To our knowledge, our study is among the very few studies have reported Bevacizumab and anti-migration effect in cancer cell lines.

*Keywords: Breast Cancer, Bevacizumab, Scratch Assay, WST-1 Analysis*  
*This study was funded by the TÜBİTAK under project no 215S169.*

## POSTER PRESENTATION – 61

### INVESTIGATION OF THE INTERACTION BETWEEN miR-203a-3p and LncRNA TUG1 IN BLADDER CANCER

Zekiye Altan<sup>1</sup>, Yunus Sahin<sup>1</sup>, Meltem Koruk Ozer<sup>1</sup>, Kaiffee Arman<sup>1</sup>, Esra Bozgeyik<sup>1</sup>, Ayshan R. Yassin<sup>1,2</sup>, Sibel Oguzkan Balci<sup>1</sup>

<sup>1</sup>Faculty of Medicine, Department of Medical Biology, University of Gaziantep, Gaziantep, Turkey

<sup>2</sup>Faculty of Medicine, Medical Department, Salahaddin University, Erbil, Irak

**Aim:** Taurine Upregulated Gene 1 (TUG1) is a long non-coding RNA (lncRNA) that increases cell proliferation in bladder cancer. However, function of the TUG1 lncRNA is not fully understood. In bladder cancer, hsa-miR-203a-3p, a short non-coding RNA, has low expression level. In this study, we aimed to investigate the relationship between lncRNA TUG1 and hsa-miR-203a-3p.

**Materials and Methods:** The commercially purchased CAL-29 cell line was cultured under appropriate conditions and treated with mimic-hsa-miR-203a-3p and its negative control. After transfection, RNA isolation was performed. For the expression analysis of TUG1 gene and hsa-miR-203a-3p, RT-PCR and qPCR methods were used. One Way ANOVA test was applied to the qPCR results. T-test was applied for the results of fold change.

**Results:** In the CAL-29 cell line treated with mimic-hsa-miR-203a-3p, there was a significant increase in hsa-miR-203a-3p expression ( $p = 0.0019$ ), the expression level of the TUG1 gene was increased relative to the negative control ( $p = 0.7988$ ). According to the fold change analysis of these obtained data, there was a significant increase in expression level of hsa-miR-203a-3p after transfection ( $p = 0.0195$ ). The expression level of the TUG1 gene is increased compared to the negative control, but this increase is not statistically significant ( $p = 0.6250$ ).

**Discussion:** According to the secondary structural fold analysis of the TUG1 gene, the structural energy of the TUG1 gene folding to be able to bind hsa-miR-203a-3p on the TUG1 gene is very high and the structure it is formed is quite unstable. Since sufficient energy could not be provided, the binding between the TUG1 gene and hsa-miR-203a-3p may not occur, or the binding may not be detectable because the binding is rather short.

**Conclusion:** In bladder cancer, a significant association between hsa-miR-203a-3p and the TUG1 gene has not been established. However, better results can be achieved with inhibitor transfection for normal bladder tissue.

*Keywords: bladder cancer, lncRNA, miRNA, miR-203a-3p, TUG1.*

## POSTER PRESENTATION – 62

### **miR-664a IS ASSOCIATED WITH OSTEOSARCOMA VIA DOWNREGULATING OF MEG3**

Yunus Sahin<sup>1</sup>, Zekiye Altan<sup>1</sup>, Kaifee Arman<sup>1</sup>, Esra Bozgeyik<sup>1</sup>, Meltem Koruk Ozer<sup>1</sup>, Sibel Oguzkan Balcı<sup>1</sup>

<sup>1</sup>Faculty of Medicine, Department of Medical Biology, University of Gaziantep, Gaziantep, Turkey

**Aim:** Osteosarcoma is the most common primary bone tumor in children and adolescents. Understanding the basic molecular mechanisms in developing cancer can be helpful in developing alternative treatment strategies. The relationship between dysregulated non-coding RNAs' (ncRNA) expression level and osteosarcoma was detected. Among those ncRNAs, the expression levels of hsa-miR-664a-5p were detected to be upregulated and MEG3 long non-coding RNA levels were detected to be downregulated in osteosarcoma tissue and cell lines. In this study, hsa-miR-664a-5p inhibitor was used in order to investigate the changes in the levels of MEG3 gene and hsa-miR-664a-5p in osteosarcoma cancer cell line (U-2 OS) and human osteoblast cell line (hFOB 1.19).

**Materials and Methods:** For the MEG3 gene expression analysis, cDNAs which are transformed from U-2 OS and hFOB 1.19 cell lines' RNAs were used at PCR and qPCR methods. In order to analysis interaction between hsa-miR-664a-5p and MEG3 gene in osteosarcoma, U-2 OS cells were transfected with antagomiR-664a-5p and negative control for 48 hours. After incubation, total RNA isolated and converted to cDNA to perform qPCR experiments. Statistical analysis of expression of MEG3 gene and hsa-miR-664a-5p in osteosarcoma after antagomiR-664a-5p transfection was done.

**Results and Discussion:** PCR and qRT-PCR expression analysis results showed that MEG3 gene has low expression level in U-2 OS cell line, high expression level in hFOB 1.19 cell line while miR-664a has high expression level in U-2 OS cell line but low expression level in hFOB 1.19 cell line. This pre-study indicated that our hypothesis is consistent. After antagomiR-664a transfection into U-2 OS cell line, according to our results, the expression level of MEG3 gene was increased while the expression level of miR-664a was decreased, as expected. The results are found to be statistically significant ( $p < 0.05$ ).

**Conclusion:** As a result of this study, it was shown that the upregulated expression of miR-664a could have an inhibitory effect on MEG3 gene expression in osteosarcoma.

*Keywords: lncRNA, MEG3, miRNA, miR-664a, Osteosarcoma.*



POSTER PRESENTATION – 63  
**IDENTIFICATION OF DUODENAL ULCERATION IN PATIENTS  
HELICOBACTER PYLORI, CLARITHROMYCIN AND FLUOROQUINOLONE  
DRUG RESISTANCE USING MOLECULAR TECHNIQUES**

Yasemin BULUT<sup>1</sup>, Gökhan ÖZDEMİR<sup>2</sup>, Cem AYGÜN<sup>3</sup>, İbrahim Hanifi ÖZERCAN<sup>4</sup>, Gül UÇAR<sup>5</sup>, Oğuzhan HANCI<sup>6</sup>

<sup>1</sup> Fırat University, Faculty of Medicine, Department of Medical Microbiology, Elazığ-Turkey

<sup>2</sup> Elazığ Fırat University Hospital

<sup>3</sup> İstanbul Acıbadem Hospital

<sup>4</sup> Fırat University, Faculty of Medicine, Department of Medical Pathology, Elazığ-Turkey

<sup>5</sup> İstanbul Rumeli University, Vocational School

<sup>6</sup> Adıyaman Çelikhan State Hospital

The aim of this study was to determine *Helicobacter pylori* clarithromycin and fluoroquinolone drug resistance by molecular techniques in patients with duodenal ulcer. In this study, 48 duodenal ulcers with 25 women (53%) of 23 male (47%) of patients biopsy specimens obtained from *H. pylori* and Clarithromycin to its resistance to Fluoroquinolone antibiotics was tested by molecular methods. The study of 48 patients with duodenal ulcers as a result of 40 (83%) the Clarithromycin resistance, 33 (69%) also Fluoroquinolone resistance in a total of 32 patients (67%) with both Clarithromycin and Fluoroquinolone resistance GenoType® HelicoDR with the method in a short time have been identified. *H. pylori* isolates 40% of length: 1.5 Kb plasmids ranging from 23.3 of contain. More than half of the world's population, 85 to 90 percent of the eradication of *H. pylori* infected our country, therefore, is of great importance. But some of antimicrobial agents used in treatment against the development of resistance of bacteria in the eradication of lead to failure. Culture and sensitivity of *H. pylori* bacteria a breeding applications in difficult due to technical difficulties, easy to implement, and have shown that cheapest of the methods is required. Studies pre-treatment the importance of the detection of the presence of resistance is emphasized.

Molecular tests in a short period of when the results are taken into account, the study has been to prevent the loss of time and unnecessary with the use of medications.

*Note to the Scientific Committee: This work was supported by Fırat University Scientific Research Projects Unit (TF.12.86). Ethics Committee Decision Number:10.05.2012-09/05*

## POSTER PRESENTATION – 64

### **DETECTION OF HEPATITIS C VIRUS (HCV) GENOTYPES BY PYROSEQUENCING IN CHRONIC HCV PATIENTS**

Yasemin BULUT<sup>1</sup>, Oğuzhan HANCI<sup>2</sup>, Cem AYGÜN<sup>3</sup>, Adnan SEYREK<sup>4</sup>, Gül UÇAR<sup>5</sup>

<sup>1</sup> Firat University, Faculty of Medicine, Department of Medical Microbiology, Elazığ-Turkey

<sup>2</sup> Adıyaman Çelikhan State Hospital

<sup>3</sup> Istanbul Acıbadem Hospital

<sup>4</sup> Firat University, Faculty of Medicine Department of Medical Microbiology, Elazığ-Turkey

<sup>5</sup> Istanbul Rumeli University, Vocational School

The aim of this study; it was aimed to determine HCV genotypes of the patients with prediagnosis or diagnosis of chronic hepatitis C in Elazığ by using pyrosequencing method. Serum samples of 50 patients with prediagnosis/diagnosis of chronic Hepatitis C were used in this study. HCV-RNA levels of all samples that were positive for anti-HCV were determined using real time PCR. RNA isolation from the samples were carried out using an automated isolation system as described by the manufacturer. HCV genotype analysis of the samples were determined by using pyrosequencing method. 46 (92%) and 1(2%) of the samples were determined as genotype 1 and genotype 3, respectively. of 46 samples that were genotype 1, 41 were found as genotype 1b and 5 as genotype 1a whereas 3 of those were not be able to subtyped. As a result, genotype 1b was found as the most common genotype in patients infected with HCV. It is very important to determine HCV genotypes if the cost of drugs is high and side effects are considerable in HCV treatment. The fact that HCV infection is a progressive disease and that there is a chance of getting rid of virustans by treatment and the prevention of hepatocellular carcinoma in treatment responders requires the initiation of early treatment in these patients and necessitates a good epidemiological study based on collecting HCV.

Genotyping HCV by pyrosequencing takes quite shorter time compared to other DNA sequencing methods. In this case, pyrosequencing can be a method of choice in routine analysis laboratories due to ease of use. Unit cost of pyrosequencing is comparable to that of DNA sequencing based methods. In fact, it is cheaper than the cost of reverse hybridization method. It is concluded that, due to the cost and required-time advantages, pyrosequencing can be used for genotyping HCV, which is an important criteria for determining the treatment response and the treatment period.

*Keywords: Hepatitis C Virus, Chronic Hepatitis C, Genotype, Pyrosequence*

*Note to the Scientific Committee: This work was supported by Firat University Scientific Research Projects Unit (TF.11.64).*

*Ethics Committee Decision Number: 13.05.2011-08/08*

## POSTER PRESENTATION – 65

### THE DETERMINATION OF THE BENEFITS WHICH CAUSED TO CARBAPENEMS IN THE HOSPITAL ORIENTED PSEUDOMONAS AERUGINOSA AND ACINETOBACTER BAUMANNII BY THE PHENOTYPIC AND GENOTYPIC METHODS

Şafak ANDIÇ<sup>1</sup>, Yasemin BULUT<sup>2</sup>, Zülal AŞÇI TORAMAN<sup>3</sup>, Kutbettin DEMİRDAĞ<sup>4</sup>, Gül UÇAR<sup>5</sup>

<sup>1</sup> Bursa Food and Feed Control Central Research Institute Directorate

<sup>2</sup> Firat University, Faculty of Medicine, Department of Medical Microbiology, Elazığ- Turkey

<sup>3</sup> Firat University, Faculty of Medicine, Department of Medical Microbiology, Elazığ-Turkey

<sup>4</sup> Firat University, Faculty of Medicine, Department of Infectious Diseases, Elazığ-Turkey

<sup>5</sup> Istanbul Rumeli University, Vocational School

Carbapenemases resisting toward carbapenems (a good treatment choice for serious infections) become significant in recent years. In our study, detection of beta-lactamase genes and investigation of clonal relationship among positive genes in isolated ornaments is aimed. Consequently, 50 *P.aeruginosa* and 50 *A.baumannii* ornaments from various clinical isolates between March-2011 and March-2012 are identified by classical methods and BD Phoenix instrument. In imipenem-resisted ornaments, beta-lactam-enzyme is investigated by kombine disk, çift disk sinerji, modifiye Hodge fenotipik tests. In ornaments with positive Fenotipik tests, OXA-group, KPC, IMP and VIM resist genes are studied by PZR. According to PZR results, in *A.baumannii* ornaments, while the beta-laktamaz genes are found to be positive in ratio of OXA-51 % 98, OXA-58 % 14, OXA-23 % 14, KPC % 8, OXA-24, VIM and IMP genes could not be detected. In *P.aeruginosa* no gene region is detected. By secans analysis in some positive samples, the relation between bacteria sequence found and that in gene bank is investigated and calculated according to 0.75. Sequences obtained are compared with the sequences in gene bank by BLAST program and following similarities are found: 97-99% in 5 samples studied OXA-23, 95-98% in 8 samples studied OXA-51, and 99-100% in 7 samples studied OXA-58 primers. Carbapenems; Are the most preferred antibiotics for Gram-negative bacterial infections, which have a wide spectrum and are able to pass rapidly through bacterial mem- branes. However, resistance to these antibiotics is now a major problem in therapy. Because of the crucial role of carbapenemases in bacterial resistance, the application of various phenotype tests to detect them in routine microbiology laboratories is epidemiologically important. In phenotypic tests, the lack of a standard method recommended by CLSI, low MIC values in carbapenem, and lack of standardized EDTA sensitivity cause difficulties in interpretation. Furthermore, these tests are not routinely used because they are not commercially available and the results are taken one day later. Rapid and accurate detection of carbapenemases, especially in severe infections in intensive care units, is crucial for the life of the patient. Since they are more sensitive than phenotypic tests, they should be used in molecular tests as well as these tests in the detection of carbapenemases.

To conclude, this study is significant for being the first in the region and for detecting common  $\beta$ -laktamaz resist genes. Identification of resist genes and their mechanisms is important for directing treatments and forming epidemiological data.

**Keywords:** *A.baumannii*, *P.aeruginosa*, OXA-51, OXA-58, OXA-23, OXA-24, VIM, IMP.

**Note to the Scientific Committee:** This work was supported by Firat University Scientific Research Projects Unit (TF.13.17).

**Ethics Committee Decision Number:** 15.03.2012-06/01

## POSTER PRESENTATION – 66 INVESTIGATION OF MTHFR C677T AND A1298C GENE POLYMORPHISM IN HUMAN KIDNEY CANCER TISSUES

Burcu Çaykara<sup>1</sup>, Hani Alsaadoni<sup>1</sup>, Fatemeh Azhari Zarnag<sup>1</sup>, Alper Ötünçtemur<sup>2</sup>, Sadrettin Pençe<sup>3</sup>

1 Istanbul University, Aziz Sancar Institute of Experimental Medicine (ASDETAE), Department of Molecular Medicine, Istanbul

2 Okmeydani Education and Research Hospital, Department of Urology, Istanbul

3 University of Health Sciences, Faculty of Medicine, Department of Physiology, Istanbul

**Background:** 5,10-Methylenetetrahydrofolate reductase (MTHFR) catalyzes the reduction of methylenetetrahydrofolate to 5-methyl tetrahydrofolate (THF) using 5,10 FAD as a cofactor, which acts as a regulator of folate coenzymes for purine, pyrimidine synthesis and methionine synthesis. 5-methyl THF provides the methyl group for the synthesis of methionine, and homocysteine is the carbon donor in methionine remethylation. The potential effect of MTHFR on DNA methylation, DNA repair and DNA synthesis, made MTHFR as a cancer-inducing gene. We aimed to evaluate C677T and A1298C gene polymorphism in kidney cancer.

**Material –Method:** 50 tumor and 50 non-tumor tissue samples were obtained from patients who had been diagnosed with kidney cancer at SB Okmeydani Training and Research Hospital after surgical operation during normal treatment. The specimens were treated with liquid nitrogen and stored at -80 °C until isolation was made at IU ASDETAE, Department of Molecular Medicine. DNA was isolated from the tissues by DNA Isolation kit and the amount of DNA was measured at 280nm. Polymerase chain reaction (PCR) was performed with locally synthesized primers containing C677T and A1298C gene polymorphism and PCR samples were run on agarose gel electrophoresis. In order to determine the region of variation, PCR products, which were subjected to digestion with Hinf I and Mbo II enzymes and visualized under UV light. The genotype and allele distributions analyzed with SPSS18.

**Results:** In the MTHFR A1298C variation, the normal AA genotype frequency was 46% and the rare CC genotype frequency was 12% in the patient group, while 24% and 18% were found in the control group, respectively [ $\chi^2(4, N=50) = 36,8 p<0.001$ ]. MTHFR C677T polymorphism normal CC genotype frequency was 48% and mutant TT genotype frequency was 12% in the patient group, while 34% and 18% were found in the control group, respectively [ $\chi^2(4, N=50) = 42,5 p<0.001$ ].

### Discussion

Our results show that MTHFR C677T and A1298C variations might have protective effects on kidney cancer. It has been thought that the highly statistically significant association of both polymorphisms in kidney cancer may be effective in assessing the risk of the disease.

**Conclusion:** MTHFR gene C677T and A1298C variants might protect against kidney cancer.

*Keywords: Kidney cancer, MTHFR, C677T, A1298C*

*Note to the Scientific Committee: This work was supported by researchers.*

*Ethics Committee's approval number: 2016/600 (Istanbul University, Istanbul Medical Faculty)*

## POSTER PRESENTATION – 67

### **micro RNA-320 AS A NOVEL POTENTIAL BIOMARKER IN RENAL ISCHEMIA REPERFUSION**

Aydın Güçlü<sup>1</sup>, Cengiz Koçak<sup>2</sup>, Fatma Emel Koçak<sup>3</sup>, Raziye Akçılar<sup>4</sup>, Yavuz Dodurga<sup>5</sup>, Aydın Akçılar<sup>6</sup>, Mücahit Seçme<sup>5</sup>

<sup>1</sup> Department of Nephrology, Ahi Evran School of Medicine, Kırşehir, Turkey;

<sup>2</sup> Department of Pathology, Dumlupınar School of Medicine, Kütahya, Turkey;

<sup>3</sup> Department of Biochemistry, Dumlupınar School of Medicine, Kütahya, Turkey;

<sup>4</sup> Department of Physiology, Dumlupınar School of Medicine, Kütahya, Turkey;

<sup>5</sup> Department of Medical Biology, Pamukkale School of Medicine, Denizli, Turkey;

<sup>6</sup> Experimental Research Unit, Dumlupınar School of Medicine, Kütahya, Turkey

**Background / Aim:** MicroRNAs (miR) are important diagnostic and treatment targets due to their different tissue expressions and their central position in the regulation of gene expressions. miR studies might pioneer emerging of new diagnostic tools and treatment goals in kidney diseases. Captopril (CAP) and telmisartan (TEL) were shown to be effective in ischemia reperfusion (IR) injury. There is not any study about the effect of TEL and CAP over miR-21-320-146a. Our aim was to study the effects of CAP and TEL over miR on renal IR model.

**Materials and Methods:** We used 12–16 weeks-old Wistar-Albino rats that weigh 300–350 g. Rats (n, 6) were randomized into four groups (Control, IR, IR+CAP, IR+TEL). Urea, creatinine, total antioxidant status (TAS), total oxidant status (TOS), oxidative stress index (OSI), super oxide dismutase (SOD), and miRNAs were analyzed.

**Results:** Urea, creatinine, TOS, OSI levels of IR+CAP, and IR+TEL groups were lower comparing to IR group. TAS and SOD levels were higher in IR group than IR+TEL group. miR-21-320-146a showed increase in renal IR injury. miR-320, 146a showed significant decrease in IR+CAP and IR+TEL groups comparing to IR group. We showed histopathological recovery and decreased apoptosis in IR+CAP and IR+T groups than IR group.

**Discussion :** We, for the first time in the literature, showed that miR-320 is increased in IR injury. miR-320 might be a novel diagnosis and treatment target in renal ischemic reperfusion injury.

**Conclusion:** In conclusion, we showed that CAP and TEL therapies decrease miR-146a and -320. Recovery effects of CAP and TEL in renal IR injury might be over miR-146a and miR-320. Furthermore, miR-320 can be a novel potential biomarker in renal ischemia reperfusion.

*Keywords: Renal ischemia-reperfusion (IR) injury; captopril; telmisartan; micro-RNAs; miR-320; miR-21 and miR-146a*  
*Ethics committee approval number: date 04 January 2016, approval number: 2016.01.05*

## POSTER PRESENTATION – 68

### INVESTIGATION OF CRITICAL ANTIOXIDANT ENZYME GENES VARIANTS IN POLYCYSTIC OVARIAN SYNDROME PATIENTS

Ali Osman Arslan<sup>1</sup>, Faruk Celik<sup>1</sup>, Ozlem Küçükhuşeyin<sup>1</sup>, Murat Diramali<sup>2</sup>, Ş. Umit Zeybek<sup>1</sup>, Selma Düzenli<sup>3</sup>, İlhan Yaylim<sup>1</sup>

<sup>1</sup>Department of Medicine, Institute of Aziz Sancar Experimental Medical Research, University of Istanbul, İstanbul

<sup>2</sup>Department of Anatomy, Abant İzzet Baysal University School of Medicine, Bolu

<sup>3</sup>Department of Medical Genetics, Abant İzzet Baysal University Medical faculty, Bolu

Polycystic ovary syndrome (PCOS) is a complex metabolic disease with a chronic course with chronic anovulation and hiperandrogenism, infertility, hirsutism, type 2 DM, endometrium and ovary cancer and affects 5-10% of the women in reproductive age. Oxidative stress has been reported to be a potential risk factor in the etiopathogenesis of PCOS in studies investigating PCOSs relationship with antioxidant enzymes and oxidative stress. Oxidative stress leads to the development of many diseases such as PCOS as a result of the destruction of balance between free radical formation and antioxidant defense mechanism. We aimed to investigate the possible effects of some important antioxidant enzymes and that coding them, such as SOD2 Ala16Val, GPX1 Pro198Leu, NOS3 Glu298Asp and CAT -21A/T on PCOS. Patient and control groups were collected at Abant İzzet Baysal University Obstetrics and Gynecology Department. Peripheral blood of 100 patients with PCOS and 100 healthy control group were collected, DNA isolation and PCR was performed. Subsequently, PCR products were digested with the specific restriction enzymes. After digestion in prepared suitable agarose gels the bands were imaged and analyzed.

In our study there is no significant results for SOD2 gene ( $p=0.512$ ) but the results obtained between GPX1, NOS3 and CAT genes were significant ( $p=0,002$ ,  $p=0,001$ ,  $p=0,031$ ). Also regression analysis was used to evaluate some PKOS risk factors in terms of genes and genotypes. Fasting blood sugar, insulin, triglyceride, waist circumference and DHEAS were found to be significant with disease, whereas FSH was found to be effective in preventing disease. In addition, when the combination of different genotypes of genes was performed, significant results were obtained in the diseases.

As a result of our study, polymorphisms in genes coding GPX1, NOS3 and CAT enzymes were found to be related to PCOS and it is thought that the genes of fasting blood sugar, triglyceride, insulin, DHEAS and waist circumference are important in the pathogenesis of the disease in the presence of homozygous mutation.

*Keywords: PCOS, SOD2, GPX1, CAT, NOS3 and antioxidant*

## POSTER PRESENTATION – 69 INVESTIGATION OF BONE STRUCTURE BY MICRO COMPUTERIZED TOMOGRAPHY IN EXPERIMENTAL DIABETES MODELS

Aycan BAŞ<sup>1</sup>, Gürcan ALBENİZ<sup>2</sup>, Leyla TÜRKER ŞENER<sup>3</sup>, Işıl ALBENİZ<sup>3</sup>

<sup>1</sup>Istanbul Kemerburgaz University, Health Services Vocational School Program of Audiometry, Istanbul

<sup>2</sup>Istanbul University, Cerrahpaşa Faculty of Medicine, Department of General Surgery, Istanbul <sup>3</sup>Istanbul University, Istanbul Faculty of Medicine, Department of Biophysics, Istanbul

**Aim:** Diabetes Mellitus (DM) is a chronic disease which course with acute and chronic complications that affect many different systems within body. Studies of the effect of DM on bone metabolism and bone mineral density (BMD) are available. The aim of our study was to investigate the bone structure and the effect of neuropathy on the BMD in rat type I and type II diabetic models with Streptozotocin (STZ) and STZ + NAD (Nicotinamide) by method of micro computerized tomography (Micro CT).

**Materials and Methods:** 8-month adult Wistar Albino rats were used in the experimental diabetes model. Type I experimental diabetes was generated by giving to 2 rats 60 mg / kg STZ and type II experimental diabetes was generated by giving to 2 rats 60 mg / kg STZ and 130 mg / kg NAD. Rats with glucose levels of 200 mg / dl and above were taken for experiment 48 hours after STZ injection, and femurs were taken under anesthesia after 28 days. With Micro CT, the image matrix was displayed at 652 × 652, voltage 50 kVp, current 800 µA and analyzed with the SkyScan1174v2 soft ware application.

**Results:** Blood sugar values and weights of rats in diabetic experimental groups were measured. When compared with the control group, it was found that the blood sugar values were high and the weights were very low. Type I diabetes group BMD was 29.8% compared to the control group, while Type II diabetes group BMD decreased by 28.5% compared to the control group. When we compare both diabetic models with the control group, after examination of the femurs with Micro CT showed that trabecular bone volumes decreased in a similar manner to BMD.

**Discussion:** It is known that diabetes affects bone metabolism. In Experimental Type I models, there is a reduction in BMD and trabecular bone volume compared to the control group and this result is consistent with the literature. In the experimental type II diabetes model, there is a decrease in BMD and trabecular bone volume compared to the control. There are controversial results in the literature but our results are in concordance with many of the literature reporting that it is declining.

**Conclusion:** After examining Type I and II diabetes induced experimental groups by Micro CT, the changes in terms of trabecular bone structure of rat femur and bone mineral density as against the control group was seen meaning fully.

The ethics committee approval is available of the Istanbul University Animal Experiments Local Ethics Board has dated 13.09.2015 numbered 2015/81.

*Keywords: Diabetes Mellitus, Type I, Type II, Micro CT, Bone mineral density*

## POSTER PRESENTATION – 70

### REAL-TIME IMPEDANCE ANALYSIS OF THE CYTOTOXICITY OF ISOTHIOCYANATE DERIVATIVES ON A549 CELLS

Ayşe Kübra Karaboğa Arslan<sup>1</sup>, Ebru Öztürk<sup>1</sup>, Rüveyde Keleş<sup>2</sup>, Şengül Dilem Doğan<sup>2</sup>, Mükerrerem Betül Yerer<sup>1</sup>

<sup>1</sup>Pharmacology Department, <sup>2</sup>Department of Pharmaceutical Basic Sciences, Faculty of Pharmacy, Erciyes University, Kayseri, 38039, Turkey

**Background:** Isothiocyanate compounds are studied on several cancer cells due to their anti-proliferative, pro-apoptotic properties and limit invasive/metastatic potential of neoplastic cells. The aim of this study was to investigate cytotoxicity of five isothiocyanate derivatives on human lung cancer cell line A549 cells at different doses in real time. These isothiocyanate derivatives have not been previously tested in A549 cell line.

**Materials and methods:** Cytotoxic effects of the isothiocyanate derivatives were monitored with xCELLigence Real-Time Cell Analyser (RTCA). A549 cells were seeded 12.500 cells/well, after then cell proliferation, attachment and spreading were monitored every 15 minutes via the impedance of E-plate wells. Approximately 24 hour post-seeding when the cells were in the log growth phase, the cells were primarily treated with B1, B2, B3, B4 and B5 compounds at 10 nM; 100 nM; 1 µM; 10 µM and 100 µM. Then to examine the exact IC<sub>50</sub> levels 1; 5; 25; 50 and 100 µM concentrations were applied quadruplicated. These experiments were run for 96 hours.

The xCELLigence technology uses electrical well impedance measurements from adherent cells and converts into CI. The RTCA software calculates logarithmic half maximum effect of concentration [log (IC<sub>50</sub>)] values at a given time point based on log concentration producing 50% reduction of CI value relative to the control CI value.

**Results:** According to results, treatment of B4 (at 100 µM) and B5 (at 25, 50, 100 µM) on cells, decreased the cell index comparing to control. B5 decreased the CI more effectively than the other compounds.

**Discussion and conclusion:** The xCELLigence system is a reliable and efficient tool for real-time screening of the cytotoxic effect of compounds in cell-based *in vitro* assays. It is the first study revealing the cytotoxic effects of the novel isothiocyanate derivatives via this xCELLigence technology.

*Keywords:* xCELLigence, A549, isothiocyanate, cytotoxicity

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## POSTER PRESENTATION – 71

### EFFECTS OF BMP1 5'UTR +104 T/C SNP SERUM LIPOPROTEIN AND APO A1 LEVELS IN CORONARY HEART DISEASE

Aysegul Basak Akadam-Teker<sup>1,2</sup>, Erhan Teker<sup>3</sup>, Zehra Bugra<sup>4</sup>, Hulya Yilmaz-Aydogan<sup>1</sup>

<sup>1</sup> Department of Molecular Medicine, Aziz Sancar Institute of Experimental Medicine, Istanbul University, Istanbul, Turkey.

<sup>2</sup> Department of Medical Genetics, Giresun University, School of Medicine, Giresun, Turkey

<sup>3</sup> Department of Cardiology, Prof. Dr. A. İlhan Özdemir Hospital, Giresun, Turkey.

<sup>4</sup> Department of Cardiology, *Istanbul Faculty of Medicine*, Istanbul University, Istanbul, Turkey.

Elevated levels of Apolipoprotein A1 (apoA1) are inversely related to risk of coronary heart disease (CHD). It is secreted as a proprotein and then cleaved by bone morphogenetic protein-1 (BMP-1). BMP-1 stimulates the conversion of newly secreted proapo A1 to its phospholipid-binding form. In this study, it was aimed to determine the role of the 5'UTR +104 T/C gene variant of BMP-1 in the development of CHD and its effects on serum apoA1 levels. This study was carried out using a sample of 131 patients with CHD and 51 controls. BMP1 5'UTR +104 T/C genotype was determined by real-time polymerase chain reaction technique. Serum ApoA1 concentrations were measured by a sandwich ELISA method. This study was supported by a grant from the Scientific Research Projects Coordination Unit of Istanbul University (Project No: 11304).

The serum ApoA1 levels were significantly higher in control subjects with the BMP1 5'UTR +104 rare CC genotype than those with the common T allele ( $p < 0.001$ ). Our findings shows an association of this SNP with serum ApoA1 and HDL-C levels, which was increased in the order of  $CT < TT < CC$  in the controls. In the CHD group, the common TT genotype showed higher serum triglyceride and VLDL-C level than the rare C allele ( $p = 0,009$  and  $p = 0,023$ , respectively). However, we didn't observe any effect of this polymorphism on serum ApoA1 and HDL-C levels in CHD patients, as it was observed in controls. We supposed that this discrepancies could be due to statin therapy. In terms of lipid-lowering effect of statins, its effect on cholesterol levels are more prominent compared to triglyceride levels. In this study, most of the CHD patients (92.6%) were receiving continued statin therapy. The inverse relationship present between serum triglyceride and HDL-C. Therefore, we can conclude that the statin therapy may be cause of different results between study groups with respect to serum ApoA1 level and triglyceride.

In conclusion, an increasing effect of the BMP-1 5'UTR rare CC genotype was shown on serum ApoA1 levels in controls, while wild type TT genotype was associated with elevated triglyceride level in CHD group. Our results suggested that the BMP-1 5'UTR +104 T/C polymorphism might be associated with serum lipids in male CHD patients.

## POSTER PRESENTATION – 72

### DOES LIPOIC ACID PREVENT VALPROIC ACID INDUCED OXIDATIVE STRESS IN LUNG?

Burcin Alev Tuzuner<sup>1</sup>, Ismet Burcu Turkyilmaz<sup>2</sup>, Hazal Ipekci<sup>1</sup>, Unsal Veli Ustundag<sup>1</sup>, Tugba Tunali-Akbay<sup>1</sup>, Ebru Emekli-Alturfan<sup>1</sup>, Refiye Yanardag<sup>2</sup>, Aysen Yarat<sup>1</sup>

<sup>1</sup>Department of Basic Medical Sciences, Biochemistry, Faculty of Dentistry, Marmara University, Maltepe, Istanbul

<sup>2</sup>Department of Chemistry, Faculty of Engineering, Istanbul University, Avcilar, Istanbul; Turkey

**Background:** Alpha lipoic acid (LA) exerts its antioxidant effects through its high reactivity to free radicals that facilitates vitamins C and E regeneration. Valproic acid (VPA) is an antiepileptic drug that has some adverse effects on tissues as it impairs the oxidant-antioxidant balance.

**Aim:** The aim of this study was to investigate the putative protective role of LA on rat lung in VPA induced oxidative stress.

**Method:** Rats were randomly divided into four groups as follows: Olive oil given control group (1mL, gavage); LA given group (50 mg/kg/day, gavage); VPA given group (500mg/kg/day, ip) and VPA+LA given group (in same doses). LA was given 1 h prior VPA administration. 16 days after VPA injection, rats were decapitated and lung samples were taken and homogenized. For biochemical analysis, glutathione (GSH), malondialdehyde (MDA), nitric oxide (NO) levels, glutathione-S-transferase (GST), superoxide dismutase (SOD) and catalase (CAT) activities were determined in 10% (w/v) lung homogenates.

**Results:** Lung GSH level and SOD activity decreased and MDA, NO levels increased significantly in the VPA group when compared with control group. In the VPA group, LA administration caused significant increases in GSH, MDA levels, SOD activity. No significant changes were observed in GST and CAT activities.

**Conclusion:** Based on these results we suggest that LA might prevent VPA induced oxidative stress in lung.

*Keywords: Lung, valproic acid, alpha lipoic acid, antioxidant-oxidant parameters*

## POSTER PRESENTATION – 73

### EVALUATION OF THE ROLE OF MMP-9 GENE rs3918242 AND TIMP-2 GENE rs8179090 VARIATIONS IN RENAL CELL CARCINOMA

Burcu Çaykara<sup>1</sup>, Hani Alsaadoni<sup>1</sup>, Alper Ötünçtemur<sup>2</sup>, Sadrettin Pençe<sup>3</sup>

<sup>1</sup> Istanbul University, Aziz Sancar Institute of Experimental Medicine (ASDETAE), Department of Molecular Medicine, Istanbul

<sup>2</sup> Okmeydani Education and Research Hospital, Department of Urology, Istanbul

<sup>3</sup> University of Health Sciences, Faculty of Medicine, Department of Physiology, Istanbul

**Background:** Matrix metalloproteinases (MMP), cell surface enzymes whose main functions are extracellular matrix degradation. The proteolytic activities of matrix metalloproteinases can be specifically inhibited by matrix metalloproteinase tissue inhibitors (TIMP). They bind irreversibly and non-covalently to MMPs and inhibit the activation of the latent enzyme form and the maintenance of catalytic activity. There are four types of TIMPs identified in humans to date, namely TIMP-1, TIMP-2, TIMP-3 and TIMP-4. Disruption of this balance between MMP and TIMPs may lead to the emergence of pathological processes. We aimed to determine the MMP-9 and TIMP-2 gene variation in renal cell carcinoma cases.

**Material –Method:** In our study, 50 tumors and 50 non-tumor surrounding tissues were obtained from the patients who were diagnosed with renal cancer at SB Okmeydani Training and Research Hospital. The specimens were treated with liquid nitrogen and stored at -80 °C until isolation was made at IU ASDETAE Department of Molecular Medicine. DNA was isolated from the tissues by DNA isolation kit and the amount of DNA was measured at 280 nm. PCR was performed with appropriate primers and samples examined by RFLP method and visualized under UV light. The genotype and allele distributions analyzed by statistical analysis (SPSS18).

**Results:** In the MMP-9 rs3918242 variation, the normal C allele frequency was 47% and the rare T frequency was 53% in the patient group, while 79% and 21% were found in the control group, respectively ( $p < 0.001$ ). MMP-9 rs3918242 TT genotype was found statically significant in patient group than in the control group [ $X^2 (4, N=50) = 10,29 p=0.036$ ]. TIMP-2 rs8179090 variation, the normal C allele frequency was 80% and the rare T frequency was 20% in the patient group, while 93% and 7% were found in the control group, respectively ( $p < 0.001$ ).

**Discussion:** In addition to other risk factors, MMP-9 rs3918242 TT genotype may be considered as an predictive marker for the investigation of renal cell carcinoma risk in individuals in Turkey. Furthermore, higher rate of TIMP-2 rs8179090 C allele in the tumor tissues ( $p < 0,001$ ) than in the control tissues may be considered that contribute to the formation of renal cell carcinoma, but it needs to be validated by more studies.

**Conclusion:** MMP-9 gene rs3918242 and TIMP-2 gene rs8179090 variants may be effective in susceptibility renal cell carcinoma.

*Keywords: Renal cell carcinoma, MMP-9, TIMP-2, rs3918242, rs8179090*

*Note to the Scientific Committee: This work was supported by researchers.*

## POSTER PRESENTATION – 74

### EVALUATION OF CD3<sup>+</sup>CD56<sup>+</sup> NKT CELLS IN PATIENTS WITH TYPE 1 AND TYPE 2 DIABETES MELLITUS

Cagdas Ugur Adas<sup>1,3</sup>, Abdullah Yilmaz<sup>1</sup>, Ilhan Satman<sup>2</sup>, Gunnur Deniz<sup>1</sup>, Ali Osman Gurol<sup>1,3</sup>, M. Temel Yilmaz<sup>1,2,3</sup>

<sup>1</sup> Istanbul University, Aziz Sancar Institute of Experimental Medicine, Department of Immunology, Istanbul

<sup>2</sup> Istanbul University, Istanbul Medicine Faculty, Department of Endocrinology and Metabolism Diseases, Istanbul

<sup>3</sup> Istanbul University, Diabetes Application and Research Center (DIYAM), Istanbul

Diabetes mellitus (DM) is a metabolic disease linked to pathogenic mechanisms leading to pancreatic beta cell damage and insulin resistance. CD3<sup>+</sup>CD56<sup>+</sup> Natural Killer T cells (NKT) and their cytokine secretions are thought to have roles in pathogenesis of DM. Their frequencies are claimed to change in relation with disease progression while they are thought to be contributors of immune attack to pancreatic beta cells.

Heparinised venous blood samples (10 ml) were drawn from patients with type-1 DM (n=10), type-2 DM (n=10) and healthy controls (n=10). The mean age of the patients with type-1 DM and type-2 DM were 30.0±7.0 years (3 males-7 females), 45.9±10.2 years (3 males-7 females), respectively. None of the healthy controls had history of DM or other chronic and autoimmune disease, and their mean age was 34.1±10.9 (3 males-7 females).

Peripheral blood mononuclear cells (PBMCs) were isolated using Ficoll-gradient centrifugation from whole blood. PBMCs were incubated with the absence and presence of IL-2 (20 ng/ml) for 24 hours at 37<sup>0</sup>C with 5% CO<sub>2</sub>, and Brefeldin A (3 µg/ml) was added 4 hours before the end of the incubation of PBMCs. After 24 hours, cells were harvested and stained for surface molecule expressions of CD3, CD56. In addition, the intracellular staining was performed for the expression of IFN-γ and IL-17. Expression of cell surface and intracellular markers was assessed using flow cytometry, and data were analyzed by FACSDiva software (BD, FACS Aria II, USA).

Frequencies of CD3<sup>+</sup>CD56<sup>+</sup> NKT cells in patients with type 1 DM were significantly lower than both patients with type 2 DM and healthy controls (p= 0.02 and 0.04, respectively). Also cytokines frequencies of these cells for IFN-g and IL-17 were significantly increased in patients with type 1 DM compared to healthy controls (p=0.05; IFN-g, p=0,03; IL-17). These results show that NKT cells and their frequencies of IFN-g and IL-17 cytokines may have roles in pathogenesis of DM.

The study followed the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Clinical Researches of the Istanbul Medicine Faculty of Istanbul University (Decision No:14).

*Keywords: Diabetes, NKT cells, IFN-g, IL-17*

*Note to the Scientific Committee: This Project was supported by the Research Fund of Istanbul University (Project No:26847).*

## POSTER PRESENTATION – 75 CONGENITAL DYSERYTHROPOIETIC ANEMIA TYPE II CASE REPORT

Cansu KARA ÖZTABAĞ<sup>1</sup>, Selma DÜZENLİ<sup>1</sup>

<sup>1</sup>Abant İzzet Baysal University, Medical Faculty, Department Of Medical Genetics, Bolu, TURKEY.

Congenital Dyserythropoietic Anemia (CDA) type II is an autosomal recessive disorder associated with morphological and functional abnormalities of erythropoiesis, which is a rare disease. Several hundred cases of CDA have been reported worldwide. Three forms became well known (I-III). CDA II is the most common type, with more than 300 reported cases. CDA type II is usually diagnosed in adolescence or early adulthood. Bone marrow is characterized by presence of binucleated or multinucleated normoblasts in CDA II patients. Mutations in the SEC23B gene on chromosome 20p11.23 cause the vast majority of the CDA type II (OMIM 224100). Approximately 60 different causative mutations have been described, localized along the entire coding sequence of the gene. Our aim is to introduce a CDA type II patient with the rare p.Glu109Lys (c.325G>A) and p.Arg313His(c.938G>A) compound heterozygous mutations.

Our patient is a 15 year old girl. She is suffering from anemia, weakness and pale skin. Her biochemical analysis revealed RBC 2,34 HGB 7,2 RDW 16,7 and reticulocyte count 0,0565. Patient's sister has the same diagnosis and same mutations. Her mother has anemia and the p.Glu109Lys (c.325G>A) heterozygous mutation. Her father has a p.Arg313His(c.938G>A) heterozygous mutations, but he hasn't got any symptoms.

First, chromosome analysis was made with her bone marrow and only 9 of 20 were observed as 46,XX chromosomal structures. So, we decided to do differential diagnosis with CDA type II. After DNA extraction, SEC23B gene mutation analysis was applied by PCR methods.

Homozygous or compound heterozygous SEC23B mutations in humans result in CDA II. We tested the SEC23B gene mutation, and found p.Glu109Lys (c.325G>A) heterozygous and p.Arg313His(c.938G>A) heterozygous mutations. The patient was compound heterozygous for two mutations. These mutations cause different symptoms. For instance, the mother with the p.Glu109Lys (c.325G>A) heterozygous mutation has anemia. On the other hand mutation of the father doesn't cause any symptoms. So, one can postulate that p.Glu109Lys (c.325G>A) heterozygous mutation but, not the other mutation induces anemia in the patients.

*Keywords: Congenital Dyserythropoietic Anemia type II; SEC23B p.Glu109Lys (c.325G>A) and p.Arg313His(c.938G>A)*

## POSTER PRESENTATION – 76

### THE INFLUENCE OF CYP2C9 AND VKORC1 POLYMORPHISMS ON WARFARIN DOSING IN PATIENTS WITH DEEP VEIN THROMBOSIS

Cansu KARA ÖZTABAĞ<sup>1</sup>, Selma DÜZENLİ<sup>1</sup>, Ali Akçahan Gepdiremen<sup>2</sup>

<sup>1</sup>Abant İzzet Baysal University, Medical Faculty, Department of Genetics, Bolu, TURKEY

<sup>2</sup>Bezmialem University, Medical Faculty, Department of Pharmacology, İstanbul, TURKEY

Deep vein thrombosis (DVT) is the blockage of a deep vein by a clot, in the upper or lower extremities. The significant danger of DVT is that it can lead to pulmonary embolism (PE). DVT treatment starts with anticoagulant drugs, and continues with warfarin. The optimum dosage that the patients need show a wide range, because, besides of the patients life style, warfarin's pharmacokinetic and pharmacodynamic features are affected by many factors. One of them is genetics. The enzymes' synthesis rate and/or quality is affected by several genes. Additionally, these enzymes show genetic polymorphism. Among these genes VKORC1 (Vitamin K Epoxide Reductase Complex Subunit 1) and CYP2C9 (Cytochromes P450), which are responsible for warfarin metabolism, are significant. Because, warfarin's metabolizers phenotypes are determined by these two genes and are classified as extensive metabolizer, intermediate metabolizer and slow metabolizer. For this reason, we tested 90 cases with DVT. In our study, the most common warfarin metabolizer phenotype is extensive metabolizer with a rate of 48.8%, while slow metabolizer is the least observed with a percentage of 12.2%. It has been shown that being aware of the genotypes of these two genes is useful for determining a close initial dose of warfarin. So, the patient's INR (international normalized ratio) stabilization is more rapid and the balance between the prevention of clotting and the risk of overbleeding is made quicker. Our aim was to reveal the benefit of knowing the metabolizer status and the effect of this two genes (CYP2C9 and VKORC1) in Turkish patients.

The results of our study, and further studies with Turkish population, will give an important clue about the distribution of the warfarin dosage genes' polymorphisms. More important, is that our study shows the necessity of genotyping patients before initial dose of warfarin injection.

*Keywords: Deep Vein Thrombosis, DVT, Warfarin, VKORC1, CYP2C9, individualized medicine, pharmacogenetics*

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*Projemiz AİBÜ BAP birimi tarafından desteklenmiştir.*

## POSTER PRESENTATION – 77

### STUDY ON POLYMORPHIC VARIANT +294T/C SNP OF *PPAR-B/D* AND SERUM OXIDIZED-LDL LEVELS IN CORONARY HEART DISEASE

Deniz Kanca<sup>1,2</sup>, Ozlem Kurnaz-Gömlüksiz<sup>2</sup>, AtikeTekeli<sup>3</sup>, Oguz Ozturk<sup>1</sup>, Hulya Yilmaz-Aydogan<sup>1</sup>

<sup>1</sup> Department of Molecular Medicine, Aziz Sancar Institute for Experimental Medicine, Istanbul University, Istanbul, Turkey.

<sup>2</sup> Department of Molecular Biology and Genetics, Faculty of Science and Arts, Halic University, Istanbul, Turkey.

<sup>3</sup> Department of Cardiovascular Surgery, Marmara University School of Medicine, Istanbul, Turkey.

Elevated level of oxidized products of low-density lipoprotein (LDL) is a very well established risk factor of coronary heart disease (CHD). The susceptibility of LDL to oxidation shows noticeable differences between individuals. These differences may be due to the manifestation of characteristic properties of LDL, determined at least in part by genetic factors. Peroxisome proliferator-activated receptors (PPARs) are nuclear transcription factors involved in the regulation of lipid and glucose metabolism. The family includes PPAR-alpha, PPAR-gamma, and PPAR-beta/delta (PPARB/D). PPAR-B/D is ubiquitously expressed and has a pivotal role in the fatty acid catabolism. It was discovered that PPAR-B/D activates the oxidation of fatty acid by increasing the expression of genes involved in utilization of fatty acid in heart and skeletal muscles. Furthermore, treatment of skeletal muscle cells with the PPAR-B/D agonists in vitro induces the expression of genes for fatty acid catabolism and promotes fatty acid oxidation. Previous studies reported an association between the rare +294 C allele of 5'-UTR +294T/C SNP of the *PPAR-B/D* gene and cardiovascular risk factors such as increased LDL-C levels and decreased levels of HDL-C. Therefore, we aimed to evaluate the potential contribution of 5'-UTR +294T/C SNP of the *PPAR-B/D* gene to serum ox-LDL levels in the development of CHD in the present study.

A total of 44 CHD patients diagnosed with at Marmara University, Department of Cardiovascular Surgery, Istanbul, and 32 healthy volunteers as controls were included in this study. Oxidized-LDL levels were measured with Elisa method (OLAB, Biomedica). The +294T/C SNP of the *PPAR B/D* gene were detected by PCR-RFLP method.

Genotypic and allelic distribution of *PPARB/D*+294T/C SNP (*rs2016520*) was consistent with the Hardy-Weinberg Equilibrium (HWE) in study groups ( $p>0.05$ ). The serum HDL-cholesterol levels were higher in *PPARB/D*- +294C allele carriers in control group ( $p=0.05$ ). However, this association was not observed in the CHD group ( $p>0.05$ ). In the CHD patients, subjects with the *PPAR-B/D* +294C allele (CC+CT genotypes) have showed a lower serum oxidized-LDL concentrations than with the *PPAR-B/D* +294TT homozygote genotype ( $226.75\pm 20.74$  vs.  $388.96\pm 73.26$ ,  $p=0.043$ ).

The findings in this study suggest that *PPAR-B/D* +294T/C SNP and the interaction of oxidized-LDL are associated with the risk of CHD development.

**Keywords:** *PPAR-B/D* ; +294T/C SNP ; ox-LDL, CHD

"This work was supported by Scientific Research Projects Coordination Unit of Istanbul University. Project number 946."

## POSTER PRESENTATION – 78

### **RHO KINASE INHIBITOR, FASUDIL INHIBITS NF- $\kappa$ B SIGNALING PATHWAY IN LUNG CANCER CELL LINE A549**

H. Malik OKUYAN<sup>1</sup>, Meral URHAN KÜÇÜK<sup>2</sup>, Cansu ÖNLEN<sup>1</sup>, Dilara SÖNMEZ<sup>4,5</sup>, Menderes Yusuf TERZİ<sup>2</sup>, Sedat KOÇAL<sup>3</sup>, Kerem KARAASLAN<sup>3</sup>, Tülin DURGUN YETİM<sup>3</sup>

<sup>1</sup>Mustafa Kemal University, Hatay Vocational School of Health Services, Hatay, Turkey

<sup>2</sup>Mustafa Kemal University, Medical Faculty, Department of Medical Biology, Hatay, Turkey

<sup>3</sup>Mustafa Kemal University, Medical Faculty, Department of Thoracic Surgery, Hatay, Turkey

<sup>4</sup>Mustafa Kemal University, Health Sciences Institute, Department of Molecular Biochemistry and Genetics, Hatay, Turkey

<sup>5</sup>Istanbul University, Institute of Aziz Sancar Experimental Medicine Research, Department of Molecular Medicine, Istanbul, Turkey

**Background/Aim:** Lung cancer is the leading cause of cancer origin deaths worldwide, with over a million deaths annually. The lack of effective treatments against lung cancer is the primary reason of high mortality rates. The nuclear factor kappa B (NF- $\kappa$ B) signaling pathway is involved in the lung cancer. The contribution of NF- $\kappa$ B to the lung cancer development is a complex process, and the underlying mechanisms of the NF- $\kappa$ B pathway have not been fully understood. Rho kinases play key roles in numerous important physiological functions such as cell proliferation, cell adhesion, migration, inflammatory responses of cells. Therefore, in our study, we aimed to have more knowledge about the pathophysiology of lung cancer by determining the effects of fasudil on NF- $\kappa$ B signaling pathway by using adenocarcinoma of the alveolar type II pneumocytes cell line (A549).

**Materials and Methods:** In the present study, A549 cell line was treated with IL-1 $\beta$  and fasudil (3 ng/ml, 50  $\mu$ M, respectively). Total RNA was isolated from cell cultures and the expression levels of NF- $\kappa$ B1, MAPK3, and MMP1 were analyzed with the real time qRT-PCR.

**Results:** Our results show that fasudil down-regulates the expression levels of NF- $\kappa$ B1, MAPK3, and MMP1 stimulated by IL-1 $\beta$ .

**Discussion:** Based on the multifunctional characteristic of Rho kinases, several studies showed the beneficial effects of Rho-kinase inhibitors in the animal models of some diseases such as glaucoma, Alzheimer's disease, diabetes, osteoporosis and cancer. Recent studies suggest that Rho kinase inhibitor, Fasudil, inhibits the activation of NF- $\kappa$ B signaling in fibroblast-like synoviocytes. However, the effect and the precise molecular mechanism of fasudil on A549 remain unclear. In the present study we investigated for the first time the effect of fasudil on NF- $\kappa$ B pathway in A549 cell line.

**Conclusion:** Our study provides sound evidence that inhibition of NF- $\kappa$ B with fasudil may be a potential therapeutic strategy for the treatment of the lung cancer. Further studies are needed to understand the underlying mechanisms of lung cancer concerning the downstream effects of the fasudil.

*Keywords:* Lung Cancer, A549, NF- $\kappa$ B1, Fasudil

*Note to the Scientific Committee:* This study was supported financially with the grant of the "Scientific Research Projects" in Mustafa Kemal University.



## POSTER PRESENTATION – 79

### MGP AS A NOVEL MOLECULAR TARGET IN OSTEOARTHRITIS

H. Malik OKUYAN<sup>1</sup>, Ahmet ARSLAN<sup>2</sup>, Menderes Y. Terzi<sup>3</sup>, Dilara SÖNMEZ<sup>4,5</sup>, Kübra Gündüz<sup>4</sup> Nilüfer BİLGİÇ<sup>4</sup>

<sup>1</sup>Mustafa Kemal University, Hatay Vocational School of Health Services, Hatay, Turkey

<sup>2</sup>Gaziantep University, Faculty of Medicine, Department of Medical Biology, Gaziantep, Turkey

<sup>3</sup>Mustafa Kemal University, Faculty of Medicine, Department of Medical Biology, Hatay, Turkey

<sup>4</sup>Mustafa Kemal University, Health Sciences Institute, Department of Molecular Biochemistry and Genetics, Hatay, Turkey

<sup>5</sup>Istanbul University, Institute of Aziz Sancar Experimental Medicine Research, Department of Molecular Medicine, İstanbul, Turkey

**Background / Aim:** Osteoarthritis (OA) is a common degenerative disease in the world and characterized by cartilage loss, inflammation, cellular changes, osteophyte formation, and extracellular matrix mineralization. The current therapy of OA has limited efficiency. Although OA is the most common articular pathology worldwide, the OA pathogenesis could not be enlightened completely so far. The understanding of the OA pathophysiology guides us to identify novel therapeutic agents for treatment and prevention. Matrix Gla protein (MGP) is a member of the growing family of vitamin K-dependent proteins, and the molecular function of MGP is yet fully unknown in OA. Recent studies have suggested that MGP may be associated with OA pathology. In the present study we aimed to investigate the role of MGP in OA by using an OA model of osteoblast (hFOB1.19) culture.

**Materials and Methods:** In our study, hFOB1.19 cell line was stimulated with IL-1 $\beta$  (5 and 10 ng/ml, for 48 and 72 hours) for *in vitro* OA model. Total RNA was isolated from the cell cultures and the expression levels of the MGP and the OA related genes (RANKL, OPG, MMP1, and BGLAP) were analyzed with the real time qRT-PCR.

**Results:** Our results indicated that the expression level of MGP significantly increased in hFOB1.19 cells. Also, OA-related genes (RANKL, OPG, MMP1, and BGLAP) showed a positive correlation with the MGP expression level.

**Discussion:** Here, we tested whether the MGP level is associated with the molecules involved in OA pathophysiology. MGP is a calcification inhibitor and an important molecule for OA. It was shown in another study that the expression levels of MMP1, RANKL and OPG are aberrant in OA patients. And also, we found in our study that MGP expression level is closely associated with the expression levels of MMP1, RANKL and OPG. Besides, MGP and BGLAP have similar structural features and both are involved in the bone mineralization. In this respect, we checked if there is any connection between these two molecules and we found that the level of MGP was associated with BGLAP in IL-1 $\beta$  induced hFOB1.19 cells.

**Conclusion:** Our study provides evidence that MGP may be a novel molecular target for OA treatment. Further studies are needed to understand mechanisms underlying OA pathogenesis concerning the role of MGP.

*Keywords: MGP, Osteoarthritis, Osteoblast*

## POSTER PRESENTATION – 80

### THE REAL TIME CYTOTOXICITY OF OXADIAZOLE DERIVATIVES ON MCF-7 CELLS

Ebru Öztürk<sup>1</sup>, Tuğçe Özyazıcı<sup>2</sup>, Marva Bader<sup>2</sup>, Mükerrer Betül Yerer<sup>1</sup>, Meriç Köksal Akkoç<sup>2</sup>

<sup>1</sup>Erciyes University, Faculty of Pharmacy, Department of Pharmacology, Kayseri/Turkey

<sup>2</sup>Yeditepe University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, İstanbul/Turkey

**Background :** Breast cancer has become the most prevalent cancer and the leading cause of death among females worldwide. In spite of most patients present with early disease and are treated with surgery, often followed by adjuvant radiotherapy and chemotherapy. Nevertheless, some patients treated with adjuvant chemotherapy ultimately relapse due to drug resistance. In this study, we aim to investigate the cytotoxic effects of novel oxadiazole derivatives on MCF-7 human breast cancer cell line.

**Materials and Methods:** Five different original oxadiazole derivatives were synthesized in Yeditepe University Department of Pharmaceutical Chemistry. To investigate the cytotoxic effects of these molecules MCF-7 was chosen and xCELLigence system was used for determination. Optimal seeding concentration of MCF-7 cells were determined and cell proliferation, attachment and spreading were monitored every 15mins via the impedance of E-plate wells. 5.000 cells/well were seeded and approximately 24h post-seeding when the cells were in the log growth phase, the cells were treated with oxadiazole derivatives (MB<sub>2,6,7,8,9</sub>: 10nM, 100nM, 1µM, 10µM, 100µM). Cell viability was observed during 48 hours after treatment and IC50 values have been calculated via xCELLigence software.

**Results and Discussion:** Cytotoxic effects of five novel oxadiazole derivatives (MB<sub>2</sub>, MB<sub>6</sub>, MB<sub>7</sub>, MB<sub>8</sub>, MB<sub>9</sub>) on MCF-7 determined with xCELLigence system at 24 and 48 hours. According to results, IC50 values in 24<sup>th</sup> and 48<sup>th</sup> hours are respectively; IC50<sub>MB2</sub>:73.8 µM and 89.3 µM, IC50<sub>MB6</sub>:22 µM and 32 µM, IC50<sub>MB7</sub>:30 µM and 32.8 µM, IC50<sub>MB8</sub>:81.5 µM and 95.4 µM, IC50<sub>MB9</sub>:190 mM and 1500 mM. According to these information; MB<sub>2</sub> and MB<sub>9</sub> have cytotoxic effects. The effects of MB<sub>9</sub> are lately seen with high concentration. MB<sub>7</sub> and MB<sub>8</sub> might be anti-proliferative with high concentration. MB<sub>6</sub> has no cytotoxic and anti-proliferative effect.

**Conclusion:** These novel molecules and data provide new information for anticancer studies. In further studies, we are planning to improve our research with identifying the action mechanisms of these compounds on MCF-7 cells.

*Keywords: xCELLigence, MCF-7, cytotoxicity, oxadiazole derivatives, breast cancer*

*\* This study is financially supported by TÜBİTAK (3001-215S157 coded project).*

## POSTER PRESENTATION – 81

### **PREDICTIVE POWER OF MEAN UTERINE ARTERY PULSATILITY INDEX, MATERNAL SERUM PLACENTAL GROWTH FACTOR AND PLACENTA ASSOCIATED PLASMA PROTEIN A LEVELS FOR THE DEVELOPMENT OF ISCHEMIC PLACENTAL DISEASES**

Gulnar Nuriyeva<sup>1</sup>, Semir Kose<sup>2</sup>, Gamze Tuna<sup>3</sup>, Melis Kant<sup>4</sup>, Merve Akis<sup>4</sup>, Sabahattin Altunyurt<sup>2</sup>, Gül Huray Islekel<sup>3,4</sup>, Omer Erbil Dogan<sup>1</sup>

<sup>1</sup> Department of Obstetrics and Gynecology, Dokuz Eylul University School of Medicine, Izmir, Turkey

<sup>2</sup> Division of Perinatology, Department of Obstetrics and Gynecology, Dokuz Eylul University School of Medicine, Izmir, Turkey

<sup>3</sup> Department of Molecular Medicine, Dokuz Eylul University, Institute of Health Sciences, Izmir, Turkey

<sup>4</sup> Department of Medical Biochemistry, Dokuz Eylul University, Institute of Health Sciences, Izmir, Turkey

**Background:** The combination of biophysical and biochemical markers of the uteroplacental perfusion provides a good starting point for selecting a group of pregnancies at high risk for the development of ischemic placental diseases during the first trimester combined test (FTCT) period. The aim of the study is to assess the predictive power of mean uterine artery pulsatility index (Ut A PI), maternal serum PIGF and placenta associated plasma protein A (PAPP-A) levels for the development of ischemic placental diseases (IPD) in a cohort of unselected singleton pregnancies during the FTCT period.

**Materials and Methods:** A sample of 880 pregnancies was registered between September 2014 and January 2016. After routine examination for FTCT, Ut A PI was measured, and maternal serum was obtained and stored at -80°C for PIGF assessment.

**Results:** Early onset preeclampsia, late-onset preeclampsia and placental dysfunction related fetal growth restriction (PD-FGR) were observed in 6 (0.7%), 17 (2.0%) and 27 (3.2%) cases, respectively. IPD requiring delivery before 34 weeks of gestation could be predicted with a sensitivity, specificity, positive predictive value and negative predictive value of 76.2%, 90.2%, 20.2% and 99.1%, respectively.

**Discussion:** Since the PAPP-A is a routine part of the FTCT, some groups have studied the predictive power of the Ut A PI and PAPP-A combination and the sensitivity was limited. The PIGF value seems to be more sensitive to the cases with restricted fetal growth than the PAPP-A. Previous studies have reported low levels of PIGF in the circulation of women with FGR without preeclampsia, and these findings lead to the definition of placental FGR. In our study, PIGF levels were low in 24/27 (88.9%) of PD-FGR cases, and this high sensitivity contributed to the prediction of IPD.

**Conclusion:** A combination of Ut A PI, PAPP-A and PIGF was proven to be successful in the first trimester prediction of IPD, with the highest sensitivity in the subgroup who required delivery before 34 weeks of gestation.

*Keywords:* Ischemic placental disease, placenta associated plasma protein A, placental growth factor, uterine artery pulsatility index

*Note to the Scientific Committee:* This research was supported by a grant from Dokuz Eylul University Scientific Research Projects Coordination Unit. The study was approved by our Institutional Ethical Committee (2014/25-26 1643-GOA).

## POSTER PRESENTATION – 82 THE EFFECTS OF GAMMA RADIATION AND HYPOBARIC CONDITIONS AND INVESTIGATION OF CDK GENES EXPRESSION *IN VITRO*

Gizem Akman<sup>1</sup>, Songül Çavdar Karaçam<sup>2</sup>, Gül Özcan<sup>1</sup>

<sup>1</sup> Istanbul University, Science Faculty, Biology Department, Vezneciler, İstanbul

<sup>2</sup> Istanbul University, Cerrahpaşa Medical Faculty, Radiation Oncology Division, Cerrahpaşa, İstanbul

**Background/Aim:** Gamma radiation has an important place in cancer treatment by harming the DNA's of cancer cells. Hypobaric stress conditions, which is a new topic for clinical trials, via creating hypoxia in cells, forms free radicals and harms the cells. It is significant to inhibit the cell cycles to stop cell division and encourage their death for the efficacy of the treatment. In this study, we aimed to show the effect of gamma radiation and hypobaric stress conditions when applied one by one and together, and the role of CDK genes in this effect.

**Materials and Methods:** The cytotoxic activities of HeLa cells which were exposed to 32 Gy gamma radiation which is also known as IC50 dose and hypobaric stress conditions were examined via MTT method, after 0 and 24 hours of incubation. The morphological changes were examined under phase-contrast and light microscopies. To detect the expression levels of cyclin dependent kinase genes, *cyclin A*, *cyclin E* and *p21* genes were examined via RT-PCR.

**Results:** In this study, under 32 Gy gamma radiation and hypobaric stress conditions, it was determined that cytotoxicity of HeLa cells was statistically significant according to control group ( $p < 0.01$ ). In the end of 0 and 24 hours of incubation, HeLa cells group it was observed that only *cyclin A* gene was expressed and expression decreased according to the control group under hypobaric stress conditions, also under hypobaric stress conditions and gamma radiation.

**Discussion:** Understanding of cell cycle's mechanisms and molecules and also cell cycle checkpoints, leads to increase the effectiveness of the treatment. For that reason, it is important that our experiment revealed gamma radiation and hypobaric stress conditions proved its effectiveness in cellular and molecular level, which would elicit an increase of the current cancer treatment, also developing new treatments.

**Conclusion:** As a result of this study, it was determined that co-administration of gamma radiation and hypobaric stress conditions to HeLa cell cultures resulted in the highest cytotoxic effect, and that this effect was reduced only at the expression level of the cyclin gene. It is important to understand the effect of the gamma radiation which is often used in cancer treatment in combination with hypobaric stress conditions for creating new treatment strategies.

*Keywords:* Gamma radiation, hypobaric stress, cyclin dependent kinase, HeLa cells

*Note to the Scientific Committee:* This work was supported by Scientific Research Projects Coordination Unit of Istanbul University. Project number 25680.

## POSTER PRESENTATION – 83

### ANTI-PROLIFERATIVE EFFECT OF NOVEL SYNTHESIZED CU(II) COMPLEX WITH 3-(3-(4-FLUOROPHENYL) TRIAZ-1-EN-1-YL) BENZENESULFONAMIDE ON COMMON GYNECOLOGICAL CANCER CELL LINES

Yasin Tuluçe<sup>1</sup>, Gokhan Gorgisen<sup>1</sup>, I. Musab Gulacar<sup>1</sup>, Ismail Koyuncu<sup>2</sup>, Mustafa Durgun<sup>3</sup>, Suleyman AKOCAK<sup>4</sup>, Halil Ozkol<sup>1</sup>, Zehra Kaya<sup>1</sup>

<sup>1</sup> Yuzuncu Yil University, Faculty of Medicine, Department of Medical Biology, Van, Turkey

<sup>2</sup> Harran University, Faculty of Medicine, Department of Biochemistry, Sanliurfa, Turkey

<sup>3</sup> Harran University, Faculty of Arts and Sciences, Department of Chemistry, Sanliurfa, Turkey

<sup>4</sup> Adiyaman University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Adiyaman, Turkey

**Background / Aim:** Chemotherapy alone or combine with radiotherapy is used as adjuvant treatment for cancer. Unfortunately, these treatment options have lots of side effects and they are often ineffective due to the development of resistance in cancer cell. Therefore, developing new anti-cancer agents is crucial for cancer treatment. In this perspective, some triazine derivatives, their complexes and Copper (II) have anti-carcinogenic effects on the cancer cells. In this study, we aim to determine the anti-proliferative effect of novel synthesized Cu (II) complex with 3-(3-(4-fluorophenyl) triaz-1-en-1-yl) benzenesulfonamide compound on common female cancer cell lines such as HeLa, MDA-MB-231, A2780 and MCF7.

**Materials and Methods:** HeLa, MDA-MB-231, A2780 MCF7 cells lines were grown in DMEM supplemented with 10% FBS, 100 mg/ml penicillin, 50 mg/ml streptomycin, and 1 mM glutamine. HeLa, MDA-MB-231, A2780 MCF7 cells were plated at a density of 5 thousand cells per well in a 96-well microtiter plates with 3 replicates. Then they were treated with different concentrations (0, 2  $\mu$ M, 5  $\mu$ M, 10  $\mu$ M, 25  $\mu$ M, 50  $\mu$ M, 100  $\mu$ M, 200  $\mu$ M) of the compound and vehicle (DMSO) for 48 hours. The MTT assay was used to test for the viability of the treated cells.

**Results:** Our results showed that Cu (II) complex with 3-(3-(4-fluorophenyl) triaz-1-en-1-yl) benzenesulfonamide compound exerted significant anti-proliferative effects at 50  $\mu$ M concentrations on common female cancers cell lines.

**Conclusion:** Our preliminary results suggest that the Copper complex is able to suppress the proliferation of the common gynecological cancer cell lines. It will be a possible candidate for cancer treatment studies but its genotoxic and apoptotic activities need to be determined by further studies.

*Keywords: Gynecological cancers, apoptosis, Copper (II), anti-cancer agents, cytotoxicity*

POSTER PRESENTATION – 84  
**ANTIPROLIFERATIVE ACTIVITY OF HYPOBARIC CONDITIONS AND  
EVALUATION OF Bcl-2 GENE EXPRESSION ON HeLa CELLS**

Gül Özcan<sup>1</sup>, Walid Khalilia<sup>2</sup>, Uğur Serbes<sup>2</sup>, Gizem Akman<sup>1</sup>, İdil Çetin<sup>1</sup>, Ercan Arıcan<sup>3</sup>

<sup>1</sup>Istanbul University, Faculty of Science, Department of Biology, Istanbul/Turkey

<sup>2</sup>Istanbul University, Institute of Science, Programme of Radiobiology, Istanbul/Turkey.

<sup>3</sup>Istanbul University, Faculty of Science, Department of Molecular Biology and Genetics, Istanbul/Turkey.

**Background/Aim:** Cancer encountered in the point that of the balance between cell proliferation and cell death is uncontrolled. Cancer causes about 13% of all annual deaths worldwide. Low pressure (hypobaric) conditions that create hypoxia promote apoptosis by inhibiting cell cycle of the cells. In this study, determination of the effects of fractional hypobaric applications at different times on HeLa cells at cellular and molecular level was purposed.

**Materials and Methods:** Experiments were carried out under hypobaric conditions (35.2 kPa) in specially designed hypobaric cabin including 2% O<sub>2</sub> and 98% N. Application of fractional hypobaric conditions was repeated two times for 3 hours with an interval of 24 hours. At the end of the implementation period cells were allowed to incubate for 24 hours for activation of repair mechanisms. Cell kinetic parameters such as growth rate (MTT) and apoptotic index were used in determination of the effect of hypobaric conditions on HeLa cells. Also in our study expression levels of the Bcl-2 gene family that have regulatory role in apoptosis were determined by RT-PCR technique to evaluate the molecular mechanism of this effect.

**Results:** The results in our study showed that antiproliferative effect of hypobaric conditions on HeLa cells started 3rd hours from the time of application and increased depending on the time of application. In our experiments as a result of this effect, while there was a significant decrease in growth rate values, there was a significant increase in apoptotic index values ( $p < 0.01$ ).

**Discussion:** Molecular studies showed that hypobaric conditions caused a significant increase in expression level of proapoptotic gene Bax that belongs to Bcl-2 gene family involved in the mechanism of apoptosis and a significant decrease in antiapoptotic Bcl-2 gene.

**Conclusion:** Consequently fractional application of hypobaric conditions on HeLa cell cultures increased both antiproliferative and apoptotic effects and these effects were triggered by Bax gene.

*Keywords: HeLa, Hypobaric, In vitro, Bcl-2 gene family*

*“Note to the Scientific Committee”: This work was supported by Scientific Research Projects Coordination Unit of Istanbul University. Project no: 4157.*

## POSTER PRESENTATION – 85

### ***G6PD*, *GPx-1* AND *CYBA* GENE VARIATION FREQUENCIES IN TYPE 2 DIABETES PATIENTS FROM ISTANBUL**

Güldal Inal-Gültekin<sup>1</sup>, Ozlem Timirci-Kahraman<sup>1</sup>, Bahar Toptaş-Hekimoğlu<sup>1</sup>, Ozlem Küçüküseyin<sup>1</sup>, A. Begüm Ceviz<sup>1</sup>, Güksu Kaşaracı<sup>1</sup>, A. Burak Dalan<sup>2</sup>, Selim Isbir<sup>3</sup>, Turgay Isbir<sup>2</sup>.

<sup>1</sup>Istanbul University, Aziz Sancar Institute of Experimental Medicine, Department of Molecular Medicine, Istanbul, Turkey.

<sup>2</sup>Yeditepe University, Faculty of Medicine, Department of Medical Biology, Istanbul, Turkey

<sup>3</sup>Marmara University, Marmara University School of Medicine, Department of Cardiovascular Surgery, Istanbul, Turkey

Type-2-diabetes (T2D) is a multigenic and complex disease, considerably influenced by life style choices. Studies focusing on molecular parameters potentially beneficial for the prevention, early diagnosis, and even possibly evolve into treatment options of this pandemic disease are becoming increasingly important.

Glucose-6-phosphate dehydrogenase (G6PD), glutathione peroxidase 1 (GPx-1), and the upper portion of the NADPH oxidase system the CYBA (p22phox) are only few of suggested parameters, as they are believed to be independent factors in the development of T2D. Mutations on these genes are suggested to either trigger or protect from the development of T2D in different populations. Hence, we investigated the frequencies of exonic c.C563T, c.C599T and c.C242T and 3' UTR c.\*A640G variations for the *G6PD*, *GPx-1* and *CYBA* genes, respectively in a cohort with T2D from Istanbul, and present preliminary results.

Volunteer T2D patients (Group 1) and healthy control volunteers (Group 2) were recruited for this study. Genomic DNA was isolated from 10 mL EDTA peripheral blood samples, and the variations were detected with PCR-RFLP and gel electrophoresis techniques.

The demographic representations of the T2D patients were in conjunction with the disease. Alcohol abuse, total cholesterol (>200 mg/dl), total glyceride (>100 mg/dl), LDL (>130 mg/dl), hypertension showed increased risk in the development of T2D ( $p=0.015$ ,  $p=0.004$ ,  $p=0.046$ ,  $p<0.001$ ,  $p<0.001$ , respectively), and women showed a higher risk of T2D ( $p<0.001$ ) in the study cohort. Patients heterozygous (CT) for c.C599T (*GPx-1*), and homozygous wild type (AA) for c.\*A640G (*CYBA*), showed increased risk for developing T2D. The c.C563T (*G6PD*) and c.C242T (*CYBA*) did not show a statistical relevance for the study group.

In conclusion, the preliminary results imply that patients heterozygous for *GPx-1* c.C599T and homozygous wild type for *CYBA* c.\*A640G mutations are at higher risk for developing diabetes. Our results are in accordance with the multigenic nature of T2D and increasing the study population will give more insight on the reciprocal influence of the genes in question.

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## POSTER PRESENTATION – 86

### IDENTIFICATION OF A SERINE-THREONINE KINASE AS A NOVEL AUTOPHAGIC REGULATOR

Seval Kilic<sup>1</sup>, Ozlem Yedier<sup>1</sup>, Devrim Gozuacik<sup>1,3</sup>, Ozlem Kutlu<sup>2,3\*</sup>

<sup>1</sup> Department of Molecular Biology Genetics and Bioengineering, Faculty of Engineering and Natural Science, Sabanci University, İstanbul, Turkey

<sup>2</sup> Department of Molecular Biology Genetics and Bioengineering, Sabanci Universitesi Nanotechnology Research and Application Center, Sabanci University, Istanbul, Turkey

<sup>3</sup> Sabanci University, Center of Excellence for Functional Surfaces and Interfaces for Nano Diagnostics (EFSUN), Istanbul 34956, Turkey

\*Corresponding author

**Background/Aim:** Phospholipid dependent Serine/Threonine kinases are shown to be involved in cellular mechanisms and disease related pathways. Upon different intracellular stimuli, these kinases are activated and functions. Several chemical analogues such as PMA and Ceramide were synthesized to mimic intracellular stimuli to study function of these kinases. For several of these kinases, activation is dependent on both PMA and a Calcium ionophore such as ionomycin. Strikingly, deregulation of these kinases has been identified in several cancers. Recent studies showed that autophagy, which evolutionary conserved cellular degradation mechanism to maintain homeostasis, is also involved in carcinogenesis. According to literature, there are no robust studies to show the interaction between autophagy and serine threonine kinases. Thus, in our study we focused to identify a novel Ser/Thr kinases through regulation of autophagy in cancer.

**Materials & Methods:** HeLa (Cervical cancer) cells exposed with chemicals, Ceramide, PMA or PMA/ionomycin to activate specific isozymes of the Ser/Thr kinase family. Upon activation of the kinases, cellular autophagic activity was investigated with GFP-LC3 puncta count, LC3 shift assay and P62 accumulation. shRNA technology is used for silencing of the specific isozyme of the Ser/Thr kinases and activation of the autophagy further analysed with the same methods and conditions. Downregulation of the gene was determined with qPCR or immunoblot. Effect of these specific stimuli was also confirmed with using MEF GFP-LC3 transgenic autophagy reporter cell line.

**Results & Discussion:** In HeLa cells, upon Ceramide exposure autophagosome formation was increased in basal condition. We also obtained the same results from MEF GFP LC3 transgenic autophagy reporter cell. Intriguingly, when the novel kinase was downregulated, the effect was reversed significantly. However, both effects were further enhanced under starvation condition.

**Conclusion:** Our findings suggest that this kinase isozyme is a suitable candidate to regulate autophagy in cervical cancer.

*Keywords: Autophagy, Cancer, Serine/Threonine Kinase*

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## POSTER PRESENTATION – 87

### **MicroRNA-125b AS A NEW POTENTIAL BIOMARKER ON DIAGNOSIS OF RENAL ISCHEMIA-REPERFUSION INJURY**

Aydın Güçlü<sup>1</sup>, Cengiz Koçak<sup>2</sup>, Fatma Emel Koçak<sup>3</sup>, Raziye Akçılar<sup>4</sup>, Yavuz Dodurga<sup>5</sup>, Aydın Akçılar<sup>6</sup>, Levent Elmas<sup>5</sup>

<sup>1</sup>Department of Nephrology, Ahi Evran School of Medicine, Kırsehir, Turkey

<sup>2</sup>Department of Pathology, Dumlupınar School of Medicine, Kutahya, Turkey

<sup>3</sup>Department of Biochemistry, Dumlupınar School of Medicine, Kutahya, Turkey

<sup>4</sup>Department of Physiology, Dumlupınar School of Medicine, Kutahya, Turkey

<sup>5</sup>Department of Medical Biology, Pamukkale School of Medicine, Denizli, Turkey

<sup>6</sup>Experimental Research Unit, Dumlupınar School of Medicine, Kutahya, Turkey

**Background / Aim:** Acute renal failure is commonly seen in the perioperative period. Ischemia reperfusion (IR) injury plays a major role in acute renal failure and delayed graft function. MicroRNAs (miRs), which are pivotal modulators of cell activities, offer a major opportunity for affective diagnosis and treatment strategies because they are tissue specific and in the center of gene expression modulation. The aim of this study is to investigate the functional and histopathological effect of bardoxolone methyl (BM) on miR-21, miR-223-5p and miR-125b in experimental renal ischemia reperfusion injury.

**Methods:** Wistar-Albino rats (12-16 wk old, weighing 300-350 g) were used in the study. Rats (n=6) were randomized into three groups (control, IR, and BM+IR). Serum urea level, total antioxidant status, total antioxidant status and oxidative stress index were also measured. Tissue levels of miRs were analyzed with quantitative real-time PCR system. Histopathologic examination of renal tissue samples were determined according to hematoxylin and eosin method.

**Results:** Significant reduction of urea and total oxidant status, increase of total antioxidant status, and oxidative stress index were identified in the IR+BM group compared with the IR group. Significant increases of miR-21 (2842.82-fold) and miR-125b (536.8-fold) were identified in the IR group compared with the control group; however, miR-223-5p levels did not show any significant difference. Also, miR-21 and miR-125b were significantly reduced in the IR+BM group compared with the IR group. Reduced histopathologic changes were observed in the IR+BM group. A significant decrease in the number of tunel-positive cells was identified in the IR+BM group compared with the IR group.

**Discussion:** The main findings of our study are that miR-21 significantly increased in IR injury. We showed for the first time that miR-125b is increased in renal IR injury. miR-125b might be a potential diagnosis and treatment target in renal IR injury. Also, we demonstrated BM significantly reduced miR-21 and miR-125b in renal IR model and made functional and histologic recoveries in kidney.

**Conclusions:** miR-125b was significantly increased in IR injury; thus, miR-125b can be a potential novel marker that can be used in diagnosis and treatment of renal IR injury. BM reduces miR-21 and miR-125b in case of IR injury and makes functional and histopathologic repairs.

*Keywords: Renal Ischemia-reperfusion injury, Bardoxolone Methyl, miR-223-5p, miR-21 and miR-125b*  
*Ethic approval number: 2016.01.05*

POSTER PRESENTATION – 88  
**IDENTIFICATION OF DIFFERENTIALLY REGULATED NON-SPECIFIC  
PROTEINS IN SH-SY5Y CELLS ENGINEERED WITH TET-REGULATED  
PROTEIN EXPRESSION SYSTEM**

Aylin Kanli<sup>1</sup>, Eylül Ece Islek<sup>1</sup>, Murat Kasap<sup>1</sup>, Gurler Akpınar<sup>1</sup>, Mehmet Dogan Gulcak<sup>1</sup>

<sup>1</sup> Department of Medical Biology, Medical Faculty, Kocaeli University, 41380, Kocaeli, Turkey

Tetracycline regulated protein expression in mammalian cells is a powerful tool to predict the physiological function, cellular localization and stability of a protein. In recent years, Tet-regulated gene expression studies were also used to predict metabolic networks that are affected by the expression of a WT or a mutant forms of a protein. To predict the metabolic networks affected, researchers generally produce a single mammalian cell clone that can express the protein of interest under tet-control and study the changes occurring in overall proteome before and after expression of a protein of interest. One limitation of tet-regulated clonal cell creation, however, is that it sometimes creates clones with changed protein levels even without the expression of the protein of interest. This side effect is due to the nonspecific insertion of the gene encoding the protein of interest into the genome. In this study, SH-SY5Y cell lines that can stably express either the WT or the mutant (V493F) FTO proteins under the control of Tet promoter were created. No tetracycline induction was performed for exogenous protein expressions in these cell lines. Protein samples were prepared from the non-induced three similar clones of each cell line and a 2DE-based comparative proteomic study was performed. Spots displaying differences in their abundance were cut from the gels and identified by MALDI-TOF/TOF. We identified 14-3-3 protein Epsilon, Vimentin, High mobility group protein B1, Heterogeneous nuclear ribonucleoprotein K, Tubulin beta-2C chain, Heat shock protein HSP 90-alpha, Heat shock protein HSP 90-beta, Alpha-enolase, TATA-binding protein-associated factor 2N proteins. In conclusion, studies utilizing tet regulated protein expression system should pay attention to the falsely regulated protein spots.

*This study was supported by TUBITAK project numbered 113S965*

## POSTER PRESENTATION – 89 IN VITRO ANTIPROLIFERATIVE EFFECTS OF LY2109761 ON HELA CELL CULTURE

Mehmet Topçul<sup>1</sup>, İdil Çetin<sup>1</sup>

<sup>1</sup>Istanbul University, Faculty of Science, Department of Biology, Istanbul/Turkey

**Background / Aim:** Because of the conventional treatment methods such as surgery, radiotherapy and chemotherapy, inhibitors as a novel approach have become important. Advances in cancer treatment is shifting particularly to target proteins and targeted therapies that stop growth signals. In this study, in vitro cytotoxic effect of TGF-Beta receptor inhibitor LY2109761 was evaluated on HeLa cells which is originated from cervix carcinoma.

**Materials and Methods:** In our project, the inhibitor that can effect TGF- $\beta$  signaling pathway was evaluated. For this purpose cell viability, cell index values obtained from xCELLigence RTCA (Real-Time Cell Analysis) DP instrument, mitotic index, apoptotic index and labelling index analysis among cell kinetic parameters were used.

**Results (quantitative and / or statistical data):** Significant decrease in cell viability and cell index, mitotic index and labelling index values was observed. Also there was a significant increase in apoptotic index values. The differences between control and all experimental groups were statistically significant ( $p < 0.01$ )

**Discussion:** In our study, promoting cytoskeletal effect of LY2109761 on HeLa cells, decreasing of cell viability, cell index, mitotic index and labelling index values and increasing of apoptotic index values are consistent with other studies.

**Conclusion:** LY2109761 offer a promising treatment modality in cervix carcinoma.

*Keywords:* LY2109761, HeLa cells, xCelligence RTCA, cytoskeletal effect.

*“Note to the Scientific Committee”:* This work was supported by Scientific Research Projects Coordination Unit of Istanbul University. Project no: 49748.

POSTER PRESENTATION – 90  
**TO INVESTIGATE THE EFFECTS OF SEDATIVE AGENTS ON NITROSATIVE  
STRESS AND DNA DAMAGE FOR IN PATIENTS, WHOM PORT CATHETER WAS  
ATTACHED ALONG WITH FOR ULTRASOUND ASSESSMENT**

Mehmet YANAR<sup>1</sup>, Seyithan TAYSI<sup>1</sup>, Yıldırım CUMA<sup>2</sup>, Yılmaz SAFİ<sup>2</sup>, Hasan ULUSAL<sup>1</sup>, Mehmet TARAKCIOĞLU<sup>1</sup>

<sup>1</sup>University of Gaziantep, Medical Faculty, Department of Medical Biochemistry, Gaziantep/Turkey

<sup>2</sup>University of Gaziantep, Medical Faculty, Department of Emergency medicine, Gaziantep/Turkey

Transvenous venous ports placed at bedside by ultrasound guidance are recently preferred for patients with intermittent and long-term infusion therapy, due to patient comfort and low infection rates. In this case, patients with long-term frequent treatment will be provided with an open vein. The aim of this study was to investigate the possible effects of this treatment on nitrosative stress and DNA damage in patients. Blood samples were taken before and after the port catheters were inserted from 40 patients whom port catheter was inserted for indication in Gaziantep University Emergency Service; malondialdehyde (MDA), nitric oxide (NO<sup>•</sup>), peroxynitrite (ONOO<sup>-</sup>), 8-hydroxy-2'-deoxyguanosine (8-OHdG) levels and nitric oxide synthase (NOS) activity were measured in the serum. MDA, (NO<sup>•</sup>), ONOO<sup>-</sup> and NOS levels were increased significantly, but no significant difference was observed in terms of 8-OHdG values. Results from the study showed that venous ports transvenously placed on bedside ultrasound guidance increase nitrosative stress parameters.

*Keywords: DNA damage, malondialdehyde, nitric oxide, nitric oxide synthase, peroxynitrite, nitrosative stress, port catheter.*

## POSTER PRESENTATION – 91

### **E2F EXPRESSION COULD BE AFFECTED BY INCREASED EXPRESSION OF MEG3 WITH miR-664 SUPPRESSION**

Yunus Sahin<sup>1</sup>, Zekiye Altan<sup>1</sup>, Kaifce Arman<sup>1</sup>, Meltem Koruk Ozer<sup>1</sup>, Khandakar A.S.M. Saadat<sup>1</sup>

<sup>1</sup>Faculty of Medicine, Department of Medical Biology, University of Gaziantep, Gaziantep, Turkey

**Aim:** The E2F family of transcription factors plays a role in proliferation, apoptosis and cell differentiation. E2F1, a member of this family, binds to the retinoblastoma protein pRb and manner cell cycle-dependent apoptosis and proliferation. E2F1 is involved in osteoblast differentiation mediated by pRb. The MEG3 gene has a tumor suppressor role in RB-related pathways and a low expression level in osteosarcoma. Based on the interaction of the MEG3 gene and E2F1 with the Rb protein, we thought that these two genes may interact with each other in osteosarcoma. The expression of the MEG3 gene was increased using antogomiR-664a in the osteosarcoma cell line. We aimed to observe changes of expression level of E2F1 after antagomiR-664a transfection.

**Materials and Methods:** The osteosarcoma cell line (U-2 OS) and normal osteoblast cell line (h.FOB 1.19) were purchased from ATCC. These cell lines were cultured to ATCC's recommended protocol and transfected with antagomiR-664a and its negative control. After the antagomiR-664a transfection, RNA isolation was performed. Transfected RNAs were converted to cDNA by RT-PCR method. Also qPCR method was used for expression analysis of MEG3, E2F and miR-664a. Statistical analysis of the data obtained as a result of qPCR were performed with student's t test.

**Results and Discussion:** MEG3, E2F and miR-664a expression levels were analyzed q-PCR before and after suppression of miR-664a. According to these results, while expression level of miR-664a was decreasing, MEG3 and E2F expression levels were increasing in U-2 OS cell line. Increased MEG3 expression was found to be statistically significant ( $p < 0.05$ ). However, increasing in E2F expression level was not found to be statistically significant ( $p = 0.0625$ ) according to two-tailed paired t test. This result suggested that expression of MEG3 and miR-664a might be involved in E2F expression level. In order to get more accurate results about interaction between MEG3 and E2F, siRNA can be used for MEG3 and E2F in hFOB 1.19 cell line.

**Conclusion:** In conclusion, increased MEG3 expression level with miR-664a suppression may have an effect on E2F expression level. Further functional analysis is need to reveal their interaction between each other in osteosarcoma.

*Keywords: E2F, lncRNA, MEG3, miRNA, miR-664a, Osteosarcoma.*

## POSTER PRESENTATION – 92

### THE INVESTIGATING OF ANTIPROLIFERATIVE EFFECTS OF CERANIB-2 ON HUMAN LUNG EPITHELIAL ADENOCARCINOMA CELLS *IN VITRO*

Pinar OZTOPCU-VATAN<sup>1</sup>, Merve YILDIZ<sup>2</sup>, Gokhan KUS<sup>3</sup>

<sup>1</sup>Department of Biology, Faculty of Arts and Sciences, Eskisehir Osmangazi University, Eskisehir, Turkey

<sup>2</sup>Graduate School of Natural and Applied Sciences, Eskisehir Osmangazi University, Eskisehir, Turkey

<sup>3</sup>Department of Health Programme, Open Faculty, Anadolu University, Eskisehir, Turkey

**Background:** Ceramide accumulation in cancer cells was found to cause inhibition of cell division and induction of apoptosis. Ceranib-2 is a ceramidase inhibitor agent that increases ceramide levels in cancer cells. Therefore, we aimed to investigate the effects of ceranib-2 on cell proliferation and morphology in human lung epithelial adenocarcinoma (A549) cells.

**Materials and Methods:** The cytotoxicity of ceranib-2 (1 to 100  $\mu$ M) was examined in A549 cells. In addition, carboplatin (1 to 100  $\mu$ M) was used as positive control and human bronchial epithelium (BEAS-2B) cells were used to determine the cytotoxic effects of the ceranib-2 in healthy cells. The cytotoxic activity of ceranib-2 was measured by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay for 24 h. One-Way ANOVA and Tukey's multiple comparison test was used for statistical analyses of MTT data. Results were considered as significant for  $p < 0.05$ . Following ceranib-2 treatment morphological changes that occurred in A549 cells were observed under inverted light microscope.

**Results:** The  $IC_{50}$  of ceranib-2 in A549 and BEAS-2B cells was determined as 22 and 49  $\mu$ M for 24 h respectively. Carboplatin was also effective on viability of A549 cells but didn't have any  $IC_{50}$  value within the dose range for 24 h. To observe morphological changes, we decided to treat A549 cells with 5, 10 and 25  $\mu$ M doses of ceranib-2 for 24 h according to MTT results. As a result, cell number was decreased compared to control cells. Also, treated cells were shrunk and observed as rounded.

**Discussion:** Inhibiting ceramidase enzyme by ceranib-2 caused reduction in cell viability for both cell lines but the effect began to detectable at lower doses in A549 cells compared to BEAS-2B cells. Also, cell shrinkage was observed in A549 cells which may be relevant to apoptosis. Our positive control carboplatin is known to be a chemotherapeutic agent which is widely used for lung cancer treatment. The results showed that ceranib-2 is more potent than carboplatin for inhibition of cell proliferation in A549 cells.

**Conclusion:** In this study, we identified cytotoxicity caused by ceranib-2 in human lung adenocarcinoma cells for the first time. Our findings suggest further research for this drug in lung cancer treatment.

*Keywords:* Ceranib-2, ceramidase inhibitor, cytotoxicity, A549.

*Note to the Scientific Committee:* This study was supported by TUBITAK (The Scientific and Technical Research Council of Turkey), (Project Number: 214Z159).

## POSTER PRESENTATION – 93 KAEMPFEROL; A POSSIBLE PRODRUG FOR GRAM (-) BACTERIA

<sup>1</sup>Elif Köse, <sup>2</sup>Esra Aydemir, <sup>3</sup>Ece Şimşek, <sup>2</sup>Orhan Koçak

<sup>1</sup>Vocational School of Health Services, Akdeniz University, 07058, Antalya, Turkey

<sup>2</sup>Biology Department, Faculty of Science, Akdeniz University, 07058 Antalya, Turkey

<sup>3</sup>Department of Nutrition and Dietetics, Antalya School of Health, Akdeniz University, 07058, Antalya, Turkey

**Background:** Kaempferol is a natural flavonol which is found in a variety of plants and plant-derived foods. Kaempferol is a yellow crystalline solid and It is slightly soluble in water and highly soluble in hot ethanol, ethers, and DMSO. It has been demonstrated that Kaempferol has an antimicrobial effect against *Helicobacter pylori*. It also has been shown to work synergistically with certain antibiotics. Gram-negative bacteria typically display diverse porins in their outer membrane that participate in the modulation of cellular permeability, outer membrane protein A (OmpA) being one of the most abundant. In this study our aim was to determine the possible interaction between Kaempferol and OmpA in a molecular docking aspect.

**Materials and Methods:** The 3D crystal structure of OmpA was obtained from RSCB Protein Data Bank (<http://www.rcsb.org/pdb/home/home.do>). The PDB code of OmpA is 1bxw. Kaempferol was used as a ligand and its molecular structure was gained from PubChem (<https://pubchem.ncbi.nlm.nih.gov>). The PubChem CID number of Kaempferol is 5280863. The interaction of OmpA with Kaempferol was determined by DockingServer (<http://www.dockingserver.com>). Docking server could be used for determining the position, geometry and energy of small molecules. This server includes rigid receptor- ligand flexible docking. OmpA - Kaempferol docking study was done by using Gasteiger charges of both receptor and ligand atoms.

**Results:** Free energy of binding was calculated as -4.84 kcal/mol (Table 1). Protein-ligand binding includes hydrogen bonds, polar, hydrophobic, pi-pi, cation-pi, and other interactions. Binding site was given in 2D format in Figure 1 and Figure 2. Amino acids in Binding site were determined as 19:HIS, 56:ASP, 58:LEU, 72:TYR, 74:ALA, 100:MET, 102: TRP, 104:ALA, 144:THR, 146:ASN, 158:ASP, 161:MET.

**Discussion:** Calculated binding energy and amino acids in binding sites indicate a possible OmpA-Kaempferol interaction site. According to the docking results, Kaempferol binds to OmpA with an 80 % frequency. It means that Kaempferol could almost completely bind to OmpA. Thus, Kaempferol exerts its antibacterial effect depending on this property. This mechanism underlies a new aspect for treating antibiotic-resistant gram (-) bacteria.

**Conclusion:** This is the first report showing that Kaempferol could interact with OmpA.

*Keywords: Kaempferol; Molecular docking; Outer membrane; OmpA,*

Table 1

Est. Free Energy of Binding	Est. Inhibition Constant, Ki	vdW + Hbond + desolv Energy	Electrostatic Energy	Total Intermolec. Energy	Frequency	Interact. Surface
-4.84 kcal/mol	281.36 uM	-5.33 kcal/mol	-0.17 kcal/mol	-5.50 kcal/mol	80%	630.01

Figure 1

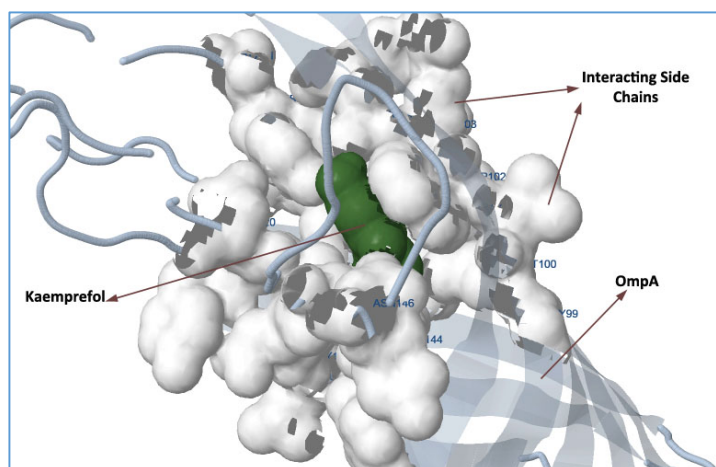
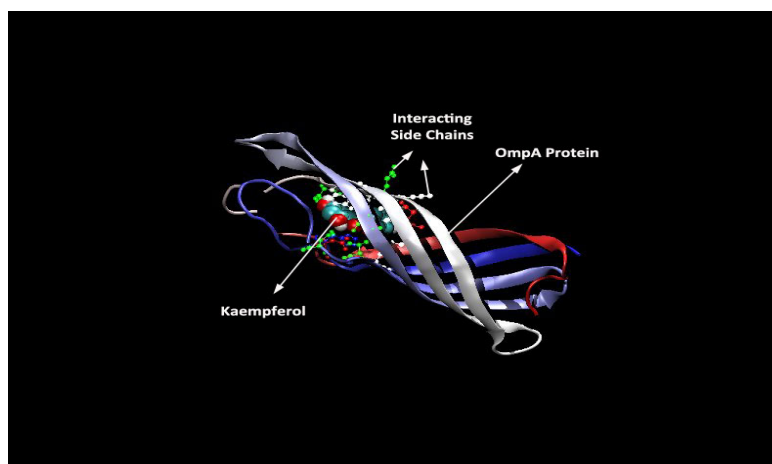


Figure 2





## POSTER PRESENTATION – 94 METAMIZOLE COULD ACT AS AN ANGIOGENIC FACTOR DEPENDING ON THE INTERACTION OF VEGFR2: A MOLECULAR DOCKING STUDY

Orhan Koçak<sup>1</sup>, Ece Şimşek<sup>2</sup>

<sup>1</sup>Biology Department, Faculty of Science, Akdeniz University, 07058 Antalya, Turkey

<sup>2</sup>Department of Nutrition and Dietetics, Antalya School of Health, Akdeniz University, 07058, Antalya, Turkey

**Background:** Pain relievers remain the main stay for treating cancer patients with chronic pain and during preoperative, intraoperative, and postoperative pain management. However, painkillers can cause side-effects including angiogenesis.

Of significance to the tumor microenvironment, painkillers interact with the endothelium and tumor cells. Painkillers can modulate the process of metastasis, which is dependent on angiogenesis, tumor cell survival, and inflammation. These cellular processes are integral to cancer progression and metastasis.

In recent decades, it has been accepted that vascular epithelial growth factor VEGF and its receptor VEGFR2, play crucial roles in angiogenesis. VEGF also acts as a potent angiogenic protein.

Metamizole-Sodium is a non-opioid, spasmolytic, analgesic drug, derived from Pyrazolone, and is generally used as a therapeutic in cancer patients. In this study, we aimed to determine the possible interaction of Metamizole with vascular endothelial growth factor receptor 2 (VEGFR2) via molecular docking.

**Materials and Methods:** The 3D crystal structure of VEGFR2 was obtained from RSCB Protein Data Bank (<http://www.rcsb.org/pdb/home/home.do>). The PDB code of VEGFR2 is 1vr2. Metamizole was used as a ligand and its molecular structure was gained from PubChem (<https://pubchem.ncbi.nlm.nih.gov>). The PubChem CID number of Metamizole is Metamizole is [21584481](https://pubchem.ncbi.nlm.nih.gov/compound/21584481). The interaction of VEGFR2 with Metamizole was determined by DockingServer (<http://www.dockingserver.com>). Docking server could be used for determining the position, geometry and energy of small molecules. This server includes rigid receptor- ligand flexible docking. VEGFR2-Metamizole docking study was done by using Gasteiger charges of both receptor and ligand atoms.

**Results:** Free energy of binding was calculated as -4.69 kcal/mol (Table 1). Protein-ligand binding includes polar, hydrophobic, pi-pi and other interactions. Binding site was given in 2D format in Figure 1 and Figure 2. Amino acids in Binding site were determined as 840: LEU, 848: VAL, 866: ALA, 918: PHE, 923: ASN, 1035: LEU.

**Discussion:** The geometry and binding Energy prediction were optimized via Gasteiger charge method in DockingServer. Calculated binding energy and amino acids in binding sites indicate the possible VEGFR2-Metamizole interaction. 868 and 1028 amino acids were determined as binding site and the active core of VEGFR2 protein. According to the docking results Metamizole could bind to VEGFR2 via 866: ALA and 1035: LEU residues. This may indicate that Metamizole might cause certain changes in the activity of VEGFR2.

**Conclusion:** This is the first report showing that Metamizole-VEGFR2 interaction could lead possible changes in receptor protein residues. These changes could affect the angiogenic switch in tumors.

*Keywords:* Metamizole, VEGFR2, molecular docking,

Table 1

Est. Free Energy of Binding	Est. Inhibition Constant, Ki	vdW + Hbond + desolv Energy	Electrostatic Energy	Total Intermolec. Energy	Frequency	Interact. Surface
-4.69 kcal/mol	363.22 uM	-5.56 kcal/mol	-0.00 kcal/mol	-5.56 kcal/mol	20%	622.206

Figure 1

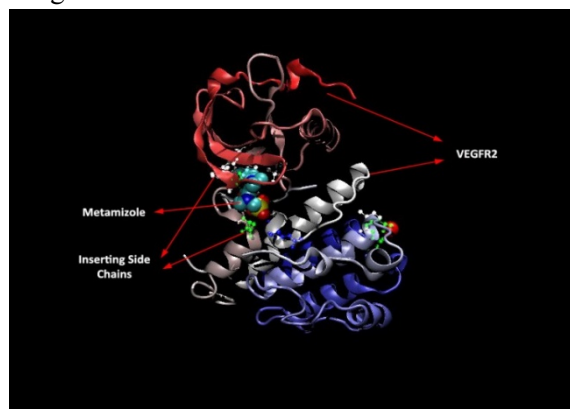
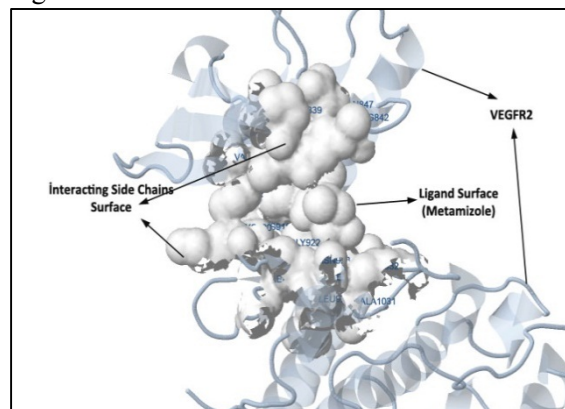


Figure 2



## POSTER PRESENTATION – 95 EVALUATION OF APOPTOTIC EFFECTS OF PACLITAXEL AND ITS MOLECULAR MECHANISM IN HeLa CELLS

Uğur serbes<sup>1</sup>, Özlem Dağdeviren Özsöylemez<sup>1</sup>, Gül Özcan<sup>2</sup>

<sup>1</sup>Istanbul University, Institute of Graduate Studies in Science and Engineering, Department of Radiobiology

<sup>2</sup>Istanbul University, Faculty of Science, Biology Department, Istanbul/Turkey.

**Background/Aim:** In this study, we aim to determine the anti-tumoral effects of paclitaxel and this drug induces the expression of specific genes involved in apoptosis signaling pathways on HeLa cells.

**Material and Methods:** In this study, PAC has been applied to HeLa cells in 6 different doses (3, 7.5, 15, 30, 60, 120 nM) for 48 hours and the IC<sub>50</sub> dose MTT method, has been determined with apoptotic index (AI) DAPI. Morphological aspects have been demonstrated using light, phase contrast and florescent microscopes, qRT-PCR have been used to evaluate pro/anti-apoptotic gene expression.

**Results:** In this study for PAC on HeLa cell cultures, IC<sub>50</sub> after 48 h has been reached at the 15 nM dose and the AI value at this dose has been determined as 42% (p<0.01). According to the results relative mRNA levels and upregulation according to the control group was detected in Akt1(1.4), Apaf1(3.4), Aven(1.6), Bad(3.1), Bax(12.3), Bcl2L11(2), Bcl2L2(1.3), Birc2(1.8), Birc3(1.4), Birc5(1.3), Caspase1(74.6), Caspase10(3.6), Caspase3(1.6), Caspase4(2.5), Caspase7(2.2), Dffa(2.5), Fas(14.68), HTRA2(3.3), Lrdd(4.2), Mcl1(1.2), NFKB1(3.2), NFKB2(2.4), PMAIP1(3.8), PTEN(1.4), RELA(2), RELB(2.2), STAT1(1.4), STAT5A(1.6), TNFRSF10A(3.3), TNFRSF10C(4.7), TNFRSF10D(8.6), TNFRSF1A(2.2), TNFRSF21(3.7), TNFRSF25(6.7), TRAF2(1.3).

We observed that BAG1(0.5), Bak1(0.8), BBC3(0.1), Bcl2L1(0.4), Bcl2L10(0.1), Bid(0.4), CAD(0.7), Caspase2(0.4), Caspase6(0.4), Caspase8(0.3), Caspase9(0.3), Diablo(0.6), EndoG(0.8), FADD(0.4), FAM96A(0.2), FAM96B(0.6), FasLG(0.07), HRK(0.4), SOCS3(0.4), STAT5B(0.6), TNF(0.04), TNFSF10(0.4), TRAF5(0.3), TRAF6(0.2) genes were showed low fold changes compared to the control group.

No difference was detected in the Bcl2(1.02), Bcl2L13(1.1), Bik(1.1), Bok(0.9), Caspase8AP2(0.9), CFLAR(1.1), CRADD(0.9), HMGB1(1), HSP90B1(0.9), REL(1.1), SOCS2(1.1), TNFRSF10B(1), TP53(0.9), TP53I3(1.1), TRAF3(1) genes compared to the control.

**Discussion:** qRT-PCR results show that Apaf1, Bad, Bax, Bcl2L11, Caspase1, Caspase10, Caspase4, Caspase7, Dffa, Fas, Htra2, Lrdd, NFKB1, NFKB2, PMAIP1, RELA, RELB, TNFRSF10A, TNFRSF10C, TNFRSF10D, TNFRSF1A, TNFRSF21, TNFRSF25 gene expressions have increased significantly. On the other hand, BAG1, BBC3, Bcl2L1, Bcl2L10, Bid, Caspase2, Caspase6, Caspase8, Caspase9, FADD, FAM96A, FasLG, HRK, SOCS3, TNF, TNFSF10, TRAF5, TRAF6 mRNA levels are significantly decreased.

**Conclusion:** Specifically the qRT-PC results, which show that Caspase2 and 10, Fas and TNFR10C and 10D show high levels of increase, suggest an external pathway. Additionally, the increase in bax gene suggests the activation of the mitochondria dependent pathway. These results provide that identifying upregulated or downregulated genes on HeLa cells helps us in better understanding cancer dynamics to identify markers and treatment targets for cervical cancer and it will make an important

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contribution to the elucidation of a novel Outlook for developing new chemo/radiotherapy combinations for clinical trials.

*Keywords: HeLa cells, Paclitaxel, apoptosis, qRT-PCR, cancer therapy.*

*Note to the Scientific Committee: This work was supported by the Research Fund of the Istanbul University, Project No: 1393 and 49547.*

## POSTER PRESENTATION – 96

### THE ROLE OF THE REPRODUCTIVE MICROBIOME ON FERTILITY AND IVF

Pembe Savas<sup>1</sup>, Fezel Nizam<sup>2</sup>

<sup>1</sup>Eastern Mediterranean University, Department of Biological Sciences, Famagusta, Cyprus,

<sup>2</sup>Eastern Mediterranean University, Department of Biological Sciences, Famagusta, Cyprus.

**Background/Aim:** While Human Microbiome Project (HMP) has been sequencing the microbiome and identifying the vast communities of microbiota that inhabit our bodies, it has already been hypothesized that microbes are involved in the physiology and pathophysiology of assisted reproduction since before the first success in in-vitro fertilization (IVF) and this relationship demands increased focus especially considering that up to forty percent of patients undergoing IVF have abnormal flora somewhere along the reproductive tract. Therefore the microbiome of the female genital tract should become an important consideration in IVF treatments and the aim of this study is to explore the current literature outlining the contribution of important bacteria on reproductive health and outlines gaps in current research in order to highlight future areas of research.

**Materials and Methods:** This relationship is evident based on the expansive literature available to date importantly after the sequencing data from the 16S rRNA subunit, we will explore the current literature and review the microbiome of the female reproductive tract focusing on the influence of the reproductive microbiome in the assisted reproductive technology.

**Results:** A transition in the microbial flora (lactobacilli species) occurred in most of the women during the course of IVF treatments due to hormonal changes (particularly with respect to variations in estradiol), or inflammation and progesterone resistance or pharmacological interventions. Hence, the vaginal microbiome has a statistically significant relationship to the live birth rate. In parallel, this study will provide a platform to discuss what a common clinical practice should include for women undergoing IVF such as screening of the vaginal microbiome and to develop a model for useful screening tools and implementation of microbial intervention strategies into modern day medicine.

**Discussion:** Although significant correlations appear to exist between the reproductive tract microbiome, hormone status and IVF success rates, a more comprehensive study is needed to better understand the mechanisms involved in a possible relationship in reproductive assisted technologies. Therefore the future research needs to validate the hypothesis generated in these studies in functional experiments and evaluate true impact on clinical practice.

**Conclusion:** In this regard, the human microbiome research should focus on the possible solutions to mitigate the various factors affecting microbiome flora, implantation and delivery rates and this research will reflect the practice of modern biomedical research.

*Keywords: microbiota, sequencing, reproduction, IVF*

POSTER PRESENTATION – 97  
**INVESTIGATION OF NITRIC OXIDE LEVELS, APOPTOSIS AND *GSK3B*  
EXPRESSIONS IN BISPHENOL A AND BIS (2-ETHYLHEXYL) PHTHALATE  
EXPOSED ZEBRAFISH EMBRYOS**

Ünsal Veli Üstündağ<sup>1</sup>, İsmail Ünal<sup>1</sup>, Perihan Seda Ateş<sup>1</sup>, Türkan Yiğitbaşı<sup>2</sup>, Nesrin Emekli<sup>2</sup>, Ebru Emekli-Alturfan<sup>1</sup>

<sup>1</sup>Department of Biochemistry, Faculty of Dentistry, Marmara University, Istanbul, Turkey

<sup>2</sup>Department of Biochemistry, Faculty of Medicine, Istanbul Medipol University, Kavacık, Istanbul, Turkey

<sup>3</sup>Department of Biochemistry, Cerrahpasa Faculty of Medicine, Istanbul University, Kocamustafa Paşa, Istanbul, Turkey

**Background and aim:** Endocrine disrupting chemicals (EDC) act by interfering with the functions of the endocrine system. Bis (2-ethylhexyl) phthalate (DEHP), Bisphenol A (BPA) are among the EDCs and they are shown to be dangerous for the public health. These chemicals can be found in the plastic boxes, milk bottles, toys, cosmetics and even in drugs and people may be exposed to them in their daily life. Glycogen synthase kinase-3 is a ubiquitously expressed protein kinase that exists in two isoforms,  $\alpha$  and  $\beta$ . Its role in glycogen biosynthesis is based on its inactivating phosphorylation of glycogen synthase and it has been found to regulate many functions through Wnt and other signaling pathways. Nitric oxide (NO) is an endogenous mediator of numerous physiological processes that range from regulation of cardiovascular function and neuro-transmission to antipathogenic and tumoricidal responses. The aim of this study was to evaluate the effects of BPA and DEHP exposure on zebrafish embryos focusing on nitric oxide levels, *GSK3 $\beta$*  expression and apoptosis.

**Materials and Methods:** Adult AB strain zebrafish were raised and housed according to Institutional Animal Care and Use Committee protocols. Newly fertilized eggs were collected and normally dividing and spherical embryos were selected and utilized for all of the described studies. Embryos were exposed to BPA and DEHP under LC50 in well plates. Developmental parameters were monitored and documented daily during embryonic and larval development. Individual malformations and abnormalities were tabulated and cell death monitored by Acrydin orange. RT-PCR was used to evaluate *GSK3 $\beta$*  expressions. RNA was isolated from the embryos and single-stranded cDNA was synthesized from RNA. Relative transcript levels were calculated by using the  $\Delta\Delta$ CT method by normalizing the values with the house keeping gene,  $\beta$  actin. Nitric oxide levels were determined by Griess method.

**Results:** In the exposure groups apoptosis, developmental delays and deformities were evident with the alterations in nitric oxide levels. *GSK3 $\beta$*  expression increased in the BPA exposed embryos.

**Conclusion and Discussion:** These findings support the role of *GSK3 $\beta$*  and nitric oxide in the metabolism of toxic effects of BPA and DEHP.

*Keywords: BPA, DEHP, Apoptosis, GSK3 $\beta$ , Nitric Oxide*

## POSTER PRESENTATION – 98

### EVALUATION OF CRESTIN EXPRESSION AS A NEURAL CREST MARKER BY *IN SITU* HYBRIDIZATION, *CYCLIN D1* AND *MYCA* EXPRESSIONS BY RT-PCR AND APOPTOSIS IN BISPHENOL F AND BISPHENOL S EXPOSED ZEBRAFISH EMBRYOS

İsmail Ünal<sup>1</sup>, Fabio D'Orazio<sup>2</sup>, Nan Li<sup>2</sup>, Ünsal Veli Üstündağ<sup>3</sup>, Perihan Seda Ateş<sup>1</sup>, Türkan Yiğitbaşı<sup>3</sup>, Ferenc Mueller<sup>2</sup>, Ebru Emekli-Alturfan<sup>1</sup>

<sup>1</sup>Department of Biochemistry, Faculty of Dentistry, Marmara University, Istanbul, Turkey

<sup>2</sup>Institute of Cancer and Genomic Sciences, College of Medical and Dental Sciences, University of Birmingham, Edgbaston, Birmingham

<sup>3</sup>Department of Biochemistry, Faculty of Medicine, Istanbul Medipol University, Kavacak, Istanbul, Turkey

**Background and Aim:** Endocrine disrupting chemicals (EDCs) are compounds in the environment that can disrupt endocrine functions. They can be found in many products such as bottles, storage boxes, canned waters. Exposure to EDCs during development is a major concern and the health consequences are mostly permanent or long-lasting. As a result of the restrictions and increasing social pressure manufacturers seek replacing Bisphenol A (BPA) with alternatives such as bisphenol S (BPS) and bisphenol F (BPF) to produce “BPA-free” products. But as BPS and BPA have similar chemical structures BPA-like adverse effects can not be excluded. The use of BPS and BPF are currently not regulated and toxicological data on BPS and BPF are scarce. Myc is well known for its participation in many malignant conversions. Cyclin D1 activates cyclin dependent kinases CDK4 and CDK6 and drives cell proliferation. The aim of this study was to evaluate the effects of BPF and BPS exposure on zebrafish embryos focusing on development, apoptosis and marker gene expression.

**Materials and Methods:** Adult AB strain zebrafish were raised and housed according to Institutional Animal Care and Use Committee protocols. Newly fertilized eggs were collected and normally dividing and spherical embryos were selected and utilized for all of the described studies. Embryos were exposed to BPF and BPS doses under LC50 in well plates. Developmental parameters were monitored and documented daily during embryonic and larval development. Individual malformations and abnormalities were tabulated and cell death monitored by Acrydin orange. *Crestin* expression was evaluated as a neural crest marker by in situ hybridization (ISH). RT-PCR was used to evaluate *cyclin D1* and *myca* expressions. RNA was isolated from the embryos and single-stranded cDNA was synthesized from RNA. Relative transcript levels were calculated by using the  $\Delta\Delta CT$  method by normalizing the values with the house keeping gene,  $\beta$  actin.

**Results:** Increased apoptosis in BPS and BPF exposed embryos, loss of pigmentation in BPF group, decreased *crestin* expression and altered expressions of *cyclin D1* and *myca* were the major findings.

**Conclusion and Discussion:** Neural crest progenitor cells are the main contributors to craniofacial cartilage and connective tissue and these progenitor cells also give rise to the pigmentation. Accordingly decreased *crestin* expression in the exposure groups reveal the need for further research to find out the potentially harmful effects of these chemicals.

*Keywords: Bisphenol S, Bisphenol F, Apoptosis, Crestin, Myca, cyclin D1*

## POSTER PRESENTATION – 99

### ANALYSIS OF *CYCLIN D1* AND *MYCA* MRNA EXPRESSIONS OF BY RT-PCR AND CELL PROLIFERATIVE NUCLEAR ANTIGEN BY WHOLE MOUNT IMMUNOHISTOCHEMICAL STAINING AND APOPTOSIS IN METHYLPARABEN EXPOSED ZEBRAFISH EMBRYOS

Perihan Seda Ateş<sup>1</sup>, İsmail Ünal<sup>1</sup>, Ünsal Veli Üstündağ<sup>2</sup>, Türkan Yiğitbaşı<sup>2</sup>, Ahmet Ata Alturfan<sup>3</sup>, Ebru Emekli-Alturfan<sup>1</sup>

<sup>1</sup>Department of Biochemistry, Faculty of Dentistry, Marmara University, Istanbul, Turkey

<sup>2</sup>Department of Biochemistry, Faculty of Medicine, Istanbul Medipol University, Kavacık, Istanbul, Turkey

<sup>3</sup>Department of Biochemistry, Cerrahpasa Faculty of Medicine, Istanbul University, Kocamustafa Paşa, Istanbul, Turkey

**Background and Aim:** Paraben is a potent endocrine disrupting chemical that can interfere with the functions of the endocrine system. It may exert effects, either directly or indirectly, through receptor-mediated processes, thus mimicking endogenous hormones and/or inhibiting normal hormone activities and metabolism. Generally alkyl esters of p-hydroxybenzoic acid (parabens) are widely used as preservatives in personal care products, foods and pharmaceuticals and their endocrine disrupting effects still haven't enlightened exactly. Due to its small size, the ease of reproduction and rearing, and short generation interval, zebrafish is one of the most commonly used fish species in xenoestrogenic potential testing. Myc, a transcription factor estimated to regulate the expression of about 15% of cellular genes, is well known for its participation in many malignant conversions. Cyclin D1 activates cyclin dependent kinases CDK4 and CDK6 and drives cell proliferation. Cell proliferative nuclear antigen (PCNA) has been shown to act a marker of proliferation. The aim of this study was to evaluate the effects of methylparaben exposure on zebrafish embryos focusing on development, apoptosis and marker gene expression.

**Materials and Methods:** Adult AB strain zebrafish were raised and housed according to Institutional Animal Care and Use Committee protocols. Newly fertilized eggs were collected and normally dividing and spherical embryos were selected and utilized for all of the described studies. Embryos were exposed to methylparaben doses under LC50 in well plates. Developmental parameters were monitored and documented daily during embryonic and larval development. Individual malformations and abnormalities were tabulated and cell death monitored by Acridin orange. RT-PCR was used to evaluate *cyclin D1* and *myca* expressions. RNA was isolated from the embryos and single-stranded cDNA was synthesized from RNA. Relative transcript levels were calculated by using the  $\Delta\Delta CT$  method by normalizing the values with the house keeping gene,  $\beta$  actin. PCNA expression was evaluated by whole mount immunohistochemical staining.

**Results:** Increased apoptosis, developmental delays and malformations in methylparaben exposed embryos, increased PCNA expressions and altered expressions of *cyclin D1* and *myca* were the major findings.

**Conclusion and Discussion:** These findings reveal the need for further research to find out the potentially harmful effects of methylparaben.

*Keywords: Methylparaben, Apoptosis, Cell Proliferative Nuclear Antigen, Myca, cyclin D1*



## POSTER PRESENTATION – 100

### INVESTIGATION OF THE EFFECTS OF SILVER NANOPARTICLES USED IN TEXTILE INDUSTRY ON APOPTOSIS AND *MYCA*, *CYCLIN D1*, *GSK3B* EXPRESSIONS

Oğuz Eryılmaz<sup>1</sup>, Perihan Seda Ateş<sup>2</sup>, Ünsal Veli Üstündağ<sup>3</sup>, İsmail Ünal<sup>2</sup>, Ahmet Ata Alturfan<sup>4</sup>, Ebru Emekli-Alturfan<sup>2</sup>, Mehmet Akalın<sup>1</sup>

<sup>1</sup>Department of Textile Engineering, Faculty of Technology, Marmara University, Istanbul, Turkey

<sup>2</sup>Department of Biochemistry, Faculty of Dentistry, Marmara University, Istanbul, Turkey

<sup>3</sup>Department of Biochemistry, Faculty of Medicine, Istanbul Medipol University, Kavacık, Istanbul, Turkey

<sup>4</sup>Department of Biochemistry, Cerrahpasa Faculty of Medicine, Istanbul University, Kocamustafa Paşa, Istanbul, Turkey

**Background and Aim:** Antimicrobial textile products are developing rapidly as functional textile products and are one of the most important points that textile sector has reached by today. Nano-sized metal and metal oxide particles are used in textile sector to provide functionality to the products. One of the most important nano metal is nano silver known especially for its antimicrobial properties. The mechanism of action is the interaction of silver with thiol groups of bacterial protein and termination of metabolic activity of the cell to and completely destroying the microorganism. Glycogen synthase kinase-3 is a ubiquitously expressed protein kinase that exists in two isoforms,  $\alpha$  and  $\beta$ . Its role in glycogen biosynthesis is based on its inactivating phosphorylation of glycogen synthase and it has been found to regulate many functions through Wnt and other signaling pathways. Myca is a transcription factor estimated to regulate the expression of about 15% of cellular genes, and it is well known for its participation in many malignant conversions. Cyclin D1 activates cyclin dependent kinases CDK4 and CDK6 and drives cell proliferation. The aim of this study was to evaluate the effects of silver nanoparticles exposure on zebrafish embryos focusing on *cmyc*, *cyclin d1* and *Gsk3 $\beta$*  expression and apoptosis.

**Materials and Methods:** Adult AB strain zebrafish were raised and housed according to Institutional Animal Care and Use Committee protocols. Newly fertilized eggs were collected and normally dividing and spherical embryos were selected and utilized for all of the described studies. Embryos were exposed to silver nano particles under LC50 in well plates. Developmental parameters were monitored and documented daily during embryonic and larval development. Individual malformations and abnormalities were tabulated and cell death monitored by Acrydin orange. RT-PCR was used to evaluate *cmyc*, *cyclin d1* and *Gsk3 $\beta$*  expressions. RNA was isolated from the embryos and single-stranded cDNA was synthesized from RNA. Relative transcript levels were calculated by using the  $\Delta\Delta$ CT method by normalizing the values with the house keeping gene,  $\beta$  actin.

**Results:** In the nano silver exposed groups increased apoptosis and alterations in the expressions of *cmyc*, *cyclin d1* and *Gsk3 $\beta$*  were evident with the malformations and developmental delays in the embryos.

**Conclusion and Discussion:** These findings support the need for further research to evaluate the effects of exposure to silver nano particles.

*Keywords:* Nano material, Silver, Apoptosis, *Gsk3 $\beta$* , *cmyc*, *cyclin d1*

## POSTER PRESENTATION – 101

### hsa-miR-501-3p IS A STABLE ENDOGENOUS CONTROL FOR BREAST TUMORS

Yasemin Oztemur Islakoglu<sup>1</sup>, Senem Noyan<sup>1</sup>, Bala Gur Dedeoglu<sup>1</sup>

<sup>1</sup>Ankara University, Biotechnology Institute, Ankara, Turkey

**Background / Aim :** Normalization is a very important process for the correct evaluation of biological data in expression analysis. It is essential to choose the correct normalization factor (endogen control), which allows the biologic difference to be revealed by eliminating technical differences. However, there is a large amount of involution related to this issue in the literature. This study was aimed to detect a stable miRNA which can be used as endogenous control in breast cancer tissues.

**Materials and Methods :** qRT-PCR studies were performed with 18 different miRNAs and 22 breast tumor tissues and data were analyzed with NormFinder.

**Results :** hsa-miR-501-3p was identified as the most stable miRNA and in the literature search, no evidence has been found that it is altered in breast tumors.

**Discussion :** Stable expression of hsa-miR-501-3p in this miRNA set, including RNU6, which is the most commonly used normalization factor in miRNA normalization, indicates the importance and criticality of endogenous control selection.

**Conclusion :** This study shows that it is not reliable to select miRNAs and genes (e.g. housekeeping genes) that were standardized in the literature for normalization. A specific endogenous control should be selected for the unique sample set to minimize the technical errors affecting the biological differences.

*Keywords : Breast Cancer, miRNA, Normalization, Endogenous Control*

POSTER PRESENTATION – 102

**THE INVESTIGATION OF ASSOCIATION BETWEEN *CLUSTERIN* GENE  
rs11136000 POLYMORPHISM IN PSEUDOEXOPHYLOSIS  
SYNDROME/GLAUCOMA**

Serbulent Yigit<sup>1</sup>, Akin Tekcan<sup>2</sup>, Helin Deniz Demir<sup>3</sup>, Ayse Feyda Nursal<sup>4</sup>, Sabire Kilicarslan<sup>1</sup>

<sup>1</sup>Gaziosmanpasa University, Faculty of Medicine, Department of Medical Biology, Tokat, Turkey

<sup>2</sup>Ahi Evran University, Faculty of Medicine, Department of Medical Biology, Kirsehi,, Turkey

<sup>3</sup>Gaziosmanpasa University, Faculty of Medicine, Department of Ophthalmology, Tokat, Turkey

<sup>4</sup>Hitit University, Faculty of Medicine, Department of Medical Genetics, Corum, Turke

**Aims:** Pseudoexfoliation (PEX), diagnosed as clinically, is a disease characterized by the presence of the gray-white fibrogranular pseudoexfoliation material located on the anterior lens capsule and/or pupillary edge, in the anterior segment examination of the substance. Glaucoma, a chronic optic neuropathy, is usually associated with increased intraocular pressure, optic nerve head cupping; make up the loss of retinal ganglion cells and degeneration of the visual field. Glaucoma is the leading cause of irreversible and preventable blindness. In this study, we aimed to investigate if there is a relationship between this single nucleotide polymorphism (SNP) of CLU gene, and PEX in Turkish population.

**Materials and Methods:** The case group included 100 PEX patients who don't have any kind ship with each other. The control group included 100 healthy volunteers who don't have any kind ship with each other. Genotyping of SNP (rs11136000) on CLU gene, was determined by using polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) method.

**Results:** A relationship between a sequence variant (rs11136000) on CLU gene and PEX was observed in different populations. C allele frequency was observed higher in the patient group. In the control group, T allele frequency was higher.

**Conclusion:** According to this, the possibility of the disease is high in people who has C allele; and the possibility of the disease is low in people who has T allele. We didn't observed a statically significant correlation between rs11136000 T> C polymorphism of CLU gene and PEX disease.

*Keywords: Pseudoexfoliation Syndrome, Clusterin gene, rs11136000, Polymorphism*

*This study was approved by the Gaziosmanpasa University Clinical Research Ethical Committee (Approval no: 15-KAEK-001).*

## POSTER PRESENTATION – 103

### THE 1800 MHZ RADIOFREQUENCY RADIATION CAN EFFECT OF HEAT SHOCK PROTEIN HSP25 GENE EXPRESSION LEVELS IN RAT RENAL TISSUE

Nurcan ARAS<sup>1</sup>, Badel ARSLAN<sup>1</sup>, Ugurgul YAS<sup>1</sup>, Aysegül CETINKAYA<sup>1</sup>, Semra ERDOĞAN<sup>2</sup>

<sup>1</sup>Faculty of Medicine, Department of Medical Biology, Mersin University, Mersin, Turkey

<sup>2</sup>Faculty of Medicine, Department of Biostatistics, Mersin University, Mersin, Turkey

Radiofrequency electromagnetic fields (RF-EMF) exposure can stimulate the cellular stress response pathways. Heat shock proteins (Hsps) are one of the most inducible proteins by RF-EMF. Some of them are Hsp25, Hsp27 and Hsp60. We determined these genes expression levels to evaluate the possible health effects of 1800 Mhz cell phone radiofrequency radiation (RF) emitted by cell phones on *Wistar albino* rat's renal tissue. Ten weeks old mature *Wistar albino* rats included in experiment. Divided them three groups and each group consist of eight rats. The exposed group was exposed by 1800 MHz RF 2h/day along 8 weeks. Sham group was the same conditions with exposed group without RF exposure. Control group was kept in their own conditions in the animal laboratory. All of them were sacrificed at the end of the eight weeks and removed their kidneys. Total RNA was extracted from renal tissue homogenate. cDNA was synthesized from RNA and then *Hsp25*, *Hsp27* and *Hsp60* genes expression levels were detected with Real-Time PCR system. The results demonstrated that exposure of 1800 MHz RF-EMF can alter the *Hsp25* ( $p=0,018$ ) gene expression level in the exposure groups renal tissue. However the *Hsp27* ( $p=0,454$ ) and *Hsp 60* ( $p=0,305$ ) genes expression levels were not altered between the groups. Longer than eight weeks exposure may be altered *Hsp27* and *Hsp60* genes expression levels too. In conclusion, our conditions of RF-EMF may lead to renal diseases like renal cell carcinoma, due to alteration some genes expression levels. Further studies should be performed to evaluate the effect of cell phone use and health effects.

*Keywords: 1800 MHz, Renal tissue, Hsp25, Hsp 27, Hsp 60, Gene Expression*

*Ethics committee decision number: 251835-013/40*

## POSTER PRESENTATION – 104

### THE INVESTIGATION OF INTERLEUKIN-6 GENE PROMOTER POLYMORPHISM IN PATIENTS WITH SCHIZOPHRENIA IN EASTERN TURKEY

Ulku OZBEY<sup>1</sup>, Gokben Ozbey<sup>2</sup>, Mustafa NAMLI<sup>3</sup>

<sup>1</sup>Departments of Genetic, Health High School, Munzur University, Tunceli, Turkey,

<sup>2</sup>Vocational School of Health Services, Firat University, Elazığ, Turkey.

<sup>3</sup>Departments of Psychiatry, Mental health and diseases hospital, Elazığ, TURKEY

**Background/Aim:** Schizophrenia is one of the most severe psychiatric disorders, with a worldwide incidence of 1%. The pathophysiological process of schizophrenia is still unclear. Immunological abnormalities have been found to be associated with schizophrenia for decades. Cytokines are key proteins involved in the immune system activation. Interleukin-6 (IL-6), an important immunoregulatory cytokine, is located on chromosome 7p21.1–22.3, a region previously reported to be linked to schizophrenia in genetic studies. In the present study it was aimed to examine the IL-6 gene promoter region's polymorphic variants in Turkish schizophrenia patients and controls.

**Materials and Methods:** Polymorphisms at position -174 in the IL-6 promoter region were determined in 103 Turkish patients who were diagnosed with schizophrenia, based on the DSM-IV, and 105 healthy controls, by polymerase chain reaction (PCR)-restriction fragment length polymorphism (RFLP).

**Results:** We analyzed allele and genotype distributions using a case-control association study. Genotyping was performed by RFLP. Statistically significant differences were observed in both allelic and genotypic frequencies of the interleukin-6 gene (IL6) rs1800795 (-174G/C) polymorphism between schizophrenia patients and control groups (Allele;  $p=0.002$ , OR 1.95, 95% CI 1.18-2.14; Genotype;  $p<0.05$ , OR 0.81, %95 CI 0.64-1.1).

**Discussion:** IL-6 rs1800795G/C gene polymorphisms differ according to geographic regions and ethnic groups. The cause of this discrepancy is associated with environmental, medical and ethnic differences as with the reflection of other social factors' effects, small sample problems, genetic background heterogeneity and publication bias.

**Conclusion:** This work has an important place in terms of being the first study which examines the relation IL-6 gene promoter polymorphism in patient and control groups in the Turkish population in Turkey. It was determined that there is a relationship between patients with schizophrenia and IL-6 rs1800795 polymorphism in the Turkish population. Genotypes of IL-6 and IL-6 receptors, and discrimination of SNP settled in this gene are believed to play an important part in determining the potential genetic code of this disease in 105 schizophrenia patients and 103 normal people. These data suggest that the IL-6 rs1800795 C allele may be a potential risk factor for schizophrenia in the Turkish population, and apparently in all humans.

*Keywords: Immunopsychiatry, Interleukin-6, Polymorphism, Schizophrenia.*

*Ethics Committee's approval number: 5-1-2006, toplanti 1/3*

*Note to the Scientific Committee: In this study was used DNAsamples obtained from blood of Schizophrenic patients and controls in the my Doctorate thesis that mentioned entitled "Ülkü ÖZBEY, Doctorate thesis, Elazığ, 2009: Investigation of Differences in P53 Gene Polymorphisms Between Schizophrenia and Lung Cancer Patients in The Turkish Population" was supported by Firat University Science Research Projects (FUBAP) (Project No-1301).*

## POSTER PRESENTATION – 105

### INVESTIGATION OF CYTOCHROME P450 1A1 (CYP1A1) GENE POLYMORPHISMS AND RISK OF BREAST CANCER IN RATS EXPOSURE TO AROCLOR 1254

Ülkü ÖZBEY<sup>1</sup>, Mürsel KÜÇÜK<sup>2</sup>, Ayşe SEYRAN<sup>3</sup>, Gökben ÖZBEY<sup>4</sup>

<sup>1</sup>Department of Genetic, Health High School, Munzur University, Tunceli, Turkey,

<sup>2</sup>Departments of zootechny, Faculty of Veterinary Medicine, Yuzuncu Yil University, Van, Turkey

<sup>3</sup>Departments of Biochemistry, Health High School, Bitlis Eren University, Bitlis Turkey

<sup>4</sup>Vocational School of Health Services, Firat University, Elazig, Turkey.

**Background/Aim:** Breast cancer is a genetic disease where breast cells proliferate abnormally. Most of the risk factors for breast cancer is associated with the increased level or prolonged exposure to estrogen. The polymorphic genes, involved in estrogen biosynthesis and conversion of the estrogen metabolites and products, play an important role in the development of sporadic breast cancer. Polychlorinated biphenyls (PCBs) can cause environmental contamination and threaten people's health due to lipophilic features. The Cytochrome P4501A1 (CYP1A1) gene is a gene that is induced by PCBs is one of the mechanisms proposed. It plays a key role in phase I metabolism of polycyclic aromatic hydrocarbons (PAH) and in estrogen metabolism. The goals of this study were to: (i) determine what is the effect on breast cancer development of Aroclor 1254 (A1254), (ii) research the relationship to breast cancer of four CYP1A1 gene polymorphisms (M1: 3801T/C, Ile462Val, M2: 4889A/G, and M3: 5639T/C) in rats experimentally exposed to an oxidizing agent such as A1254 and (iii) analyze polymorphic variants of this gene promoter region in all groups.

**Materials and Methods:** In this study, 30 normal female (control) and 30 Sprague-Dawley female rats exposed to A1254 provided from the center for experimental studies of Firat University Medical Faculty were used. The rats were given A1254 at 2 mg/kg/day by injection at 20 days. After the injections, rats were decapitated. Genotypes were searched by the polymerase chain reaction-based restriction fragment length polymorphism (PCR-RFLP) method.

**Results:** We compared gene activity (M1, M2, M3 and codon 462) between the A1254 infected rats and a control group. For all of the four genes, there were no significant differences found in the genotype and allele frequencies in both groups ( $p>0.005$ ).

**Discussion:** The functional significance of the polymorphisms remains unclear. In the other 17 studies, no association was identified between breast cancer and CYP1A1 genotype. Metaanalysis observed no significant risk for the genotypes. In our study, the effects of A1254 because of the short length of the application period could not be determined.

**Conclusion:** We highlighted that Aroclor1254 has different and harmful effects on oxidant and anti-oxidant systems in all groups. The reaction of rats exposed to PCB gave obvious evidence of oxidant damage. Future studies should required to explore possible interactions between CYP1A1 and sources of PAH, markers of estrogen exposure, and other genes involved in PAH metabolism.

*Keywords: Aroclor1254, oxidative stress, breast neoplasms; cytochrome P-450 CYP1A1; polymorphism.*

*Ethics Committee's approval number: Ethics Committee's approval number: 2010/02-3 Tarih: 25.02.2010*

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*Note to the Scientific Committee: This study was supported by Yüzüncü Yıl University Science Research Projects (YYUBAP) (Project No: 2011-VF-B033). We thank YYUBAP for contribution. However, for the extraction of genomic DNA in this work was performed by blood obtained from rats in her doctorate thesis that mentioned entitled "Ayşe SEYRAN, PhD thesis, Elazığ, 2010: "entitled "Investigating the oxidative stress in pregnant rats and their offsprings exposed to Aroclor1254 and the Protective effects of Vitamin E against this stress" was supported by Fırat University Science Research Projects (FUBAP) (Project No-1575).*

## POSTER PRESENTATION – 106

### THE DETERMINATION OF THE CYP2C19 GENE POLYMORPHISM IN STENT-INSERTED PATIENTS

Yasemin Ekinci<sup>1</sup>, Emine Dıraman<sup>1</sup>

<sup>1</sup>Ondokuz Mayıs University, Faculty of Science & Arts, Department of Biology, Samsun

The aim of this study is to investigate the distribution of CYP2C19 (cytochrome 4502C19) gene polymorphism in stent-inserted patients and the healthy control group from Samsun and the surrounding provinces, thus the possibility to adjust the dosage of antithrombotic drugs by looking at this polymorphism in patients who are inserted stents.

250 patients over 18 years old who had been inserted stents in the cardiology department as the patients group and 115 healthy people as the control group were involved in the study. Peripheral blood samples obtained from the patients and the controls were placed in 2 ml heparinized tubes and genotyped at molecular genetics laboratory. From the DNA obtained from these blood samples, the CYP2C19 gene was identified by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) technique. CYP2C19\*2 PCR products were cut with the SmaI enzyme respectively, and the resulting fragments were identified by agarose gel electrophoresis. As a result of the identification, the genotypes of 250 stent-inserted patients and 115 healthy people were determined and compared. Accordingly, 188 wild type, 58 heterozygote and 4 mutant types were described in 250 stent-inserted patients. And in the healthy control group, 87 wild, 27 heterozygote and 1 mutant type were defined.

The proportion of CYP2C19 slow metabolizers varies between communities. The frequency of slow metabolism of the caucasian race varies from 2-5% in the eastern population to 11-23% in the eastern populations. Başçı et al. (1994) found the proportion of slow metabolizers in healthy people to be 0.94% and this study was the first researched in Turkish people. And Aynacıoğlu et al. (1999) found it 1% in 404 healthy people. CYP2C19 plays a role in the metabolism of many drugs used clinically (Hunfeld 2008). For this reason, it is crucial to adjust the dose of medication for the patients in whom it is determined that the CYP2C19\*2 allele is heterozygote or mutant. Clopidogrel is a drug appearing in the antithrombotic drug group and taking effect by inhibiting the aggregation of thrombocytes causing blood-clotting. In the case of poor metabolizer patients with stents attached, the risk of serious effects such as stroke, infarction and death is increased following the use of clopidogrel. Therefore, by looking at this polymorphism in advance, the drug and drug dose can be adjusted. We also think that the result of our study will contribute to the literature.

When statistical analysis was performed, it was observed that there was no correlation between the genotype distributions in the patient and control groups ( $p > 0.05$ ). It was also observed that there wasn't a correlation between gender and genotype distribution in both groups ( $p > 0.05$ ). Our study is the first study to determine CYP2C19 gene polymorphism in patients from both Samsun and the surrounding provinces, who were inserted stent and the results are parallel with those of Başçı et al. (1994) and Aynacıoğlu et al. (1999).

*Keywords: CYP2C19, Stent, RFLP, Allele*

*Project Order No: 30.01.2012*

*Ethical Board Order No: 30.12.2011*



## POSTER PRESENTATION – 107

### PMA FUNCTIONS AS AN AUTOPHAGY INHIBITOR THROUGH ACTIVATION OF A SERINE THREONINE KINASE

Ozlem Yedier<sup>1</sup>, Seval Kilic<sup>1</sup>, Devrim Gozuacik<sup>1,3</sup>, Ozlem Kutlu<sup>2,3,\*</sup>

<sup>1</sup> Department of Molecular Biology Genetics and Bioengineering, Faculty of Engineering and Natural Science, Sabancı University, İstanbul, Turkey

<sup>2</sup> Nanotechnology Research and Application Center, Sabancı University, İstanbul, Turkey

<sup>3</sup> Sabancı University, Center of Excellence for Functional Surfaces and Interfaces for Nano Diagnostics (EFSUN), İstanbul 34956, Turkey

\*Corresponding author.

**Background/Aim:** Serine-threonine kinases have vital roles in various signalling pathways such as proliferation, differentiation and apoptosis. Thus, they served as crucial players in health and disease including cancer. Isozymes of these families show tissue specific expression patterns and function specifically in different pathways. Autophagy is another major process in the cell which degrades long-lived, non-functional organelles and proteins to sustain the homeostasis. Moreover, as well as serine threonine kinases, autophagy was also found to relate with cancer in different stages. Here, we investigated the relation between autophagy and these kinases in cancer.

**Materials & Methods:** Several stimuli including ceramide and PMA were used to activate different isozymes of this family in HeLa cells. Upon stimulus, activation status of the isozymes was checked in terms of self or substrate phosphorylation. Cellular autophagic activity was determined via GFP-LC3 dot counting, LC3 shift assay and p62 accumulation. Moreover, effect of these stimuli was investigated upon autophagy induction with starvation. Silencing of these kinases were performed to reveal which isozyme is responsible for this phenomenon. MEF GFP-LC3 transgenic autophagy reporter cells were also used to confirm the effect of these stimuli on autophagy.

**Results & Discussion:** One of the stimuli (PMA) used in this study showed very prominent changes in autophagic activity of cancer cells. This effect was even more evident when starvation was used together with the PMA. Interestingly, PMA caused a very robust self-phosphorylation only one of these isozymes. This effect was further validated through silencing of this isozyme.

**Conclusion:** According to our findings, it is showed that this particular serine-threonine kinase has a regulatory effect on autophagy upon activation with PMA.

*Keywords : Autophagy, serine-threonine kinases, cancer*

*\*This work was supported by The Scientific and Technological Research Council of Turkey (TUBITAK) 1001- 114Z836 Grant*

## POSTER PRESENTATION – 108

### IS THERE THE RELATIONSHIP BETWEEN IL-33 LEVELS WITH OXIDATIVE STRESS IN OBESITY?

Maide Hacer ALAGOZ<sup>1</sup>, Türkan YİĞİTBAŞI<sup>2</sup>, Nesrin EMEKLİ<sup>2</sup>

<sup>1</sup>Department of Clinical Biochemistry, Okmeydanı Educational and Research Hospital, Istanbul, Turkey

<sup>2</sup>Department of Biochemistry, Medical Faculty, Medipol University, Istanbul, Turkey.

Increased ROS secretion into peripheral blood from accumulated fat tissue in obesity is involved with induction of insulin resistance in skeletal muscle and adipose tissue and impaired insulin secretion by  $\beta$  cells. Recent studies have demonstrated a protective role for IL-33 against obesity-associated inflammation, atherosclerosis and metabolic abnormalities. In this study, we aimed to investigate the IL-33 levels oxidative stress relationship in obese individuals.

Measurements of height, weight, were obtained and 80 participants were classified according to their body mass indices (BMI, kg/m<sup>2</sup>,) into health-weight (BMI < 25 n=21), overweight (25  $\leq$  BMI < 30 n=21) and obese (30  $\leq$  BMI, n=38) Peripheral blood was obtained and the fasting glucose and lipid profiles (TGL, total cholesterol, LDL-C, high density lipoprotein cholesterol (HDL-C)), Total oxidant level (TOL) and total antioxidant capacity (TAC) measured by photometric method. HbA1c, CRP levels measured by chemiluminescence immunoassay. IL-33 serum levels measured by ELISA method. All statistics were calculated using the SPSS 17.0 software. *p* values < 0.05 were considered statistically significant.

Obese subjects had significantly (*p* < 0.001) lower levels of TAC compared to control and overweight subjects. No difference was detected in TOL levels among subjects (*p* > 0.05). OSI and CRP levels were found to be significantly higher in obese subjects (*p* < 0.001; *p* < 0,05, respectively). Overweight subjects had numerically higher levels of IL-33 compared to health-weight and obese subjects. However, no significant difference was observed in IL-33 levels among the three groups (*p* > 0.05). BMI was negatively correlated with TAC (Spearman *r* = -0.52, *p* = < 0.001) in subjects. Furthermore, BMI was found to be positively correlated with OSI (Spearman *r* = 0.45, *p* = < 0.001), Glukoz (Spearman *r* = 0.36, *p* = 0.001) and HbA1c (Spearman *r* = 0.37, *p* = 0.001). No correlation was between BMI and IL-33 in groups

This results suggest that diminished levels of TAC and increased levels of OSI may be associated with obesity. We concluded that further studies were needed to understand possible antioxidant, anti-inflammatory and protective metabolic effects of IL-33 in obesity.

*Obesity, IL-33, TAC, TOS, OSI*

*Ethics Committee approval number: 335 / 25.06.2015*

POSTER PRESENTATION – 109

**DIAGNOSIS OF BLADDER OUTLET OBSTRUCTION-ASSOCIATED ACUTE KIDNEY INJURY: DIFFERENTIAL ROLES OF SERUM CREATININE, AND URINARY NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN**

Emre Karabay<sup>1</sup>, Ugur Yucetas<sup>1</sup>, Erkan Erkan<sup>1</sup>, Esmâ Yucetas<sup>2</sup>, Huseyin Aytac Ates<sup>1</sup>,  
Mustafa Kadihasanoglu<sup>1</sup>, Kemal Behzatoglu<sup>3</sup>, Mahmut Gokhan Toktas<sup>1</sup>

Istanbul Training and Research Hospital, Department of Urology<sup>1</sup> and Pathology<sup>3</sup>  
Haseki Training and Research Hospital, Department of Biochemistry<sup>2</sup>

**Objective:** To compare the urinary NGAL levels with serum creatinine levels in rats with bladder outlet obstruction (BOO).

**Materials-Methods:** Twenty male Wistar Albino rats, each weight 300-350 gr, were divided into 4 groups: (i) sham-operated control; (ii) 14 days partial BOO (iii) 28 days partial BOO; and (iv) complete BOO. In each group, basal serum creatinine and urinary NGAL levels were measured. Serum creatinine levels and urinary NGAL levels were assessed in group-4 on the third day of the study, in group-2 on the 14th day, and in group-3 on the 28th day. Measurements of urinary NGAL levels were performed with ELISA. The results were compared with plasma creatinine levels and creatinine clearance values. The excised bladder and renal tissues were histopathologically examined.

**Results:** The increase in plasma creatinine levels was statistically significant in only group-4 (13.79±1.57 mg/dL, p=0.011). Also, in group-4, the increase in plasma creatinine levels (p=0.043) and urinary NGAL levels (p=0.003) were statistically significant. In group-3, increase in urinary NGAL levels were higher (p=0.007). However, plasma creatinine levels did not increase. There was no correlation between the levels of urinary NGAL and plasma creatinine, the positive correlation between urinary NGAL and creatinine clearance levels was shown (r=-0.445, p=0.004). There was no significant difference in renal tubular injury between the groups, however there was a positive correlation between the duration of the obstruction and the increase of fibrosis in the bladder tissue (p=0.016).

**Conclusion:** It can be concluded that urinary NGAL levels might be an early biomarker for renal dysfunction in partial bladder outlet obstruction.

## POSTER PRESENTATION – 110

### COMPARISON OF OXIDATIVE STRESS PARAMETERS IN PERIPHERAL AND INTERNAL SPERMATIC VEINS OF INFERTILE PATIENTS WITH VARICOCELE

Ugur Yucetas<sup>1</sup>, Mehmet Gokhan Culha<sup>1</sup>, Esmâ Yucetas<sup>2</sup>, Erkan Erkan<sup>1</sup>, Mustafa Kadihasanoglu<sup>1</sup>, Mahmut Gokhan Toktas<sup>1</sup>

<sup>1</sup>Department of Urology, Istanbul Training and Research Hospital, Istanbul

<sup>2</sup>Department of Biochemistry, Haseki Training and Research Hospital, Istanbul

**Introduction:** The aim of this cross-sectional study is to compare the level of oxidative stress in peripheral and internal spermatic vein blood of varicocele patients with fertile men.

**Method:** Between October 2012 and July 2014. 30 primary infertile varicoceles and 30 fertile control patients were included in the study. Physical examination and scrotal Doppler ultrasonography were performed in each patient with varicocele. Peripheral venous (Group 1) and internal spermatic venous blood (Group 2) of the patients with varicocele and peripheral venous blood (Group 3) of the control group were compared in terms of ischemia modified albumin (IMA), total oxidant capacity (TOC), total antioxidant capacity (TAC), oxidative stress index (OSI), Kruskal-Wallis and Spearman correlation tests were used for statistical analysis, and  $p < 0.05$  was considered as significant.

**Results:** The mean age of the patients was  $27.33 \pm 5.40$  (18-36) years, and the mean age of the control group was  $28.17 \pm 5.50$  (19-36) years. When median IMA and TAC levels were compared, there was no significant difference between groups ( $p = 0.326$  and  $p = 0.433$ , respectively) (Table). However, median TOC and OSI levels were significantly lower in control group ( $p = 0.007$ , and  $p = 0.005$ , respectively). The age of the patients was significantly correlated with IMA, TAC, and OSI levels of internal spermatic vein ( $r = -0.72$   $p = 0.043$ ,  $r = 0.397$   $p = 0.03$ ,  $r = 0.367$   $p = 0.046$ , respectively).

**Conclusion:** This study showed the harmful effect of varicocele induced oxidative stress in the local and the systemic circulation. Further research is needed on varicocele and oxidative stress mechanisms.

Table: Comparison of IMA, TOC, TAC, and OSI levels between groups.

	<b>Group 1</b> (n=30)	<b>Group-2</b> (n=30)	<b>Group-3</b> (n=30)	<b>p</b>
IMA [ng/mL, median(IQR), min-max]	136.59 (215.16) [20.87-779.44]	119.91 (163.88) [38.33-785.06]	108.14 (72.54) [32.02-656.63]	0.326
TOS [ $\mu$ mol/L, median(IQR), min-max]	41.05 (45.3) [3.5-96.3]	30.85 (34.3) [14.2-89.6]	9.25 (45.8) [0.7-102]	<b>0.007</b>
TAS [mmol/L, median(IQR),min-max]	4.25 (0.7) [3.1-4.8]	4.15 (0.6) [3.4-7.7]	4.20 (0.5) [3.4-10.6]	0.433
OSI [median(IQR), min- max]	1.05 (1.16) [0.08-2.47]	0.79 (0.86) [0.30-1.91]	0.21 (1.19) [0.02-2.21]	<b>0.005</b>

IMA: ischemia modified albumin, TOC: total oxidant capacity TAC: total antioxidant capacity, OSI: oxidative stress index, IQR: interquartile range

## POSTER PRESENTATION – 111

### **EFFECT OF LOW DOSE $\alpha$ -LIPIC ACID ON BODY WEIGHT, FOOD INTAKE, LIPID PROFILE AND ADIPOSE TISSUES IN ELDERLY RATS FED A HIGH FAT DIET**

Sehkar Oktay<sup>1,2</sup>

<sup>1</sup>Department of Basic Medical Sciences, Faculty of Dentistry, Marmara University, Maltepe, Istanbul, Turkey

<sup>2</sup>North Florida/South Georgia Veterans Health System, Geriatric Research, Education, and Clinical Center, Gainesville, FL, USA

**Background/Aim:** The aim of the study was to investigate the effect of administration of  $\alpha$ -lipoic acid (LA) on body weight, blood lipids and adipose tissue parameters in elderly rats fed a high fed (HF) diet.

**Materials and Methods:** Male Fischer F344 XBN rats (24 months old) were divided into groups as follows: Control (provided the standard chow) (n=5); HF (provided the HF diet contains 60% fat) (n=5); HF+ LA (with provided the HF diet and LA injection 1mg/kg ip. for 1 week, then double dose for 1 week) (n=6). Rats were sacrificed, blood and adipose tissues were collected. Body weight (BW), kilocalorie intake (KCal), food intake (FI), blood lipid parameters: total cholesterol (TC), triglycerides (TG), high and low density lipoproteins (HDL, LDL) and white adipose tissue parameters: retroperitoneal (RTWAT), perirenal (PWAT), epididymal (EWAT) and brown adipose tissue (BAT) were investigated in experimental groups.

**Results:** As expected, BW increased in HF and HF+LA groups compared to the controls but the result was insignificant in HF group. KCal significantly increased in HF group compared to the controls and also in HF+LA group compared to the HF group. There was no difference in FI result in HF group, but significantly decreased in HF+LA group compared to the both controls and HF group. No significant change was observed in lipid parameters of either HF and HF+LA groups compared to the controls. Even so, RTWAT, PWAT and EWAT significantly increased both in HF and HF-LA groups, BAT significantly increased only in HF group compared to the controls. Treatment with LA to HF did not change the parameters.

**Discussion:** LA administration did not decrease lipid and adipose tissue parameters in HF group. This result may be a reason of administration of low dose LA, but the elderly animals prevented the application higher doses of LA. Also a long term treatment with low dose may be effective on these parameters.

**Conclusion:** It is well known LA is effective on reduction of feed efficiency and modulate lipid metabolism. But it is necessary to determine the appropriate dose and duration of the treatment for the beneficial effects of LA in elderly rats.

*Keywords:  $\alpha$ -Lipoic Acid, high fat diet, food intake, adipose tissue*

## POSTER PRESENTATION – 112

### ***ANALYSES OF SUKKULA RETROTRANSPOSON IN HUMAN GENOME***

Buket Cakmak<sup>1,2</sup>, Sevgi Marakli<sup>1</sup>, Nermin Gozukirmizi<sup>1</sup>

<sup>1</sup>Department of Molecular Biology and Genetics, Faculty of Science, Istanbul University, Vezneciler, 34134 Istanbul, Turkey

<sup>2</sup>Biruni University Vocational Health High School, Medical Laboratory Techniques, Topkapi, 34104 İstanbul, Turkey

**Background / Aim:** Retrotransposons, mobile genetic elements, constitute 15-90% of the plant genomes. There are many studies related to retrotransposons, increasing knowledge about evolution. They are classified as autonomous or nonautonomous based upon whether they encode proteins required for their retrotransposition or not. Our aim is to identify plant-specific nonautonomous retrotransposon (*Sukkula*) in human genome.

**Materials and Methods:** In this study, we isolated genomic DNA from 24 different individuals and *Sukkula* retrotransposon movements were analysed by IRAP molecular marker technique. IRAP PCR products resolved by agarose gel electrophoresis. After agarose gel electrophoresis, the gel was scanned and photographed on an ultraviolet (UV) transilluminator. The polymorphism rates were calculated using Jaccard similarity coefficient.

**Results:** Polymorphism rates were calculated among samples by comparing each sample with the other samples. At the end of analyses we detected that there were 8-100% polymorphism ratios among all samples.

**Discussions:** *Sukkula* is known among the most active retrotransposons in barley genome. There are a number of studies to detect *Sukkula* retrotransposon with different species. These studies demonstrated that *Sukkula* is also active in different organisms. Our study supports previous studies.

**Conclusions:** This study is one of the first reports related to plant-specific retrotransposon in human genome. The obtained findings are expected to contribute to increase knowledge about plant retrotransposon in human genome and also their roles in human genome evolution. This work was carried out in accordance with ethical rules.

*Note to the Scientific Committee: This work was supported by the Scientific Research Projects Coordination Unit of Istanbul University [grant number FDK-2017-22142].*

*Keywords: Mobile Genetic Elements, human, IRAP, polymorphism*

## POSTER PRESENTATION – 113

### DEVELOPMENT OF A FAST, ECONOMICAL & PRACTICAL METHOD FOR THE MOLECULAR DETECTION OF BACTERIAL MENINGITIDIS PATHOGENS

<sup>1</sup>Volkan Demir, <sup>1,5</sup>Canan Ketre, <sup>1,3</sup>Gözde Girgin Özgümüş, <sup>2</sup>Selin Nar Ötgün, <sup>2</sup>Meral Turan, <sup>2</sup>Selçuk Kılıç, <sup>1</sup>Halil İbrahim Miraloğlu, <sup>1</sup>Mehmet Genç, <sup>4</sup>Mustafa Kolukırık

<sup>1</sup>Bioeksen Research and Development Technologies Ltd. Co., Istanbul Technical University, ARI TEKNOKENT Istanbul/Turkey

<sup>2</sup>Reference Microbiology Laboratories Department, Turkish Public Health Institute (TPHI), Ankara/Turkey

<sup>3</sup>Marmara University, Medical School, Medical Genetics Department Istanbul/Turkey

<sup>4</sup>ENGY Environmental and Energy Technologies Biotechnology Ltd. Co., Bogazici University Technopark, Istanbul/Turkey

<sup>5</sup>Department of Environmental Engineering, Istanbul Technical University, Istanbul/Turkey

In the detection and serotyping of bacterial meningitides, conventional polymerase chain reaction (PCR) and real time/qualitative PCR (qPCR) based tests where fast and reliable result can be obtained in hours scale, that doesn't have disadvantages of gold standard culture based methods, is present in American Center for Disease Control and Prevention (CDC) guidelines. Adapting laboratory personnel that are familiar with conventional microbiological methods, to complicated molecular analysis protocols that is present in CDC guidelines, is impossible. The aim of this project is to render the molecular methods for the detection and serotyping of bacterial meningitides pathogens that are present in CDC guidelines, simpler and cheaper by revising them, so that they can be effectively applied by personnel that doesn't have any knowledge about these methods.

A method was developed for fast (15 min) bacterial DNA isolation from Cerebrospinal Fluid (CSF) and serum samples based on cell disruption with guanidium thiocyanate and purification of DNAs with silica columns. The qPCR protocol is optimized using "Bio-Rad CFX Connect" and "Roche Light Cycler 96" instruments. The qPCR master mixes that have two years of shelf life when kept at -20 °C, are ready for use just by adding the template DNA was developed and the reaction conditions are optimized under this project. In the validation steps, target and non-target reference sub species and plasmid vectors harboring target DNAs are used. Reference samples are prepared by inoculating CSF and serum samples that didn't contain targets.

qPCR detection limit, for all the DNA targets, is 3 copies of DNA/reaction. While, the detection limits, in the studies conducted with bacterial targets, are determined in the range of 10-100 cfu/ml. None of the developed tests have given cross reaction with non-target organisms. DNA isolation from 12 samples, qPCR set-up, scanning of 3 targets of bacteria with qPCR and analysis of the results, takes, maximum of 105 min with Bio-Rad CFX Connect, maximum of 90 min with Roche Light Cycler 96, in a single run. The foreseen application cost of the test per sample including all the plastics and consumables, manufacturing, distribution, training, technical support and all the like is 9.4€. In a single sample, serotyping of *N.meningitidis*, *H.influenzae* and *S.pneumoniae* can be completed in 75 min in Bio-Rad CFX Connect, in 60 min in Roche Light Cycler, where the cost is foreseen as 9.9 and 15 € respectively.

*Keywords: Bacterial meningitides, IVD NAT, Neisseria meningitidis, Haemophilus influenzae, and Streptococcus pneumoniae*



## POSTER PRESENTATION – 114

### DETERMINATION FREQUENCY OF XRCC1 (rs25487) GENE POLYMORPHISM IN TURKISH OVARIAN CANCER PATIENTS

Aslı Tetik Vardarlı<sup>1</sup>, Duygu Aygüneş<sup>1</sup>, Levent Akman<sup>2</sup>, Çığır Biray Avcı<sup>1</sup>, Coşan Terek<sup>2</sup>, Nur Selvi Günel<sup>1</sup>

<sup>1</sup>Ege University, Faculty of Medicine, Department of Medical Biology, Izmir, TURKEY

<sup>2</sup>Ege University, Faculty of Medicine, Department of Obstetrics and Gynecology, Izmir, Turkey

**Aim:** Ovarian cancer is the fifth leading cause of cancer-related death among women. Implementation of early diagnosis and effective treatments have great importance to increase survival rate. In recent studies, gene mutations in DNA repair genes defined as an important risk factor for cancer development behind patient's age, obesity, family history of cancer. In DNA repairing pathway, The X-ray repair cross-complementing group 1 (*XRCC1*) gene plays a crucial role in base excision and nucleotide excision repair. The aim of our study was to determine the frequency of XRCC1 (rs25487) single nucleotide polymorphism (SNP) in Turkish patients with ovarian cancer.

**Materials&Methods:** Our study group consisted of 33 patients with ovarian cancer. Genomic DNA was extracted from patients ovarian tissue samples using QIAamp DNA Mini Kit. The gene-specific primers were synthesized. A total of 33 cases with ovarian cancer were genotyped for the XRCC1 (rs25487) SNP by Sanger sequencing method.

**Results:** XRCC1 (rs25487) AA, AG and GG genotype distributions were found in 3%, 0%, and 97% of patients with ovarian cancer. Significant associations was determined between the GG genotype and ovarian cancer.

**Discussion:** A study from Caucasians revealed that AA genotype have a protective effect in both basal cell and squamous cell cancers whereas GG genotype defined as a risk factor in development of basal cancers, breast cancers in studies of Koreans and Western New York, respectively. This is the first study to determine the frequency of XRCC1 (rs25487) SNP in ovarian cancers.

**Conclusion:** GG genotype of XRCC1 (rs25487) SNP may be used as a marker to detect the ovarian cancer development. Further studies are needed to determine the potential role of GG genotype on disease development with larger patient numbers.

*Keywords: XRCC1, (rs25487, ovarian cancer)*

## POSTER PRESENTATION – 115

### EVALUATION OF ACACETIN AS AN ANTICANCER AGENT AGAINST BREAST CANCER

Eren Yılmaz<sup>1</sup>, Ayşe Begüm Ceviz<sup>1</sup>, Allison Pınar Eronat<sup>1</sup>, Mehmet Fatih Seyhan<sup>1</sup>, Sema Bilgiç-Gazioğlu<sup>2</sup>, Hülya Yılmaz Aydoğan<sup>1</sup>, Oğuz Öztürk<sup>1</sup>

<sup>1</sup>Department of Molecular Medicine, ASDETAE, Istanbul University, Istanbul

<sup>2</sup>Department of Immunology, ASDETAE, Istanbul University, Istanbul

Flavanoids are natural compounds, abundantly found in medicinal and aromatic plants. Acacetin, a member of the flavone subclass of flavonoids, have been shown to have anti-proliferative effects on many cancer types following its anti-peroxidative, anti-inflammatory, anti-plasmodial and anti-mutogenic properties.

Breast cancer, most common cancer of women worldwide, comes second among all cancers. Surgery, radiation therapy, endocrine therapy and chemotherapy are beneficial in treatment. Chemotherapeutics that are commonly used in the treatment, damage the cancer cells by generating free radicals, concurrently impairing the DNA-RNA, proteins and lipids of the normal cells. Therefore, chemotherapeutics that cannot discriminate between healthy and cancer cells, damage normal cells and lead to numerous adverse effects. Hence, natural products with their low toxicity and adverse effects are intensely being investigated for the treatment of breast cancer. The objective of this study was to investigate the possible cytotoxic or apoptotic impact of Acacetin due to its low toxicity/adverse effects on MCF-7, a cell line representing the most common breast cancer type, Luminal A ER/PR +, and MCF10A, non-tumoregenic breast epithelial cell line.

The MCF-7 and MCF-10A cell lines were treated with Acacetin with various doses and time intervals. The cytotoxic effects were determined via the WST-1 assay at the 24th, 48th, 72nd hours and the apoptotic effects by the Annexin V-PI assay.

Acacetin exposure lead to a significant decrease in cell viability starting from a dose of 20-30 µg/ml on the MCF-7 cells compared to MCF-10A at all three time points ( $p < 0.001$ ). Conversely, on the control cell line, MCF-10A, no significant effects were observed except the highest doses ( $p > 0.05$ ). The Annexin V-PI assay revealed that while treatment of 10µg/ml Acacetin on MCF-7 induced apoptosis on 89% of the cells in 24 hours, MCF-10A cells displayed 88% viability. The findings suggest that Acacetin may be used as a supplementary phytochemical in the treatment of Luminal type breast cancer with minimal adverse effect.

*Keywords: Breast cancer, acacetin, flavonoids, apoptosis, cytotoxicity*

## POSTER PRESENTATION – 116

### SYNTHESIS AND BIOLOGICAL ACTIVITY OF INDOLINE AND TRIAZOLE-SUBSTITUTED DERIVATIVES AS GLYCOSIDASE INHIBITORS

Zeynep Özge Yılmaz<sup>1</sup>, Emel Karakılıç<sup>1</sup>, Arif Baran<sup>1</sup>

<sup>1</sup>Department of Chemistry, Faculty of Arts and Sciences, Sakarya University, Sakarya, Turkey

**Background/Aim:** Inhibitors of glycosidases, already used or tested in the treatment of diabetes and HIV infection and as antifungal agents, are expected to arouse increasing interest as therapeutic agents as our understanding of the role of glycosidases in recognition processes improves<sup>a</sup>. And is to synthesize new indoline and triazole derivatives which was investigate their inhibitory effects in glycosidase enzymes.

**Materials and Methods:** In the study, cyclohexane and thiazole derivatives scaffold were synthesized as hybride molecule. In ringe of study, 3,4;5,6-diepoxy cyclohex-1-ene<sup>b</sup> was treated with indoline ring and than affording residue. The residue was reacted with propargyl bromide for protection of hydroxyl groups. Reactive tri bound of propargylate compound was subjected to benzyl or alkyl azide compounds using catalytic amount of copper sulfate afforded reactive triazole molecule<sup>c</sup>.

**Results:** Here in, we synthesized two new compounds for the first time in the literature and probed their biological activities with the  $\alpha$  and  $\beta$ -glucosidases. IC50 value of the compounds were compared according known acarbose as glucosidase inhibitor. In the result our new molecule have more active as acarbose against glucosidases.

**Conclusion:**, Affection activity of  $\alpha$  and  $\beta$  glucosidase inhibition, due to their potential indoline, triazole and aromatic scaffold, were secrened for their promising therapeutic potential in the management of wide ranging disorder like diabetes as known in literature.

*Keywords: Glycosidase, 1,2,3-Triazole, Indoline.*

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POSTER PRESENTATION – 117

**REAL-TIME PCR (qPCR) BASED METHOD FOR DETECTION AND SPECIES  
DIFFERENTIATION OF *BORDETELLA PERTUSSIS*, *BORDETELLA  
PARAPERTUSSIS*, *BORDETELLA HOLMESII* VE *BORDETELLA  
BRONCHISEPTICA***

<sup>1</sup>İbrahim Halil Miraloğlu, <sup>1,3</sup>Canan Ketre, <sup>2</sup>Selin Nar Ötgün, <sup>1</sup>Volkan Demir, <sup>2</sup>Meral Turan, <sup>2</sup>Nuriye Ünal,  
<sup>1,4</sup>Gözde Girgin Özgümüş, <sup>1</sup>Mehmet Genç, <sup>1</sup>Esra Arslan Ganiler, <sup>5</sup>Mustafa Kolukırık

<sup>1</sup>Bioeksen R&D Technologies Ltd., İstanbul Technical University Arı Teknokent, İstanbul/Turkey

<sup>2</sup>Reference Microbiology Laboratories Department, Turkish Public Health Institute (TPHI), Ankara/Turkey

<sup>3</sup>Department of Environmental Engineering, İstanbul Technical University, İstanbul/Turkey

<sup>4</sup>Marmara University, Medical School, Medical Genetics Department İstanbul/Turkey

<sup>5</sup>ENGY Environmental and Energy Technologies Biotechnology Ltd. Co., Bogazici University Technopark, İstanbul/Turkey

Although pertussis is a vaccine-preventable disease, it continues to be an endemic and epidemic disease all over the world. In Turkey, Whooping cough is a notification mandatory disease, under the Expanded Immunization Program. In nasopharyngeal swab and / or aspirate specimens taken from suspected cases of pertussis, it is known that genomic elements specific to *Bordetella* spp. are detected in hours by conventional polymerase chain reaction (PCR) and real time PCR (qPCR) based methods. However, a qPCR-based method that can distinguish *B.pertussis* / *B.parapertussis* / *B.holmesii* / *B.bronchiseptica* species has not yet been developed. The purpose of this project is to develop an accurate, fast and reliable DNA isolation and qPCR based laboratory method which could distinguish these pathogenic species.

A method based on cell lysis with guanidinium thiocyanate for bacterial DNA isolation (15 min) from nasopharyngeal swab and aspiration samples and purification of DNA using silica columns was developed. A qPCR method targeting IS481, IS1001, IS1002, ptxP, hIS1001 and flaA genes for the detection and isolation of *B.pertussis* / *B.parapertussis* / *B.holmesii* / *B.bronchiseptica* is developed by using primers and probe sequences published in the guidelines of the Centers for Disease Control and Prevention (CDC), The European Center for Disease Prevention and Control (ECDC) and the World Health Organization (WHO). Target and non-target reference strains were used in the validation stages. In the study, representative clinical specimens containing targeted and/or non-targeted bacteria at different concentrations are produced by using nasopharyngeal swabs / aspiration specimens that did not include the targeted species. QPCR master mixtures with a shelf life of 2 years when stored at -20 ° C, ready for use with the addition of template DNA only, have been developed under this project and the reaction operating conditions have been optimized.

In experiments, swabs contaminated with 9 targeted *Bordetella* strains and non-target 12 different bacterial strains, the developed test was able to differentiate *Bordetella* species and did not cross-react with non-target bacteria. For all DNA targets, qPCR detection limit is 3 copies of DNA / reaction. In studies conducted with bacterial targets, the detection limit for all targets was determined as 100 cfu / ml.

It will be possible to develop new Whooping cough vaccination strategies for prevention and control in the light of the data acquired from the large-scale field studies by using the qPCR based, accurate, rapid and reliable laboratory-made molecular method produced in this study.

## POSTER PRESENTATION – 118

### **HUMAN TISSUE AND CANCER CELL LINE SPECIFICITY OF LOC105372161: A TAIL-TO-TAIL NATURAL ANTISENSE TRANSCRIPT OF BCL2**

Esra BOZGEYİK<sup>1</sup>, Yusuf Ziya IGCI<sup>1</sup>, Ecir Ali CAKMAK<sup>1</sup>, Ahmet ARSLAN<sup>1</sup>

<sup>1</sup>University of Gaziantep, Faculty of Medicine, Department of Medical Biology and Genetics, Gaziantep, Turkey

Natural antisense transcripts (NATs) are endogen RNA molecules that make complementary base pairing with other transcripts. It has been proposed that NATs regulate their target genes at various levels of cellular processes including transcription, mRNA processing, splicing, stability, cellular transport and translation. NATs are divided into HTH (head-to-head), TTT (tail-to-tail), and EMB (embedded) subgroups according to their genomic localization and degree of overlapping with other transcripts. Accordingly, the aim of the present study was to investigate the expression levels of BCL2 and LOC105372161, a tail-to-tail natural antisense transcript of BCL2, in various human tissue samples and cancer cell lines. A total of 19 different cell lines and 20 different human tissue sample (Human Total RNA Master Panel II) were included in the study. For the analysis of gene expression levels qPCR and RT-PCR were used. As a result, LOC105372161 was found to be tissue specific. Particularly, while it is highly expressed in placenta, prostate, spleen, and thymus tissues, its expression almost lost in heart, bone marrow, kidney, and thyroid gland tissues. LOC105372161 was also found to be differentially expressed in cell lines. While its expression highly elevated in HEK293, CAL29, and DU-145 cells, it is found to be highly reduced or lost in CRL4010, A172, and HeLa cells. Also, while expression levels of LOC105372161 was found to be elevated in breast cancer cell lines compared to CRL-4010 cells and BCL2 expression was decreased. Lastly, expression of LOC105372161 was found to be decreased in DU-145 and PC3 prostate cancer cells as compared to normal prostate tissues. Results of the current study suggest that LOC105372161 may be involved in the regulation of anti-apoptotic BCL2 gene. In the future studies, it is of great interest to determine the interrelation between LOC105372161 and BCL2.

## POSTER PRESENTATION – 119

### DEVELOPMENT OF A RAPID AND HIGH RESOLUTION BRUCELLA GENOTYPING METHOD BASED ON MISMATCH AMPLIFICATION

<sup>1</sup>Mehmet Genç, <sup>2</sup>Selçuk Kılıç <sup>1,3</sup>Canan Ketre, <sup>1,4</sup>Gözde Girgin, <sup>1</sup>Volkan Demir, <sup>1</sup>Esra Arslan Ganiler, <sup>5</sup>Mustafa Kolukırlık

<sup>1</sup>Bioeksen Research and Development Technologies Ltd. Co., Istanbul Technical University, ARI TEKNOKENT Istanbul/Turkey

<sup>2</sup>Reference Microbiology Laboratories Department, Turkish Public Health Institute (TPHI), Ankara/Turkey

<sup>3</sup>Department of Environmental Engineering, Istanbul Technical University, Istanbul/Turkey

<sup>4</sup>Marmara University, Medical School, Medical Genetics Department Istanbul/Turkey

<sup>5</sup>ENGY Environmental and Energy Technologies Biotechnology Ltd. Co., Bogazici University Technopark, Istanbul/Turkey

Brucellosis, which is caused by the agent *Brucella spp.*, is a contagious disease. It is hard to put forth the inter-species and intra-species genome differences of *Brucella* species because of their genetically monomorphic nature. Methods that give so much information but also have high cost values like Next Generation Sequencing, which targets thousands of single nucleotide polymorphisms (SNP) and microarray are used in *Brucella* Genotyping. As a result of these studies 17 SNP regions have been defined that are able to differentiate inter-species and intra-species genotypic variations of *B. abortus*, *B. melitensis* and *B. Suis*. These SNPs are already being scanned by methods that have high cost and high workload such as capillary electrophoresis and DNA sequence analysis. The aim of this study is to develop a cost effective and rapid method that can genotype *Brucella* species by targeting those 17 SNPs with specific primers in a quantitative real time PCR (qPCR) process.

A rapid Bacterial DNA Extraction method (15 min) was developed that is based on Guanidinium thiocyanate (GITC) and usage of silica columns. QPCR protocol was optimized by the usage of “Biorad CFX Connect” and “Roche Light Cycler 96” instruments. A master mix, which can be stored for 2 years at -20 °C, and that is ready to use only after template DNA addition was developed and reaction conditions were optimized. QPCR specificity was verified by DNA sequence analysis. 3 Primers were designed which is based on the mismatch amplification rationale. That has modifications in the 3' end of primers. Samples have been genotyped according to difference of threshold cycle numbers (Cq) of after qPCR process, which are applied to *Brucella* DNA samples with these modified primer pairs those target 17 SNP regions.

34 isolates which are isolated from blood cultures and obtained from THSK were studied. 32 of these isolates showed 100% genotypic similarity and have SNP profile which belongs to *B.melitensis*. The other two isolates showed different genotype profiles, one is *B.abortus* and the other showed a genotype which is represented in all three of *B.melitensis/canis and suis*.

These results indicates that there are one dominant strain in our country. Much more isolates should be studied in order to determine the accurate genotype disposition related to time and area. This genotyping method takes <80 min, which is the fastest method, yet. And because of the low cost of qPCR it is the most cost effective method for now.

*Brucella, Brucellosis, Genotyping, SNP, qPCR, Mismatch Amplification*

## POSTER PRESENTATION – 120

### INVESTIGATION OF EFFLUX PUMPS IN ANTIBIOTIC RESISTANCE OF *KLEBSIELLA PNEUMONIAE*

Burak Yazgan<sup>1</sup>, İbrahim Türkel<sup>2</sup>, Rıdvan Güçkan<sup>3</sup>, Çetin Kılınc<sup>3</sup>, Tuba Yıldırım<sup>2</sup>

<sup>1</sup>Central Research Laboratory, Amasya University, İpekköy, Amasya, Turkey

<sup>2</sup>Department of Biology, Faculty of Arts and Sciences, Amasya University, Amasya, Turkey

<sup>3</sup>Microbiology Laboratory, Amasya Sabuncuoglu Serefeddin Education and Research Hospital, Amasya, Turkey

**Background / Aim:** The increasing antibiotic resistance seen in *Klebsiella pneumoniae*, including extended-spectrum  $\beta$ -lactamase (ESBL) and more recently, carbapenem resistant strains is a source of concern in the medical area. In this study, we aimed to determine possible role of *AcrA* and *kexD* (RND family), *ketM* and *kdeA* (MATE family) and *kpnEF* (SMR family) related to efflux pump genes involved in multidrug resistance.

**Materials and Methods:** Bacterial isolates (n=52) were collected from Amasya Sabuncuoglu Serefeddin Education and Research Hospital between January 2013-January 2017. The isolates were divided into three group; ESBL positive (+), carbapenem resistance and none ESBL/carbapenem resistance (susceptible). The fold change levels of *AcrA*, *ketM*, *kdeA*, *kpnEF*, and *kexD* was determined by quantitative real-time PCR (qRT-PCR). *Klebsiella pneumoniae* ATCC 700721 was used for normalization. All statistical analyses were performed using Student's t test in Graphpad Prism 7.0 ( $p < 0.05$ ).

**Results:** Data analyses showed that fold change expression levels of *AcrA* ( $p < 0.0019$ ), *ketM* ( $p < 0.0023$ ), *kdeA* ( $p < 0.0001$ ), *kpnEF* ( $p < 0.0001$ ) and *kexD* ( $p < 0.0207$ ) was higher in susceptible isolates than ESBL (+) isolates. In addition to this, only *AcrA* expression level was higher in carbapenem resistant isolates than ESBL (+) isolates ( $p < 0.0310$ ). No significant difference was found between susceptible and carbapenem resistance isolates for all other efflux pumps.

**Discussion:** This study describes the role of *AcrA*, *ketM*, *kdeA*, *kpnEF* and *kexD* efflux pump genes in clinical ESBL (+), carbapenem resistance and susceptible isolates. It seems that export of antimicrobial agents is not the primary function of these efflux pumps and they can act as a life-saving properties for susceptible isolates.

**Conclusion:** It seems these biological vacuums of bacterial cells didn't have a role in antibiotic resistance and have a function in the survival of *Klebsiella pneumoniae*. Obtained findings are expected to contribute to our understanding of the gene expressions related to efflux pumps and the development of new antimicrobials.

**Keywords:** *Klebsiella pneumoniae*, ESBL, antibiotic resistance, efflux pump

**Note to the Scientific Committee:** We would like to thank specialists at Central Research Laboratory for helpful approach and technical assistance.

## POSTER PRESENTATION – 121

### LACK OF ASSOCIATION BETWEEN LOX-1, IL17A GENETIC VARIANTS AND CLINICAL PHENOTYPES IN TURKISH CORONARY ARTERY DISEASE PATIENTS

Aymen Rjab<sup>1</sup>, Burcu Bayoglu<sup>2</sup>, Deniz Goksedef<sup>1</sup>, Mujgan Cengiz<sup>2</sup>, Caner Arslan<sup>1</sup>, Gokhan Ipek<sup>1</sup>

<sup>1</sup>Istanbul University, Cerrahpasa Medical Faculty, Department of Heart and Vessel Surgery, Istanbul, Turkey.

<sup>2</sup>Istanbul University, Cerrahpasa Medical Faculty, Department of Medical Biology, Istanbul, Turkey.

**Background/Aim:** Coronary artery disease (CAD) is defined as the formation of plaque on the inner walls of coronary arteries and results narrowing or blockage due to atherosclerosis. The clinical and pathological spectrum of CAD can go up to chronic stable angina, myocardial infarction (MI) and sudden cardiac death. Increased oxidative stress during atherogenesis rises lipid oxidation in arterial walls. Oxidized low-density lipoprotein (ox-LDL) accumulated in the intima, makes the progression of plaque development and causes an imbalance between cell proliferation and death. Experimental and epidemiological data suggest that IL17A is a pro-inflammatory cytokine involving in the innate and adaptive immune responses. Recently, IL17A was shown to recruit and activate macrophages in atherosclerotic lesions. IL17A may participate in inflammatory processes in plaque destabilization. Based on this information, the aim of our study, is to investigate the roles of IL17A and LOX-1 genes on CAD etiology and prognosis.

**Materials and Methods:** In this prospective case-control study, LOX-1 K167N (rs11053646) and IL17A rs3819025 and rs8193037 variants were determined with real-time polymerase chain reaction (RT-PCR) in 100 CAD diagnosed patients and 100 healthy controls.

**Results:** There was no significant difference in LOX-1 rs11053646, IL17A rs3819025 and rs8193037 genotype frequencies between CAD patients and controls ( $p > 0.05$ ). CAD group was determined to have single-, double-, or triple-vessel disease according to the angiographic evaluation depending on the number of diseased vessels. No significant difference in LOX-1 rs11053646, IL17A rs3819025 and rs8193037 genotype frequencies was observed between the single-, double- and triple-vessel disease in CAD patient group ( $p = 0.77$ ,  $p = 0.61$ ,  $p = 0.18$ ). When CAD risk were evaluated with logistic regression model, waist circumference were found to increase CAD risk with 1.14 fold ( $p = 0.002$ ). Also, body mass index, fasting glucose and triglyceride levels were found to increase CAD risk significantly ( $p = 0.013$ ,  $p = 0.006$ ,  $p = 0.035$ ).

**Discussion:** Studies have reported significant relationships in LOX-1 and IL17A gene variants in various populations. A significant relation was reported in K167N polymorphism of LOX-1 gene in patients with MI in a Japanese population. Also, another study reported the significant relationship between IL17A rs8193037 G allele frequency in Chinese CAD patients.

**Conclusion:** Since no significant differences were observed in the genotype frequencies of LOX-1 and IL17A gene variants between CAD patients and controls, it is suggested that LOX-1 rs11053646, IL17A rs3819025 and rs8193037 variants were not associated with CAD risk in Turkish patients. This result may be due to the limited number of patients in our study group.

*Keywords:* Coronary artery disease, ox-LDL, LOX-1, IL17A, genetic variants

*Note to the scientific committee:* This work was supported by the Scientific Research Projects Coordination Unit of Istanbul University. The research project number: 50188. Ethics Committee's approval number: 83045809/604.01/04-288196



## POSTER PRESENTATION – 122

### ANALYSES OF ANTIBIOTIC RESISTANCE RELATED TO BIOFILM ACTIVITY AND ESBL GENES OF *KLEBSIELLA PNEUMONIAE*

Ceren Yavuz<sup>1</sup>, Rıdvan Güçkan<sup>2</sup>, Çetin Kılınc<sup>2</sup>, Burak Yazgan<sup>3</sup>, Seda Mesci<sup>1</sup>, Tuba Yıldırım<sup>1</sup>

<sup>1</sup>Department of Biology, Faculty of Arts and Sciences, Amasya University, Amasya, Turkey

<sup>2</sup>Microbiology Laboratory, Amasya Sabuncuoğlu Serefeddin Education and Research Hospital, Amasya, Turkey

<sup>3</sup>Central Research Laboratory, Amasya University, Amasya, Turkey

**Background / Aim:** *Klebsiella pneumoniae* is one of the most common pathogens, producing extended-spectrum beta-lactamases (ESBL). Our aim was to investigate the antibiotic sensitivity, expression levels of *IntI*, *TEM*, *SHV* and *CTX* genes involved in multidrug resistance and biofilm formation.

**Materials and Methods:** A total of 52 isolates were collected from tracheal aspirate and urine in Amasya Sabuncuoğlu Serefeddin Education and Research Hospital between 2013-2017. Identification was performed by using VITEK2 system and phenotypic confirmation of the ESBL producing isolates by using combined disc test. Antibiotic sensitivity was performed by Kirby-Bauer disc diffusion method against cefazolin, cefuroxime, ceftriaxone, cefepime, piperacilin-tazobaktam, imipenem, meropenem, gentamicin, amikacin, ciprofloxacin and levofloxacin. Moreover, biofilm formation was investigated by microtitration plate method. The relative expression of *IntI*, *TEM*, *SHV* and *CTX* was performed in qRT-PCR.

**Results:** Among 52, 19 were sensitive to all antibiotics. 17 were ESBL positive and 16 were carbapenem resistant. Moreover, 13 of the sensitive strains, all of the ESBL strains and 7 of the carbapenem resistant strains produced biofilm. *IntI* expression of 2 sensitive and 15 ESBL(+) were upregulated but 2 carbapenem resistant were downregulated. *TEM* expression of 4 sensitive and 8 ESBL(+) were upregulated but 8 carbapenem resistant were downregulated. *SHV* expression of 1 sensitive was downregulated but 15 ESBL(+) and 1 carbapenem resistant were upregulated. *CTX* expression of all sensitive were downregulated on the other hand 15 ESBL(+) and 2 carbapenem resistant were upregulated.

**Discussion:** *IntI*, *TEM*, *SHV* and *CTX* are responsible for antibiotic resistance. Supporting to this, the expression of these genes were upregulated in ESBL(+) strains. All ESBL(+) samples produced biofilm and also the expression of these genes were downregulated. We concluded that there might be a correlation between expression of these genes and biofilm formation. Moreover, sensitive and carbapenem resistant showed varying results in terms of gene expressions because some strains produced biofilm.

**Conclusion:** Our results revealed possible role of these genes in biofilm formation and antibiotic resistance, providing the development of new drugs. Further studies will be needed in order to define when or how these systems involved in antibiotic resistance and biofilm formation.

*Keywords:* *Klebsiella pneumoniae*, antibiotic resistance, biofilm, *IntI*, *TEM*, *SHV*, *CTX*

## POSTER PRESENTATION – 123

### DEVELOPING NEXT GENERATION SEQUENCING BASED BRCA1/BRCA2 MUTATIONS DIAGNOSTIC ASSAY AND BIOINFORMATICS ANALYSIS SOFTWARE

Gözde Girgin Özgümüş<sup>1,2</sup>, Canan Ketre<sup>1,3</sup>, Volkan Demir<sup>1</sup>, Mehmet Genç<sup>1</sup>, İbrahim Halil Miraloğlu<sup>1</sup>, A. İlder Güney<sup>2</sup>

<sup>1</sup>Bioeksan Research and Development Technologies Ltd. Co., Istanbul Technical University, ARI TEKNOKENT Istanbul/Turkey

<sup>2</sup>Marmara University, Medical School, Medical Genetics Department Istanbul/Turkey

<sup>3</sup>Department of Environmental Engineering, Istanbul Technical University, Istanbul/Turkey

The most common known cause of hereditary breast and ovary cancer syndrome is genetic changes in BRCA 1 and 2 genes. Early identification of germline BRCA mutations can help physicians make informed decisions on risk reduction strategies such as hormone replacement therapy, chemoprevention and prophylactic surgery.

The objective of this study was to design and validate a next-generation sequencing assay (NGS) to detect BRCA1 and BRCA2 mutations that have a lower financial cost compared to current routine methods; and to develop a bioinformatics software for practical data analysis.

DNA from 50 patient samples previously tested for BRCA1/2 mutations with NGS on Illumina Miseq platform using Multiplicom BRCA MASTR™ Dx Kit were acquired from Marmara University Medical Genetics Department. A total of 10 DNA samples with known pathogenic germline mutations were used to calibrate the routine procedure, that is, multiplex PCR amplification, library preparation, and bioinformatics analysis parameters. Samples were pooled and sequenced together but remained readily identifiable using barcodes (indices) ligated to the amplicons during library preparation. We performed NGS on Illumina Miseq platform. Data was analyzed using our bioinformatics tool based on Galaxy software specifically designed for this study; and compared with previous data from Sophia software.

The library preparation kit developed in this project covers all *BRCA1* and *BRCA2* coding regions, including 50 bp intron-exon junctions. We found that more than 99.9% of the targeted regions were covered at greater than 30% of the mean coverage. 1546 clinically significant variations have been detected by our Galaxy based bioinformatics tool.

The application of optimized experimental conditions resulted in a full coverage of the BRCA1 and BRCA2 regions of interest with uniform representation of each PCR amplicon in the coverage distribution. The average number of reads mapped per sample was 137,418 resulting in an average coverage of 721x. We showed that our BRCA1/BRCA2 Library preparation kit provides complete exon coverage of all coding sequences of *BRCA1* and *BRCA2* genes DNA resulted in high sensitivity ( $\geq 99.7\%$ ), specificity ( $\geq 99.99\%$ ) and accuracy ( $\geq 99.99\%$ ). Our in-house developed software correctly identified the known variants in all 50 retrospective samples and correctly assigned homozygosity and heterozygosity, with no false-positive or false-negative variant predictions.

We describe an integrative diagnostic solution for the analysis of the BRCA1 and BRCA2 genes. This method offers the possibility of detecting different mutation types such as point mutations, small deletions, and exon or allele losses both from germline. The complete workflow is based on a multiplex PCR amplification strategy to generate patient DNA library followed by NGS sequencing and data analysis. For NGS data analysis we developed our own bioinformatics pipeline.

*Keywords: BRCA1/BRCA2, NGS, Mutations, Snp, Variation Analysis, NGS Library*

*Ethics committee: Marmara University, School of Medicine, Clinical Research Ethics Committee Date: 06.01.2017 and the protocol number 09.2017.101*

*Note to the Scientific Committee: Research grant by TUBITAK*

## POSTER PRESENTATION – 124

### DEVELOPMENT OF A NEW QPCR BASED METHOD FOR QUANTIFICATION OF VIABLE *ESCHERICHIA COLI*

Canan Ketre<sup>1,2</sup>, Mustafa Kolukırkı<sup>3</sup>, Bahar Ince<sup>3,4</sup>, Orhan Ince<sup>1,3</sup>

<sup>1</sup>Department of Environmental Engineering, Istanbul Technical University, Istanbul/Turkey

<sup>2</sup>Bioeksen Research and Development Technologies Ltd. Co., Istanbul Technical University, ARI TEKNOKENT Istanbul/Turkey

<sup>3</sup>ENGY Environmental and Energy Technologies Biotechnology Ltd. Co., Bogazici University Technopark, Istanbul/Turkey

<sup>4</sup>Institute of Environmental Sciences, Bogazici University, Istanbul/Turkey

Food and water safety remains one of the most important global health issues. *Escherichia coli* are capable of toxin production and threaten both human and animal health. However, routine methods are incapable of detecting viable but non-culturable (VBNC) bacteria in food and water samples, leading to false-negative identification.

In this study, a new and fast DNase I (FD) treatment-based method was developed to quantify viable *Escherichia coli* in water samples by quantitative real-time PCR (qPCR), and it was compared with the previously described DNase I and Proteinase K (DN/PK), propidium monoazide (PMA) and platinum (Pt) treatment-based methods. The FD-qPCR-based limits of detection (LOD) values for *E. coli* in the presence of 107 dead cells were 10, 20 and 60 viable cells, respectively, in 250-mL sample volumes. The FD-qPCR-based lower limits of quantification (LLOQ) values for *E. coli* in the presence of 107 dead cells were 30, 50 and 150 viable cells, respectively, in 250-mL sample volumes. The LOD and LLOQ values of the FD and PMA-qPCR assays were equal to or lower than those of the Pt and DN/PK qPCR assays. The apparent advantages of the FD-qPCR assays over the PMA and other viability qPCR assays included their higher quantitative accuracy and their ease of use. FD-qPCR and traditional culture-based assays were applied to field tap water and water resource samples. The FD-qPCR was positive for all culture-positive samples and was able to quantify viable but non-cultivable (VBNC) bacteria in the culture-negative samples. The quantitative results also allowed a correlation between the physicochemical characteristics and the VBNC cell abundance in each sample. To our knowledge, our study is the first to comparatively evaluate all methodological options for DNA-targeted viability qPCR assays.

## POSTER PRESENTATION – 125

### PROTECTIVE EFFECTS OF CHARD (*BETA VULGARIS* L. VAR. *CİCLA*) ON VALPROIC ACID INDUCED KIDNEY INJURY IN RATS

Sevim Tunalı<sup>1</sup>, Esin Ak<sup>2</sup>, Sule Cetinel<sup>3</sup>, Refiye Yanardag<sup>1</sup>

<sup>1</sup>Istanbul University, Faculty of Engineering, Department of Chemistry, Istanbul, Turkey,

<sup>2</sup>Marmara University, Faculty of Dentistry, Department of Histology and Embryology, Istanbul, Turkey,

<sup>3</sup>Marmara University, Faculty of Medicine, Department of Histology and Embryology, Istanbul, Turkey,

**Background / Aim:** Valproic acid (VPA) is an antiepileptic drug (AED) which is widely used for the treatment of epilepsy and other neurological and psychiatric disorders such as bipolar affective disorder and migraine headache. Adverse effects of VPA have been documented in liver, kidney, pancreas and hemotopoietic system. Chard (*Beta vulgaris* L. var. *cicla*) is a common plant in Turkey and has an antioxidant and antiacetylcholinesterase effects. The aim of this study was to examine the potential protective effects of chard on VPA induced kidney injury.

**Materials and Methods:** Female rats were divided into four groups as intact control animals, VPA (0.5 g/kg/day, i.p.), chard (100 mg/kg/day, oral) and VPA+chard (in the same dose and time) given to the groups for seven days. Chard extract was given 1 h prior to the administration of VPA. On the 8th day the animals were sacrificed under anesthesia and serum and kidney tissue samples were taken. For light microscopic investigation, kidney tissue samples were fixed in 10% formaldehyde and routinely processed for paraffin embedding. Approximately 5- $\mu$ m thick paraffin sections were stained with Hematoxylin and Eosin (H&E). Urea and creatinine levels were also determined in the serum samples.

**Results:** In the VPA group, there were tubular degeneration with severe epithelial desquamation and cast formation, and prominent congestion in interstitium and glomeruli. Following the chard treatment in the VPA-induced group, reduced interstitial and glomerular congestion and tubular epithelial regeneration were observed. In the VPA group, serum urea and creatinine levels were increased compared to controls. Administration of chard extract decreased serum urea and creatinine levels in VPA group.

**Discussion:** Adverse effects of VPA on many vital organ systems have remained as a challenging issue. A protective treatment of VPA induced adverse effects has yet to be developed.

**Conclusion:** The present study demonstrates that chard might have a protective effect on VPA induced kidney damage.

*Keywords: Valproic acid, chard, kidney, histology.*

## POSTER PRESENTATION – 126

### NATURAL ANTISENSE TRANSCRIPTS IN HUMAN GENOME AND THEIR CLASSIFICATION

Esra BOZGEYİK<sup>1</sup>, Ecir Ali ÇAKMAK<sup>1</sup>

<sup>1</sup>University of Gaziantep, Faculty of Medicine, Department of Medical Biology and Genetics, Gaziantep, Turkey

Natural antisense transcripts are endogenous RNA molecules which makes complementary base pairing with their target transcripts. NATs are divided into four different subgroups as HTH (head-to-head), TTT (tail-to-tail), EMB (embedded) and INT (intronic) according to their location in the genome and the degree of overlap with the other transcripts. NATs are reported to be either positively or negatively correlated with their targets, indicating that the mechanism of action of these transcripts might be different. Although the mechanisms of action of NATs are not completely clear, it has been suggested that they regulate their target with various mechanisms including RNA masking, double-strand RNA depended mechanisms and chromatin remodeling. In this study, according to the GRCh38.p7 Primary Assembly in “Gene” interface of NCBI database, NATs that are identified until February 2017 were determined. Additionally, Ensembl and Genome Browser were used. All chromosomes were checked for the presence of NATs. Previously, NATs were defined as non-coding transcripts encoded in the opposite strand of the protein-encoding gene. However, our results showed that NATs may also include proteins, lncRNAs, miRNAs, snoRNAs and tRNAs which are encoded from the opposite strand of a protein coding gene. Similarly, lncRNA, miRNA, snoRNA and tRNA molecules encoded by the opposite strand of a lncRNA may also be referred to as NAT. We also calculated the number of NATs and their types in human chromosomes. In human genome, EMB subtype was most common in NATs. Among lncNAT INT subtype was most common and in pNATs TTT subtype was most common. In addition, there are transcripts synthesized in the same direction and / or opposite direction as small RNA molecules such as miRNA, tRNA, scnRNA, snRNA and snoRNA. As a result of whole transcriptome and microarray analysis, it has been shown that about 20% of the human genome makes sense-antisense pairs. In addition to sense- antisense pairs (bi-directional), the human genome has also been shown to have sense-sense pairs (non-bi-directional). The effects of antisense transcripts on the complex regulation of the human genome seem to be quite high and the identification of these mechanisms is important for molecular biology studies.

## POSTER PRESENTATION – 127

### DEVELOPMENT OF A LAMP-BASED METHOD FOR RAPID DIAGNOSIS OF GROUP A B-HEMOLYTIC STREPTOCOCCI (AGBHS)

Gözde Girgin Özgümüş<sup>1,2</sup>, Canan Ketre<sup>1,3</sup>, Selçuk Kılıç<sup>4</sup>, Selin Nar Ötgün<sup>4</sup>, Volkan Demir<sup>1</sup> Meral Turan<sup>4</sup>, Mustafa Kolukirik<sup>5</sup>

<sup>1</sup>Bioeksen Research and Development Technologies Ltd. Co., Istanbul Technical University, ARI TEKNOKENT Istanbul/Turkey

<sup>2</sup>Marmara University, Medical School, Medical Genetics Department Istanbul/Turkey

<sup>3</sup>Department of Environmental Engineering, Istanbul Technical University, Istanbul/Turkey

<sup>4</sup>Reference Microbiology Laboratories Department, Turkish Public Health Institute (TPHI), Ankara/Turkey

<sup>5</sup>ENGY Environmental and Energy Technologies Biotechnology Ltd. Co., Bogazici University Technopark, Istanbul/Turkey

Because of the long duration of the throat culture method, rapid antigen tests are inconclusive and high cost of DNA amplification based methods are used, AGBHS diagnostic test is performed in only 5% of acute tonsillopharyngitis patients in our country. This results in an excessive amount of antibiotic prescription if not necessary. The purpose of this project is to develop an AGBHS diagnostic method based on Loop Mediated isothermal DNA amplification (LAMP) that is rapid, precise and economical profit.

Our team developed and validated a rapid method to isolate bacterial DNA from throat swab samples collected with nylon swab for 10 minutes.

A quantitative real-time PCR (qPCR) method for AGBHS diagnosis compatible with this isolation method has also been developed and validated by our team.

In this study, AGBHS-targeted LAMP diagnostic method, which was used in suitable with the DNA isolation method we have already validated, has been developed.

Bu çalışmada, daha önce valide ettiğimiz DNA izole yöntemi ile birlikte kullanılan, AGBHS hedefli LAMP tanı yöntemi geliştirilmiştir.

For this purpose, 7 sets of AGBHS speB wide target 6 LAMP primer sets were designed. LAMP reactions were carried out in heating blocks at 65 ° C for 30 min. During the evaluation of the LAMP reactions, both positive and negative samples were detected by UV light using both SybrGreen and detected with naked eye to which the HNB (*hydroxynaphthol blue*) dye was added to the reaction. LAMP reactions were also prepared to include SybrGreen, amplification reactions in qPCR devices were performed at 65 ° C for 50 minutes, product formation was monitored in real time, and melting curve analyzes of the resulting products were performed.

The performances of the designed LAMP primer sets were evaluated comparatively on the 10<sup>0</sup>-10<sup>4</sup> AGBHS / dilution of swab, counted by qPCR and culture. The specificity of LAMP primer sets was tested using 10<sup>4</sup>-10<sup>6</sup> cfu / mL non-target strains, *Staphylococcus epidermidis*, *Arcanobacterium haemolyticum*, *Staphylococcus aureus*, *Corynebacterium pseudodiphtheriticum*, *Corynebacterium diphtheria*, *H.influenzae*, *Neisseriae meningitidis*, *Neisseria pharyngis*, *Moraxella catarrhalis*, *Escherichia coli*, *Streptococcus agalactiae*, *Streptococcus dysgalactiae*, *Streptococcus dysgalactiae subspecies equisimilis*, *Streptococcus pneumoniae*, *Streptococcus mutans*.

All of the LAMP primer sets didn't give cross reaction with non target bacterial strains. Limit of detection for 30 min of LAMP reaction for different primer sets were determined. speB- 2.3 primer set's limit of detection for 10<sup>3</sup> AGBHS/Swab concentration is determined as shorter than 25 min.

By qPCR based method detection is determined in 55 min including DNA extraction. By the developed LAMP based method the 10<sup>1</sup> AGBHS/Swab concentration detection could be done in 45 min including DNA extraction and 25 min for 10<sup>3</sup> AGBHS/Swab concentration.

## POSTER PRESENTATION – 128

### EFFECT OF VITAMIN D ON CELL GROWTH IN GASTRIC CANCER AND BLADDER CANCER CELL LINES

İlhan Yaylım<sup>1</sup>, Özlem Küçük Hüseyin<sup>1</sup>, Onur Temoçin<sup>2</sup>, Mediha Süleymanoğlu<sup>3</sup>, Damla Çelik<sup>3</sup>, Ammad Ahmad Farooqi<sup>4</sup>, Ceylan Hepokur<sup>5</sup>, Güneş Özen<sup>1</sup>, Emine Bilge<sup>6</sup>, Serap Kuruca<sup>3</sup>

<sup>1</sup>Istanbul University, The Institute of Experimental Medicine, Department of Molecular Medicine, Istanbul, Turkey,

<sup>2</sup>VU University Amsterdam, Faculty of Earth and Life Sciences (FALW), Biomolecular Sciences, Amsterdam, Netherlands,

<sup>3</sup>Istanbul University, Istanbul Medical Faculty, Department of Physiology, Istanbul, Turkey,

<sup>4</sup>Laboratory for Translational Oncology and Personalized Medicine, Rashid Latif Medical College, Lahore, Pakistan

<sup>5</sup>Cumhuriyet University, Faculty of Pharmacy, Department of Basic Pharmaceutical Sciences, Division of Biochemistry, Sivas, Turkey

<sup>6</sup>Istanbul University, The Institute of Experimental Medicine, Department of Neuroscience, Istanbul Turkey

Vitamins, as essential elements in the organisms, were recently shown to be involved in more processes than thought in the past. Vitamin D, which is a hormone-like fat-soluble molecule, is a widely studied vitamin in today's research. Despite the fact that there are studies on effects of Vitamin D on cell growth of different cell lines *in vitro*, there is a lack of information about the selective effects of different doses of Vitamin D on different cell lines. In addition, the mechanisms how this vitamin influences cell proliferation and cell viability are not fully identified. In this study, we aimed to investigate effects of Vitamin D on cell growth and cell viability in ECV bladder cancer cells and AGS gastric cancer cells. We used different doses of Calcitriol, the most active form of Vitamin D for *in vitro* treatment of these cell lines and investigated its effects on cell growth by MTT (Methyl-Thiazol Tetrazolium) assays and cell viability by Trypan Blue staining. Moreover, we analyzed the effect of this vitamin on levels of a few critical proteins involved in cell proliferation (c-Myc and  $\beta$ -catenin), the Vitamin D receptor protein VDR, and apoptotic markers such as Bax, cytochrome C and Caspase 3 in protein extracts of ECV cells, by Western Blot analysis. As an outcome of our study, we observed that Vitamin D inhibited cell growth. This effect was different on different cell lines, at different doses and treatment times. We also detected changes in levels of the proteins indicated in these cell lines upon Calcitriol treatment. In our project, we showed the expressional changes in mitochondrial apoptotic markers upon Calcitriol treatment, and by using the cell lines never being tested with Calcitriol, we believe that the anti-proliferative and apoptotic effects of Vitamin D in these cells will improve the insights on this topic.

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*Keywords: Vitamin D, cell growth, gastric cancer, bladder cancer*

POSTER PRESENTATION – 129

**SYNTHESIS AND INVESTIGATION OF BIOLOGICAL PROPERTIES FOR  
 4-(DI(1H-INDOL-3-YL)METHYL)PHENOL BEARING COBALT PHTHALOCYANINE**

İrem Oral<sup>1</sup>, Gökay Aydın<sup>1</sup>, Arif Baran<sup>1</sup>

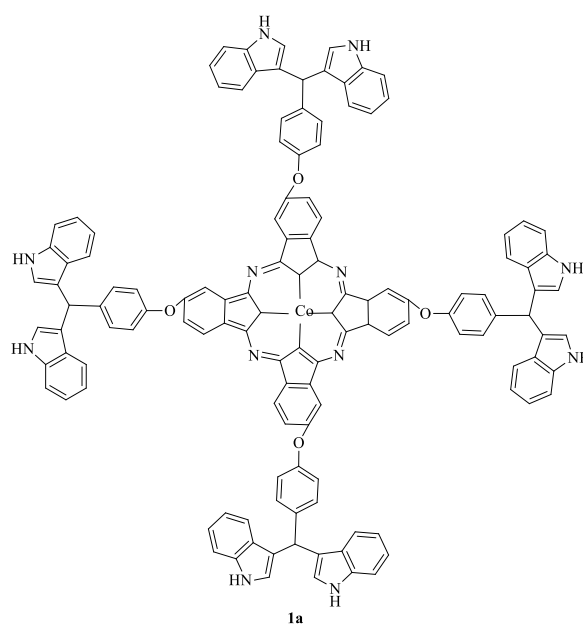
<sup>1</sup>Department of Chemistry, Faculty of Arts and Sciences, Sakarya University, Sakarya, Turkey

**Background/Aim:** The indole structure is one of the most important compound of natural products, pharmaceuticals and agrochemicals. They represents a privileged structural moiety with a broad spectrum of biological activities. Therefore, we have disclosed a approuche for phtalocyanine synthesis starting from indole.

**Materials and Methods:** In this study, indole and p-hydroxybenzaldehyde were reacted according to procedure<sup>a</sup>, afforded hybride molecule, 4-(di(1H-indol-3-yl)methyl)phenol as a sole, which was reacted with 4-nitrofphtalonitrile for acquiring didentate molecule. This was treated with Co(OAc)<sub>2</sub>.2H<sub>2</sub>O for investigation of new ball-type dinuclear Co(II)–Co(II) (**1a**) metallophthalocyanines successfully.

**Results:** Xanthine oxidase and Carbonic anhydarase inhibition activity were measured for phtalocyanine-Co (**1a**) and phtalocyanine-Zn in 5-40 µM and 0.125-20 µM concentration respectively.

**Conclusion:** The best enzyme inhibition activity was observed for phtalocyanine-Co as 0.290 µM. but not observed for phtalocyanine-Zn.



*Keywords: Indole, Xanthine oxidase, Carbonic anhydarase  
 (P.S. supported by TUBITAK-ARDEB, 115Z446 and 113Z699 projects)*



## POSTER PRESENTATION – 130

### **MENTALLY AND PHYSICALLY RETARDED PATIENT WITH NUMEROUS PATHOGENIC VARIANTS REVEALED BY WHOLE EXOME SCREENING: A CASE REPORT**

Naser GILANI<sup>1,2</sup>, Rozhgar A. KHAILANY<sup>1,3</sup>, Ahmet ARSLAN<sup>4</sup>, Khandakar A. S. M. SAADAT<sup>1</sup>, Amir ARIAMAND<sup>2</sup>, Mohammad R. ABBASZADEGAN<sup>5</sup>

<sup>1</sup>Department of Medical Biology, Health Science Institute, Faculty of Medicine, Gaziantep University, Gaziantep, Turkey

<sup>2</sup>Farabi Medical Laboratory, Erbil, Iraq

<sup>3</sup>Department of Biology, College of Science, Salahaddin University, Erbil, Iraq

<sup>4</sup>Department of Medical Biology, Faculty of Medicine, Namık Kemal University, Tekirdag, Turkey

<sup>5</sup>Medical Genetic Research Center, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

**Background:** There are extensive variety of inherited disease could lead to mental and physical retardation. Distinguishing the genetics variants caused these abnormalities are crucial to decide next steps in determining appropriate treatment, support and additional molecular investigation in close relatives or making arrangements for further pregnancies. In this study we have a 5-year-old boy that physically and mentally is impaired. He has other clinical features such as; speechlessness, seizure and uncontrolled defecation. His two male siblings have died in their first year of life due to severe diarrhea and vomiting.

**Materials and Methods:** Genomic DNA was extracted from proband's whole blood sample. Whole exome enrichment was performed using Agilent SureSelect V6 TargetEnrichment Kit. Followed by Next Generation Sequencing using Illumina HiSeq4000 platform. All exons and flanking 10bp were detected and analyzed.

**Results:** Three mutations were detected in the patient in homozygous pathogenic state, includes; c.185T>C in *HEXB* gene resulting Sandhoff disease, c.97A>G in *HPD* gene resulting Tyrosinemia type III and c.209G>A in *BBS2* gene leading to Bardet-Biedl syndrome. Additionally, other compound heterozygous pathogenic mutations were detected in the patient includes; c.242C>T and c.133C>T in *AMPD1* gene cause muscle AMP deaminase deficiency.

**Discussion and Conclusion:** As we see there is a multiple genetic variations detected in proband that could lead to various type of genetic disorders. They have some common and some unique clinical features. Lastly, ⚠ genetic counseling and segregation analysis of mentioned mutations in family members should be considered.

*Key words:* Genetic defect, Mutation, Next Generation Sequencing.

POSTER PRESENTATION – 131  
**INVESTIGATION OF DNA-BINDING PROPERTIES OF  
METALLOPHTHALOCYANINE COMPOUNDS CONTAINING CYCLOHEX-4-ENE**

Yunus Mercan<sup>1</sup>, Furkan Özen<sup>1</sup>, Arif Baran<sup>1</sup>

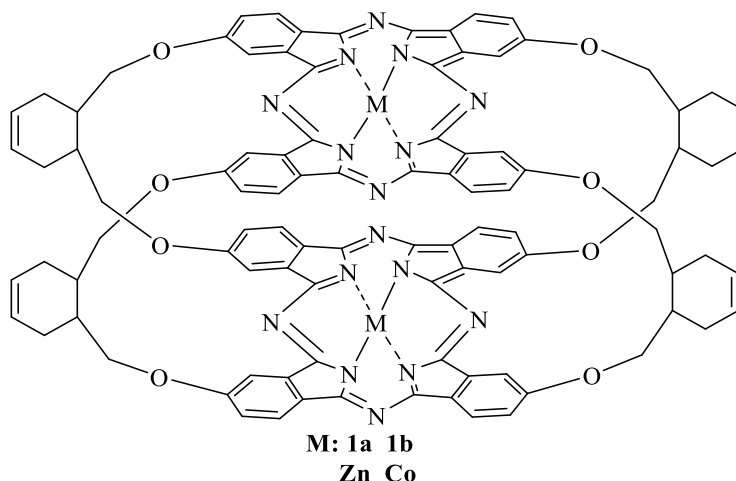
<sup>1</sup>Sakarya University, Faculty of Arts and Sciences, Chemistry Department, 54187, Sakarya, Turkey

**Aim:** In this study new ball-type dinuclear Zn(II)–Zn(II) (**1a**) and Co(II)–Co(II) (**1b**) metallophthalocyanines were synthesized. Then DNA-binding properties of these molecules were investigated.

**Materials and Methods:** DNA binding properties of complexes was investigated by fluorescence spectroscopic method. In this study, calf thymus DNA (CT-DNA) is used and constant amount of complexes was titrated by increasing amount of CT-DNA. Concentration of compounds is 10  $\mu$ M and CT-DNA concentration range was 15-100  $\mu$ M for **1a**, 10.3-72  $\mu$ M for **1b**. Reaction mixture composed of CT-DNA and compounds in 5 mM Tris. HCl buffer pH 7.4 and this mixture incubated at 37 °C for 10 min. Excitation of compounds **1a** and **1b** is 348 and 361.6 nm respectively. Emission wavelength of **1a** and **1b** is 684 nm.

**Results and Discussions:** When we titrate the **1a** complex with increasing the DNA concentration, fluorescence intensity is increased. This means **1a** complexes binds to DNA with hyperchromistic manner. DNA structure and confirmation were changed with agent that possesses hyperchromic feature because DNA double strands open and these molecules with intercalator property intervene between the DNA strands. Whereas titration of **1b** with rising DNA concentration results in decreasing fluorescence intensity, these effect is named as hypochromistic effect. The molecules binding to DNA with hypochromicity exhibit electrostatic, hydrogen bonding and hydrophobic interactions and therefore these molecules approximate to the sugar-phosphate backbone. These kind of agents are generally groove binders [1].

**Conclusions:** **1a** complex with increasing DNA concentration, the fluorescence intensity is increased.



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**Reference:**

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*Keywords: Metallophthalocyanine, DNA-binding*

*Supported by TUBITAK-ARDEB, 115Z446 and 113Z699 projects*

## POSTER PRESENTATION – 132

### **HUMAN PAPILLOMAVIRUS PREVALANCE, GENOTYPES DISTRUBUTION AND CERVICAL CYTOLOGICAL PROFILES AMONG FEMALE OUTPATIENTS IN THE WESTERN BLACK SEA REGION OF TURKEY**

Safi Oz Z<sup>1</sup>, Ozdamar SO<sup>2</sup>, Kandemir N<sup>2</sup>, Dogan Gun B<sup>2</sup>, Bahadır B<sup>2</sup>, Barut F<sup>2</sup>, Yurdakan G<sup>2</sup>, Harma M<sup>3</sup>

1. Bulent Ecevit University, School of Medicine, Department of Medical Biology, Zonguldak,

2. Bulent Ecevit University, School of Medicine, Department of Pathology, Zonguldak, Turkey

3. Bulent Ecevit University, School of Medicine, Department of Gynecology and Obstetrics, Zonguldak, Turkey

**Background :** Human papillomavirus (HPV) is the main cause of cervical cancer. The aim of the present study was to evaluate HPV prevalence, genotype distribution and cervical cytological profiles of female patients in Western Black Sea Region of Turkey.

**Materials and Methods:** This study was conducted between April 2015 and January 2016, covering a total of 628 women. The mean age of the patients was 44, 52 ± 13, 2 years (19-85 years). Cervical samples were collected with a cervical brush and preserved in a liquid-based cytology medium (BD SurePath™) and then stained with Papanicolaou technique for routine cytological examination. Remaining samples were transported to the COBAS 4800 system for further processing of High Risk-HPV (HR-HPV) detection and simultaneous HPV-16 and HPV-18 genotyping. HPV was detected in 101 patients (16,08 %).

**Results:** The prevalence of HPV 16, HPV 18, HR-HPV types (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68) and double HPV (HPV18 + HR- HPV) were 45 (7,16 %), 3 (0,47%), 50 (7,96%), 3 (0,47%) respectively. Routine cytological examination revealed 47 (46,53%) women with cytologic abnormality, 38 (37,62%) with inflammation, 11 (10,89%) with normal cytology and 2 (1,98%) with vaginal atrophy in HPV positive patients. In HPV 16 infected patients, ASCUS (8;17,77%), ASCH (5; 11,11%), LSIL (5; 11,11%), HSIL (1; 2,22%), AGUS (1; 2,22%) and AGC (1; 2,22%) were diagnosed. In HR-HPV infected patients, ASCUS (8; 16%), LSIL (9;18%), HSIL (7;14 %) and squamous cell carcinoma (1; 2%) were diagnosed.

**Conclusion:** HPV prevalence that was found in this study is in the range of previously reported values in Turkey and we found that High risk HPV types (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68) are the most common ones in our region.

*Keywords: Human Papilloma Virus (HPV), HR-HPV, liquid-based cytology, Papanicolaou technique.*

## POSTER PRESENTATION – 133

### MICRONUCLEUS DETECTION IN CERVICAL SMEAR AND COMET TESTS IN BLOOD SAMPLE OF REPRODUCTIVE AND MENOPAUSAL PERIODS FOR DNA DAMAGE EVALUATION

Okan SANCER<sup>1</sup>, Pınar ASLAN KOŞAR<sup>1</sup>, Zehra SAFİ ÖZ<sup>2</sup>, Esra Nur TOLA<sup>3</sup>, V. Atahan TOGAY<sup>1</sup>, Ibrahim Metin CIRIS<sup>4</sup>

<sup>1</sup>Department of Medical Biology, Faculty of Medicine, Süleyman Demirel University, Isparta, Turkey.

<sup>2</sup>Department of Medical Biology, Faculty of Medicine, Bulent Ecevit University, Zonguldak, Turkey

<sup>3</sup>Department of Obstetrics and Gynecology, Faculty of Medicine, Süleyman Demirel University, Isparta, Turkey.

<sup>4</sup>Department of Pathology, Faculty of Medicine, Süleyman Demirel University, Isparta, Turkey.

**Background:** Hormones control different body functions. In the vaginal pH is normally 3,5-5, which increases with falling estrogen during menopause, it may go up to 6-8. The resulting alkaline environments make the vagina susceptible to numerous pathogenic bacteria. COMET and Micronucleus (MN) techniques are widely used for determining the DNA damage, as they might allow the detection of increased genetic instability women in menopause and it may be an early marker for cancer.

**Materials and Methods:** In the present study, 30 reproductive, 30 menopausal period and 30 control DNA damage were monitored by COMET assay. EtBr-stained DNA was observed by using image analysis software magnification of x 40 objective. For Micronucleus assay; 30 reproductive and 30 menopausal period cervical smears were prepared. Epithelial cells were assessed using image analysis software at a magnification of x400.

**Results:** Higher DNA damage was found in the menopausal period compared to reproductive period. DNA damage in menopausal period was found to be statistically significant ( $p < 0,05$ ). For micronucleus assay, the mean frequency of chromatin damage and cell proliferation difference wasn't found to be statistically significant ( $p > 0,05$ ).

**Conclusion:** As we show that, DNA damage levels increase in menopausal period which could contribute to disease progression in elderly women, it is necessary to develop therapeutics targeting this problem.

*Keywords: Micronucleus, Comet assay, menopausal period*

POSTER PRESENTATION – 134  
**EXPRESSION ASSOCIATION OF MIR-22 AND MIR-452 IN RENAL CELL  
CARCINOMA**

Rozhgar A. KHAILANY<sup>1,2</sup>, Mehmet OZASLAN<sup>3</sup>, Naser GILANI<sup>1,4</sup>, Belan O. KANABE<sup>3</sup>, Muhamad SAFDAR<sup>1</sup>

<sup>1</sup>Department of Medical Biology, Faculty of Medicine, University of Gaziantep, Gaziantep, Turkey

<sup>2</sup>Department of Biology, College of Science, University of Salahaddin, Erbil, Iraq

<sup>3</sup>Department of Biology, Gaziantep University, Gaziantep, Turkey

<sup>4</sup>Farabi Medical Laboratory, Erbil, Iraq

**Background:** Renal cell carcinoma is the third most common urologic cancer and the seventh most common malignancy overall. MicroRNAs (miRNAs) initiate translational controlling and play a critical role in developmental timing. Presently, it is determined miRNAs play an important roles in several physiological and pathological conditions, particularly deregulation in various type of cancers. The goal of this study is to evaluate the expression level of MiR-22 and MiR-452 in renal cell carcinoma.

**Materials and Methods:** MicroRNAs expression level of 40 paired tumor and normal tissue samples were measured by quantitative real time polymerase chain reaction (qRT-PCR) technique. The samples were grouped according to the types of renal carcinoma and clinical characteristics of patients, including gender and average age.

**Results:** Expression level of MiR-22 was significantly decreased (down-regulated) while the expression level of MiR-452 was significantly increased (up-regulated) in renal cell carcinoma tissues compared to normal tissues.

**Discussion and Conclusion:** Consequently, these two miRNAs could be potentially used as diagnostic biomarkers in renal cell carcinoma. However, further studies are mandatory to a better understanding and confirmation of our preliminary findings.

*Keywords: Renal cell carcinoma, Expression analysis, MicroRNAs, qRT-PCR*

## POSTER PRESENTATION – 135

### THE LONG NON-CODING RNA GENE HOTAIR EXPRESSION IN THE ADIPOSE TISSUES OF OBESE PATIENTS

Burcu Bayoglu<sup>1</sup>, Gulseren Billur Akdeniz<sup>1</sup>, Feyzullah Ersoz<sup>2</sup>, Mutlu Niyazoglu<sup>3</sup>, Saadet Busra Aksoyer<sup>1</sup>, Murat Sarici<sup>4</sup>, Mujgan Cengiz<sup>1</sup>

<sup>1</sup>Istanbul University, Cerrahpasa Medical Faculty, Department of Medical Biology, Istanbul, Turkey.

<sup>2</sup>Istanbul Training and Research Hospital, Department of General Surgery, Istanbul, Turkey.

<sup>3</sup>Istanbul Training and Research Hospital, Department of Endocrinology, Istanbul, Turkey.

<sup>4</sup>Dr. Lutfi Kirdar Kartal Training and Research Hospital, Department of Plastic Reconstructive and Aesthetic Surgery, Istanbul, Turkey.

**Background/Aim:** Obesity is a condition of excessive fat accumulation and it is a risk factor for certain human diseases like type 2 diabetes, cardiovascular diseases and some cancer types. Recent studies suggested the significance of long non-coding RNAs (lncRNAs) on adipogenesis regulation. lncRNAs associate with DNA binding proteins and have major roles in the regulation of gene expression with an epigenetic manner. HOTAIR (Hox transcript antisense intergenic RNA) is a lncRNA expressed from developmental HoxC locus located on chromosome 12q13.13. HOTAIR acts with polycomb repressive complex 2 to reprogram chromatin organization. Alterations in HOTAIR expression levels have been shown to participate in various pathogenic processes. The aim of this study is to determine the lncRNA gene HOTAIR expression levels in the abdominal adipose tissues of obese patients and non-obese individuals and to compare HOTAIR gene expression levels with obesity related phenotypes and serum lipids in a group of Turkish population.

**Materials and Methods:** In this study, 31 obese patients, body mass index (BMI)  $\geq 30$ , undergoing metabolic surgery and 35 non-obese individuals, BMI  $< 25$ , having liposuction were used. HOTAIR expression levels were determined by real-time quantitative polymerase chain reaction (RT-qPCR) from the abdominal adipose tissue specimens of obese patients and controls. Relative changes in non-coding RNA expression levels were calculated using the  $2^{-\Delta\Delta C_t}$  method.

**Results:** BMI, total-cholesterol, LDL-cholesterol, triglycerides, fasting glucose and fasting insulin levels were significantly higher in obese patients than in controls ( $p < 0.001$ ). HbA1c and HOMA-IR values were also significantly higher in obese patients when compared with controls ( $p = 0.003$ ,  $p < 0.001$ ). HOTAIR levels were down-regulated in 7 (22.58 %) and up-regulated in 22 (70.97 %) of adipose tissue specimens. In 2 of 31 (6.45 %) tissues, there was no change in the expression levels. The patient group in which HOTAIR expression has not changed, HDL-cholesterol levels were higher with borderline significance ( $p = 0.056$ ). However, no significant correlation was found between HOTAIR expression levels and serum lipid profiles, fasting glucose and insulin levels ( $p > 0.05$ ).

**Discussion:** Recent studies have shown that, HOTAIR is highly expressed in gluteal fat tissue in comparison with other fat depots. Also, in a recent study, HOTAIR has been identified as a pro-adipogenic lncRNA and highly expressed in gluteal-femoral fat suggested to facilitate intestinal progenitor cell proliferation in wildtype mice.

**Conclusion:** We suggest that, HOTAIR expression may have an important role in obesity. However, further studies should confirm our results with larger sample size.

*Keywords:* Obesity, long non-coding RNAs, HOTAIR, gene expression

*This work was supported by the Scientific Research Projects Coordination Unit of Istanbul University. The research project number: 20787. Ethics Committee's approval number: 83045809/604.01/02-40791*

## POSTER PRESENTATION – 136

### EFFECT OF ALDOSE REDUCTASE INHIBITION ON LPS-INDUCED NEUROINFLAMMATION IN MICROGLIAL CELLS

Ahmet Cumaoglu<sup>1</sup>, Mukerrem Betül Yerer<sup>2</sup>

<sup>1</sup>Faculty of Pharmacy Department of Biochemistry, <sup>2</sup>Department of Pharmacology. Erciyas University, Kayseri, Turkey

**Aim:** In the central nervous system, microglial over-activation is considered to be a central event in neuroinflammation. Aldose reductase (AR) has a key role in several inflammatory diseases. Therefore, AR inhibition seems to be a useful strategy for anti-inflammation therapy.

**Results:** In the present study, we found that Quercetin and monochloropivaloylquercetin showed potent inhibition on aldose reductase expression and anti-neuroinflammatory effects in Lipopolysaccharide (LPS) induced inflammatory process by inhibiting expression of inflammatory mediators in microglial cells. Monochloropivaloylquercetin suppressed COX-2 expression and quercetin suppressed iNOS expression, which further resulted in downstream inhibition prostoglandin E2 (PGE2) release (monochloropivaloylquercetin pretreated cells). Also treatment with Sorbinil (AR inhibitor) caused to decrease PGE2 release. Additionally, LPS treatment resulted with activation of MAPK (phosphorylation of c-Jun N-Terminal kinase(JNK), extracellular signal-regulated kinase (ERK) and mitogen-activated protein kinase p38) Especially pretreatment with monochloropivaloylquercetin and sorbinil significantly reduced the activation of MAPK. Furthermore, inhibition of MAPK pathway with monochloropivaloylquercetin and sorbinyl treatment caused a dimunition in proinflammatory cytokine (TNF- $\alpha$ ) release in LPS induced neuroinflammation.

**Conclusion:** These findings suggested that AR is a potential target for treatment of neuroinflammation and that quercetin and monochloropivaloilquercetin could be an effective agent for treating or preventing neuroinflammatory diseases.

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POSTER PRESENTATION – 137  
**ANTI-INFLAMMATORY EFFECTS OF ETHANOL EXTRACT FROM LICHENS  
ON LPS-STIMULATED RAW 264.7 CELL**

<sup>1</sup>Ahmet CUMA OGLU, <sup>2</sup>Hatice BEKCI, <sup>3</sup>GOKHAN HALICI

Erciyes University, <sup>1</sup>Faculty of Pharmacy, Department of Biochemistry, <sup>2</sup>Faculty of Engineering, Department of Food Engineering, <sup>3</sup>Faculty of Science, Department of Biology

**Aim:** Lichens provide a large array of compounds with the potential for pharmaceutical development. In the present study, extracts from three lichen species (*Usnea articulata*, *Umbilicaria crustulosa*, *Bryoria fuscescens*) were examined for anti-inflammatory activity.

**Materials and Methods:** To measure the effects of extract on pro-inflammatory mediators, we used the following methods: MTT assay (cell viability or cytotoxicity), reverse transcriptase-polymerase chain reaction (COX-2, iNOS mRNA), western blotting analysis (COX-2, iNOS mRNA).

**Results:** Stimulation of the RAW 264.7 cells with LPS+IFN- $\gamma$  (1  $\mu$ g/mL LPS/100 ng/mL IFN- $\gamma$  3 hrs treatment) increased mRNA and protein expression of cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) which were markedly inhibited by the pre-treatment with *Usnea* extract (40  $\mu$ g/mL) and *Umbilicaria* (40  $\mu$ g/mL) extracts without causing any cytotoxic effects. Interestingly, pre-treatment with *Bryoria* sp (30  $\mu$ g/mL) extract caused a raising in the levels of COX-2/iNOS mRNA and protein levels.

**Conclusions:** These results suggest that *Usnea* and *Umbilicaria* extract may have potential for development into an effective anti-inflammatory agent.

## POSTER PRESENTATION – 138 ANALYSIS OF MAPK 7 IN COLORECTAL CANCER RISK

Canan Cacina<sup>1</sup>, Soykan Arıkan<sup>2</sup>, Esra Kaytan Sağlam<sup>3</sup>, Ümit Zeybek<sup>1</sup>, Saime Turan<sup>1</sup>, İlhan Yaylım<sup>1</sup>

<sup>1</sup> Institute Of Aziz Sancar Experimental Medicine Department Of Molecular Medicine, Istanbul University

<sup>2</sup> Istanbul Education And Research Hospital Surgery Clinic, Istanbul, Turkey

<sup>3</sup> Institute Of Oncology , Department Of Radiation Oncology, Istanbul University

### Background / Aim

The MAPKs extracellular signal regulated protein kinases 1 and 2 (ERK1/2) were first identified in the early 1980s, but in the following years, the MAPK family was ascertained to include three c-Jun N-terminal Kinases (JNK), ERK3 isoforms, ERK5 and ERK7, four p38 isoforms. MAP kinases are regulated by phosphorylation cascades and they are a family of highly conserved signal transduction pathways, allowing the cells to respond to multiple extracellular inputs. MAPKs are activated by different stimuli, such as hormones and growth factors acting through tyrosine or serine/threonine kinases, inflammatory cytokines, peptides acting through G protein-coupled receptors, as well as environmental stresses such as ionising radiation or osmotic stress. The aim of present study was to investigate relationship between the MAPK7 gene variations and colorectal cancer risk in a Turkish population.

### Materials and Methods

In present study 100 genomic DNA samples (50 colorectal cancer patients and 50 controls) were analyzed by the next generation sequencing methods to identify possible variations in MAPK7 gene.

### Results

A total of 15 different variants (232+131C>A, 1216C>T --6+19G>T, 399-70G>A, 1613G>A 1191A>G, 1477+22T>G, 233-97\_233-96insA, 399-70G>A, 399-91G>T, 2110A>G, 2164-111C>T, -6+21C>A, -39G>A, -5-381T>G) were identified in 100 individuals. -5-381T>G gene variant was observed in 76% of colorectal cancer cases, 66% in controls but this distinction was not statistically significant (p=0.378). We also didn't find any significant differences in frequency of the other variations (p=1.00).

### Discussion

According to results of MAP7 kinase gene analyses we did not observe any significant association between variations and colorectal cancer risk. Further studies in a larger population is needed to confirm the our results.

**Conclusion:** We are of the opinion that our study offer an insight into the other studies which will analyse the importance of MAPK7 gene variations in identification of colorectal cancer risk.

*Keywords:* protein kinase, pathways, signaling

*Acknowledgement:* This project was supported by Istanbul University Scientific Research Projects Unit (IU/BAP) (Project no:28852).

## POSTER PRESENTATION – 139

### EXPRESSION LEVELS OF MICRORNAS RELATED TO AUTOPHAGY PATHWAY IN SERUM OF COLORECTAL CANCER PATIENTS AND HEALTHY CONTROLS

Umit Yilmaz<sup>1</sup>, **Nesibe Yilmaz**<sup>2</sup>, Arzu Ergen<sup>2</sup>, İlhan Yaylim<sup>2</sup>, Soykan Arıkan<sup>3</sup>, Umit Zeybek<sup>2</sup>

<sup>1</sup> Department of Physiology, Faculty of Medicine, Inonu University, Malatya, Turkey

<sup>2</sup> Department of Molecular Medicine, Aziz Sancar Institute of Experimental Medicine, Istanbul University, Istanbul, Turkey

<sup>3</sup> Department of General Surgery, Istanbul Training and Research Hospital, Istanbul, Turkey.

**Background/Aim:** Colorectal cancer is the fourth leading cause of cancer-related death in the world and is responsible for approximately 610 000 deaths each year. Autophagy is defined as a self-eating “auto (self) phagy (to eat)”, used for under normal physiological conditions, the breakdown of cellular components in order to nutrients during starvation. MicroRNAs (miRNAs) are endogenous non-protein coding, single stranded RNA of 18-24 nucleotide length that negatively modulate gene expression by binding to the 3’-UTR of mRNA. MiRNAs play important roles almost every cellular process including autophagy. The aim of this study was to investigate the use of miR-17-5p, miR-30b, miR-30b, miR-216a and miR-216b as biomarkers for the diagnosis of colorectal cancer from serum.

**Materials and Methods:** Forty seven patients with colorectal cancer and 50 healthy individuals who did not have a cancer history were included in this study. In the serum of colorectal cancer patients and of healthy controls, expression levels of miR-17-5p, miR-30b, miR-30b, miR-216a and miR-216b were measured by qRT-PCR.

**Results:** The expression level of miR-30d in the patient group was found to be decreased statistically, when the serum samples of colorectal cancer patients and healthy subjects were compared ( $p=0.001$ , 95% confidence interval=1.32-3.52).

**Discussion:** In recent years, many studies has suggested that serum levels of miRNAs can be used as noninvasive biomarkers in the diagnosis of cancer. Also, hundreds of miRNAs have been studied in the serum and plasma of cancer patients, but there are still many contradictions about its usefulness as a biomarker in the diagnosis of cancer.

**Conclusion:** Our results indicated that miR-17-5p, miR-30b, miR-216a, miR-216b can not use as a highly reliable biomarker in serum for colorectal cancer diagnose.

*Keywords: Colorectal Cancer, Autophagy, miRNA, qRT-PCR.*

*This study was supported by TUBITAK (Project no: 215S540).*

## POSTER PRESENTATION – 140

### K-RAS GENE EXPRESSION IN TUMOR AND ADJACENT NORMAL TISSUES OF COLORECTAL CANCER PATIENTS

**Nesibe Yilmaz**<sup>1</sup>, Umit Yilmaz<sup>2</sup>, Arzu Ergen<sup>1</sup>, İlhan Yaylim<sup>1</sup>, Nihat Aksakal<sup>3</sup>, Umit Zeybek<sup>1</sup>

<sup>1</sup> Department of Molecular Medicine, Aziz Sancar Institute of Experimental Medicine, Istanbul University, Istanbul, Turkey

<sup>2</sup> Department of Physiology, Faculty of Medicine, Inonu University, Malatya, Turkey

<sup>3</sup> Department of General Surgery, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey

**Background/Aim:** Colorectal cancer is one of the most common cancers throughout the world.

The *K-ras* oncogene is mutated in approximately 35%-45% of colorectal cancers, and *K-ras* mutational status testing has been highlighted in recent years. The *K-ras* gene, which has been extensively studied for more than three decades, has been demonstrated to be a strong negative predictive biomarker to indicate whether a CRC patient will respond to treatment. The purpose of the present study was to investigate the *K-ras* gene expression in colorectal cancer.

**Materials and Methods:** Forty seven colorectal cancer patients were included in this study and the tumor tissue and adjacent normal tissue were collected from these patients during the surgical operation. *K-ras* gene expression levels were detected by quantitative Real-Time PCR in the tumor and adjacent normal tissues of colorectal cancer patients.

**Results:** Our results showed that *K-ras* gene expression levels were increased in tumor tissue by 7.19 fold compared to adjacent normal tissue.

**Discussion:** In many studies, it has been showed that *K-ras* plays a role as an oncogene in different cancer types such as colon, pancreatic and lung cancer. When we investigated *K-ras* gene expression levels in tumor and adjacent normal tissues, *K-ras* gene expression levels were increased in tumor tissue.

**Conclusion:** According to our data, we are suggesting that *K-ras* gene may acts like an oncogene in colorectal cancer.

*Keywords: Colorectal Cancer, K-ras, Gene expression, qRT-PCR.*

## POSTER PRESENTATION – 141

### THE EFFECTS OF SOLUBLE-RAGE PLASMA LEVELS TO THE DEVELOPMENT OF CHILDHOOD OBESITY IN GIRLS

Ozlem Kucukhuseyin<sup>1</sup>, E. Hande Karagedik<sup>1</sup>, Emel Torun<sup>2</sup>, Tolga Ozgen<sup>3</sup>, Ilhan Yaylım<sup>1</sup>, Hulya Yılmaz-Aydoğan<sup>1</sup>, H.Arzu Ergen<sup>1</sup>

<sup>1</sup>Department of Molecular Medicine, Aziz Sancar Institute of Experimental Medicine, Istanbul University, Istanbul, Turkey

<sup>2</sup>Department of Pediatrics, Bezmî Alem University, Istanbul, Turkey

<sup>3</sup>Department of Pediatric Endocrinology, Bezmî Alem University, Istanbul, Turkey

**Background.** The worldwide prevalence of obesity and its metabolic complications have increased substantially in recent decades. Accumulating evidence suggests that the synthesis and release of pro-inflammatory and anti-inflammatory cytokines from adipose tissue may play a critical role in the development of obesity-related metabolic disorders by affecting insulin sensitivity, generation of reactive oxygen species or inducing macrophage-derived factors leading to a chronic low-grade inflammatory state in obesity. It was proposed that formation of advanced glycosylation end-products (AGE) or advanced lipoxidation end-products can be one of the molecular mechanism for damaged adipokine release. The effects of AGEs are mediated by binding to specific multiligand cell-surface receptors, RAGEs. A part from cell-surface RAGE, soluble RAGE (sRAGE), a circulating isoform, circulates in human plasma and has emerged as a reliable biomarker in a number of RAGE-mediated metabolic disorders. The aim of this study is to investigate sRAGE levels in obese female children and to determine its association with adipose tissue dysfunctioning and the development of obesity.

**Material-Method.** 50 obese female children and 51 normal weight children were included in this study. Plasma sRAGE levels were determined by using a commercially available enzyme-linked immunosorbent assay kit (Quantikine; R&D systems) (Biovendor Research and Diagnostic Products, Czech Republic) according to manufacturer's protocol. Measurements were performed in duplicate, and the results were averaged.

**Results.** The levels of BMI, hip or waist ratio, systolic and diastolic blood pressures, insulin, HOMA-IR, insulin resistance, TG, ALT and free T4 were higher, and HDL-C levels were lower in obese cases than controls ( $p < 0.05$ ). Besides, obese group had significantly higher sRAGE ( $892.07 \pm 87.23 \rightarrow 517.45 \pm 49.76$ ;  $p < 0.001$ ) levels. However, any significant difference was observed in clinical parameters in obese girls with sRAGE levels greater than the median of sRAGE level in controls. In obese cases with BMI  $> 30$  higher levels of systolic and diastolic blood pressures and lower total cholesterol, LDL-C and HDL-C levels were observed ( $p < 0.05$ ). In addition sRAGE levels were higher in those cases with no statistical significance ( $p > 0.05$ ).

**Discussion.** In recent years, studies on advanced glycation end products (AGE) and their interaction with their receptors (RAGE) has increasingly become prevalent. However, studies concerning AGE-RAGE interaction in obesity was scarce and the results are conflicting. As this preliminary study was the first one to determine the effects of sRAGE plasma levels to the development of childhood obesity in Turkish girls, it was found that obese girls had higher plasma levels of sRAGE and, our results suggest that higher plasma levels of sRAGE may have a protective role against obesity by affecting lipid profiles.

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## POSTER PRESENTATION – 142

### BECLIN-1 GENE EXPRESSION IN TUMOR AND ADJACENT NORMAL TISSUES OF COLORECTAL CANCER PATIENTS

**Umit Yilmaz**<sup>1</sup>, Nesibe Yilmaz<sup>2</sup>, Arzu Ergen<sup>2</sup>, İlhan Yaylim<sup>2</sup>, Nihat Aksakal<sup>3</sup>, Umit Zeybek<sup>2</sup>

<sup>1</sup> Department of Physiology, Faculty of Medicine, Inonu University, Malatya, Turkey

<sup>2</sup> Department of Molecular Medicine, Aziz Sancar Institute of Experimental Medicine, Istanbul University, Istanbul, Turkey

<sup>3</sup> Department of General Surgery, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey

**Background/Aim:** Colorectal cancer accounts for approximately 10% of all cancer cases, is the third most common type of cancer worldwide and over 1.24 million people are diagnosed with colorectal cancer each year. Autophagy means self (auto) - eating (phagy) and Beclin-1 is the most important protein that plays a key role in autophagy. Autophagy shows tumor suppressor effect during cancer development, while it contributes to survive of cancer cells during cancer progression. The purpose of the present study was to investigate the role of the Beclin-1 gene and autophagy in colorectal cancer.

**Materials and Methods:** Forty seven colorectal cancer patients were included in this study and the tumor tissue and adjacent normal tissue were collected from these patients during the surgical operation. Beclin-1 gene expression levels were detected by quantitative Real-Time PCR in the tumor and adjacent normal tissues of colorectal cancer patients. In tumor and adjacent normal tissue samples of patients, Beclin-1 protein levels were examined by Western Blot method.

**Results:** Our results showed that Beclin-1 gene expression levels were decreased in tumor tissue by 5.64 fold compared to adjacent normal tissue ( $p=0.001$ ). Also, according to our results, Beclin-1 protein levels in the tumor tissue were decreased statistically, when Beclin-1 protein levels were compared between the tumor tissue and the adjacent normal tissue samples ( $p=0.001$ , 95% confidence interval=0.19-4.71).

**Discussion:** The role of autophagy in cancer development and progression is still poorly understood. However, Beclin-1 gene has been identified as tumor suppressor gene in many cancer studies. The results of this study showed that Beclin-1 gene may be a tumor suppressor gene and autophagy may be a mechanism leading to cell death in colorectal cancer.

**Conclusion:** According to our data, we are suggesting that Beclin-1 gene may acts like a tumor-suppressor gene in colorectal cancer.

*Keywords: Colorectal Cancer, Autophagy, Beclin-1, Gene expression*

*This study was supported by TUBITAK (Project no: 215S540).*

## POSTER PRESENTATION – 143

### MIRNAS EXPRESSION DIFFERENCES BETWEEN SERUM AND TUMOR TISSUE OF COLORECTAL CANCER PATIENTS

**Umit Yilmaz**<sup>1</sup>, Nesibe Yilmaz<sup>2</sup>, Arzu Ergen<sup>2</sup>, İlhan Yaylim<sup>2</sup>, Nihat Aksakal<sup>3</sup>, Umit Zeybek<sup>2</sup>

<sup>1</sup> Department of Physiology, Faculty of Medicine, Inonu University, Malatya, Turkey

<sup>2</sup> Department of Molecular Medicine, Aziz Sancar Institute of Experimental Medicine, Istanbul University, Istanbul, Turkey

<sup>3</sup> Department of General Surgery, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey

**Background/Aim:** In recent years, many studies have suggested that miRNAs can be used as important biomarkers in the diagnosis and prognosis of diseases. However, several studies have indicated that expression levels of miRNAs is determined in tumor tissue while expression levels of these miRNAs can not be detected in serum samples. The aim of this study was to determine whether the expression differences of miR-17-5p, miR-30b, miR-30d, miR-216a and miR-216b in the tumor tissue and serum of colorectal cancer patients.

**Materials and Methods:** Forty seven colorectal cancer patients were included in this study and the serum and tumor tissue were collected from these patients. MiR-17-5p, miR-30b, miR-30d, miR-216a and miR-216b expression levels were detected by quantitative Real-Time PCR in the serum and tumor tissue of colorectal cancer patients.

**Results:** Expression levels of miR-17-5p, miR-30b, miR-30d, miR-216a and miR-216b in serum samples of patients were statistically decreased compared to tumor tissues of patients ( $p=0.001$ ).

**Discussion:** During our real-time PCR analysis, we found that miRNAs in serum were more difficult to detect than tissues, and because Ct value of serum samples were found to be later than tissue samples.

**Conclusion:** Before using miRNAs as non-invasive biomarkers, it is necessary to determine whether there is an expression difference between serum and tumor tissue of patients.

*Keywords: Colorectal Cancer, miRNA, qRT-PCR.*

*This study was supported by TUBITAK (Project no: 215S540).*



POSTER PRESENTATION – 144  
**THE NMR QUANTIFICATION OF PROPOLIS CONSTITUENTS FROM  
NORTHERN TURKEY**

Meltem Maras ATABAY<sup>1</sup> Zehra Safi OZ<sup>2</sup>, Meryem Ferah AKPOLAT<sup>3</sup>

<sup>1</sup>Bulent Ecevit University, Faculty of Education, Department of Mathematics and Science Education, Kdz Ereğli, Zonguldak, Turkey

<sup>2</sup>Bulent Ecevit University, Faculty of Medicine, Department of Medical Biology, Kozlu, Zonguldak, Turkey

<sup>3</sup>Bulent Ecevit University, Faculty of Medicine, Department of Histology and Embriology, Kozlu, Zonguldak, Turkey

**Background :** Propolis contains a rich variety of chemical compounds. The chemical composition of propolis varies significantly depending on the specific plant resin used by the honeybees in propolis production. Multivariate analysis of data from propolis extracts has proven to be a useful technique to show differences among propolis components.

**Material and methods:** In this study, ethanol extract of propolis was obtained. The propolis extract was subjected to a NMR technique.

**Results:** The structure of compounds in propolis was obtained from its NMR spectrum. Correlations from COSY, HSQC and NOESY confirmed the structure of the compound as well as the carbon and proton chemical shifts.

**Conclusion:** NMR quantification is a rapid, easy to perform, reliable method for finding highly bioactive popular propolis constituents. Differences were observed in the qualitative and quantitative values of constituents in the propolis from Northern Turkey.

## POSTER PRESENTATION – 145

### DETERMINATION OF RADIOACTIVITY IN THE PROPOLIS SAMPLES COLLECTED FROM BLACKSEA REGION IN TURKEY

Zehra SAFI OZ<sup>1</sup>, Meltem MARAS ATABAY<sup>2</sup>, Meryem FERAH AKPOLAT<sup>3</sup>

<sup>1</sup> Bulent Ecevit University, Faculty of Medicine, Department of Medical Biology, Kozlu, Zonguldak, Turkey

<sup>2</sup> Bulent Ecevit University, Faculty of Education, Department of Mathematics and Science Education, Kdz Ereğli Zonguldak, Turkey

<sup>3</sup> Bulent Ecevit University, Faculty of Medicine, Department of Histology and Embryology, Kozlu, Zonguldak, Turkey

**Background :** Propolis is a sticky substance that bees make which is better known as "bee glue". The process begins when an expert propolis-making bee gathers resin from cone-producing evergreen trees or from the buds of trees. it is being used as a natural food by the people. The aim of this study was to do the radioactivity analysis of propolis samples collected from ten cities at weastern blacksea region in Turkey by considering pollution agents and geographical and botanical factors. The effect of the Chernobyl atomic power station accident in 1986 was on bee products. Pollen and propolis are considered to be better indicators for radioactive contamination than honey.

**Materials and Methods:** The propolis samples were collected from bee farms in cities of Blacksea region, determined by the sampling method.

**Results:** <sup>40</sup>K were present in propolis samples at all studied blacksea region. The concentration of 40K was: minimum: 27 Bq/kg, maximum: 73 Bq/kg.

**Conclusion:** At the end of the analyses, the most radioactive propolis samples and their regions were determined. It has been 25 years since a disastrous explosion in Chernobyl nuclear power plant happened, yet its effects still continue to appear in the region, especially on the Black Sea coast of Turkey. Radioactivity is not currently a problem for honey and for other bee products. However, after thermo-nuclear incidents, bee products should be controlled before consumption.

*Keywords: Propolis, radioactivity, radioactivisotops, Potasium.*

## POSTER PRESENTATION – 146

### 4-METHYLCATECOL INDUCES NECROTIC CELL DEATH BY JNK PATHWAY IN INSULINOMA INS-1 CELLS

A. Karatug Kacar, S. Bolkent

University of Istanbul, Faculty of Science, Department of Biology, Istanbul, Turkey

**Background / Aim :** İnsülinoma is a tumor originating from the beta cells of the Langerhans islets, which form the endocrine part of the pancreas and secretes insulin. 4-methylcatechol is a catecholamine derivative and show a cytotoxic effect by generating reactive oxygen species. The aim of this study was to determine type of cellular death in insülinoma INS-1, and to investigate the molecular mechanism of occurred cellular death.

**Materials and Methods :** We have used INS-1 cell line. The cells were marked with acridine orange/ethidium bromide to determine the death rate. Lactate dehydrogenase (LDH) with cytotoxicity kit and reactive oxygen species (ROS) by using dichlorofluorescein diacetate were measured. Mitochondrial membrane potential ( $\Delta\Psi_m$ ) loss was indicated with 3,3'-dihexyloxycarbocyanine iodide. HPLC was used to determine the intracellular ATP and GTP levels. Both active and total JNK and ERK amounts were shown with the ELISA method. p-RAF1, both active and total Elk1, c-Jun and ATF2 transcription factors, Hsp 70 and Hsp 90 were shown with western blotting and their expression levels were analyzed with q-RT-PCR.

**Results :** More necrotic cells than apoptosis were observed in between 250-450  $\mu\text{M}$  doses of 4-methylcatechol in INS-1 cells. An increase in LDH levels and ROS, a decrease in  $\Delta\Psi_m$ , ATP and GTP, a decrease in RAF1 expression, total JNK amount, JNK expression, ATF2 expression, active ERK amount, ERK expression and Elk1 expression, an increase in p-RAF1 activity, active JNK amount and total c-Jun amount were found by 4-methylcatechol administration in compared to control group at determined doses.

**Discussion :** The cellular death occurred when 4-methylcatechol was applied to insülinoma INS-1 cells at 250-450  $\mu\text{M}$  doses. Giving 350, 400, and 450  $\mu\text{M}$  4-methylcatechol led to more necrotic death of the cells.

**Conclusion:** The cells perform necrotic death by the following options: i) phosphorylated RAF1 activates the JNK pathway with the activity of transcription factor c-Jun, ii) Hsp 70 and Hsp 90 did not show a change inside the cell, rendering the JNK pathway active.

*Keywords: 4-Methylcatechol, Insulinoma, INS-1 cells, Cell death, Necrosis, JNK pathway*

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POSTER PRESENTATION – 147  
**EFFECTS OF DIETARY CONTENTS ON REDOX HOMEOSTASIS ACCORDING  
TO AGE AND GENDER IN *DROSOPHILA MELANOGASTER***

***Karolin YANAR<sup>a,b</sup>, Seval AYDIN<sup>a</sup>,Ufuk ÇAKATAY<sup>a</sup>***

<sup>a</sup>*Istanbul University Cerrahpaşa Medical Faculty, Department of Biochemistry İstanbul,Turkey*

<sup>b</sup>*Istanbul University, Institute of Aziz Sançar Experimental Medicine, Department of Molecular Medicine İstanbul,Turkey*

*Drosophila melanogaster* is one of the extensively used model organisms for experimental purposes as life span, aging, various disease models and nutritional research areas. In our current study, we aimed to evaluate the effects of dietary nutrients types related to redox homeostasis according to age and gender. *Drosophila melanogaster* colonies were raised on a different dose of fructose and protein containing media as low, median and high dose of fructose and protein combination.

Flies were separated according to their gender and age as 10 and 30 day-old. Biomarkers related to oxidative protein (protein carbonyl groups, advanced oxidation protein products, dityrosine, kynurenine, N-fomylkynurenine), lipid (lipid hydroperoxides) and carbohydrate damage (advanced glycation end products) and enzymatic antioxidant marker (Cu,Zn-superoxide dismutase) were evaluated according to age and gender. Statistical analysis was performed by SPSS20.

Our experimental observations showed that aging and gender are important factors on oxidative damage. It was also concluded that the extend of basal oxidative stress levels and Cu,Zn superoxide dismutase activity were higher in male flies than females ( $p<0.001$ ). On the other hand, flies as considered elderly (30- day-old) represented impaired redox status than relatively young ones (10 -day-old).

We also observed that high levels of protein content in fructose based media fecundity rate was increased and also transition to adult flies and survival ratio were decreased.

Our results showed that nutrition plays important role in redox homeostasis. Studies have shown that *Drosophila* flies are sensitive to nutrient type and their life span depends on it. Thus, there is no definitive life span period; median life span is varying between 30 to 120 days. We found that male flies affected more than female flies due to-nutrition type. It is well known that females more sheltered to oxidative damage than males because of estrogen. In older age this situation changes. We think 30-day-old flies agreed relatively aged flies when compared to 10-day-old flies.

Further studies are needed to focus on evaluation of the relation between life span, molecular mechanisms and oxidative stress biomarkers.

*Keywords: Drosophila melanogaster, aging, nutrition, gender*

*This study was supported by Istanbul University Scientific Research Fund (49223)*

POSTER PRESENTATION – 148  
**EXPERIMENTS LEADING TO A FALSE SENSE IN INTERPRETATION OF ACTIN  
PRODUCTION IN *ESCHERICHIA COLI***

Eylül Ece Islek<sup>1</sup>, Mehmet Sarihan<sup>1</sup>, Gurler Akpınar<sup>1</sup>, Aylin Kanlı<sup>1</sup>, Murat Kasap<sup>1</sup>

<sup>1</sup> Department of Medical Biology, Medical Faculty, Kocaeli University, 41380, Kocaeli, Turkey

Beta ( $\beta$ ) Actin, a 42 kDa intermediate filament protein is a housekeeping protein that is made constitutively in the cell. This intrinsic property of  $\beta$ -Actin makes it a good candidate for normalization of the gene or protein expression data. That's why in numerous studies,  $\beta$ -Actin is used as an internal control. In order to produce an antibody against  $\beta$ -Actin, we attempted synthesize  $\beta$ -Actin in *E. coli*. Optimized  $\beta$ -Actin gene for expression in *E. coli* was cloned into pQE-2 and expressed in *E. coli* BL21(DE3) strain. Western blot analysis with an anti- $\beta$ -Actin and an anti-His antibodies produced a single specific band with a MW of 35kDa indicating that  $\beta$ -Actin might be produced by this *E. coli* strain in its modified form. Metal affinity purification of the putative  $\beta$ -Actin protein gave a relatively sharp single peak and SDS-PAGE analysis of the purified fractions generated a protein band with respective MW of 35 kDa. The 35 kDa band was predicted to be the band corresponding to the one observed in Western blots. We sliced the band from an SDS-PAGE gel and identified by MALDI-TOF-TOF analysis. Our expectation was to see that the 35 kDa band belonged to  $\beta$ -Actin gene product. However, the results demonstrated the otherwise indicating that Western blot analysis as well as protein purification data generated a false sense in interpreting experiments for protein production in *E. coli*.

POSTER PRESENTATION – 149  
**COMPARATIVE ANALYSIS OF NUCLEAR PROTEIN ISOLATION METHODS  
USING 2D-BASED APPROACH**

Abula Ayimugu<sup>2</sup>, Murat Kasap<sup>1</sup>, Aylin Kanli<sup>1</sup>, Gurler Akpınar<sup>1</sup>, Kubra Karaosmanoglu<sup>2</sup>

<sup>1</sup> Department of Medical Biology, Medical Faculty, Kocaeli University, 41380, Kocaeli, Turkey

<sup>2</sup> Department of Biomedical Engineering, Technology Faculty, Kocaeli University, 41380, Kocaeli, Turkey

Nucleus, the regulatory hub of the eukaryotic cell is a dynamic system and nuclear proteins (NPs) are predicted to comprise about 10–20% of the total cellular proteins, suggesting the involvement of the nucleus in a number of diverse functions. However, NPs are often under-represented in proteomic studies due to their low abundance. In this study, we aimed to find an optimal nuclear protein isolation method for comparative nuclear proteome analysis. SH-SY5Y cells were grown under standard culture conditions and nuclear proteins were extracted using either commercially available kits or discontinuous density gradient centrifugation. The purity of the isolated nuclear proteins were verified by Western Blot (WB) analysis with antibodies against Histon H3, LaminA/C, for nuclear proteins and GAPDH and Cyclophilin A for cytoplasmic proteins. Further analysis was performed by 2-DE gels and the proteins were identified with MALDI-TOF/TOF. An improved density gradient centrifugation method was developed and were successfully used for highly pure nuclear protein isolation. The collected fractions harboring nuclear proteins produced bands only with anti-histone H3 and anti- LaminA/C antibodies but not with anti-GAPDH and anti-cyclophilin antibodies. In addition, 70% of the proteins on 2-DE gels were resident nuclear proteins and 10% of the proteins were predicted to be nuclear-associated. The newly developed method may be used for the discovery of not-yet identified proteins and for comparative nuclear proteome studies.

POSTER PRESENTATION – 150  
**COMPARATIVE PROTEOMIC ANALYSIS OF SH-SY5Y CELLS STABLY  
EXPRESSING THE WT FTO OR THE MUTANT FTO PROTEINS**

Aylin Kanli<sup>1</sup>, Murat Kasap<sup>1</sup>, Gurler Akpinar<sup>1</sup>, Mehin Zulfigarova, Mehmet Dogan Gulkac<sup>1</sup>

<sup>1</sup>Department of Medical Biology, Medical Faculty, Kocaeli University, 41380, Kocaeli, Turkey

The FTO protein displays DNA and RNA demethylase activity. Intronic mutations of the FTO gene are associated with obesity, whereas exonic mutations affect catalytic activity, structure and function. Although there are numerous studies regarding its catalytic function, the overall existence or absence of FTO on cellular proteome has not been investigated. The V493F mutation, located on the C-terminus, does not affect its demethylase activity. However, this does not mean that the mutation is behaving like a silent mutation and does not affect other possible functions of FTO. The purpose of this study, thus, was to investigate the changes in soluble proteome of SH-SY5Y cells upon expression of the WT or the mutant FTO proteins. For this purpose, SH-SY5Y cells stably expressing either the WT or the mutant FTO proteins under the control of tet promoter were used in 2D-SDS-PAGE studies. Spots displaying differences in their abundance were cut from the gels and identified by MALDI-TOF/TOF analysis. We observed changes in abundance of seven and nine protein spots in the WT-FTO and the V493F-FTO over-expressing cells, respectively. Keratin type II cytoskeletal 1 and Peroxiredoxin-2 proteins were up-regulated, while proliferating cell nuclear antigen, 14-3-3-zeta delta, Peroxiredoxin-6, phosphoglycerate mutase 1, guanine nucleotide binding protein subunit- 2 like 1 proteins were down-regulated in the WT-FTO expressing cells. While heat shock 70 kDa protein 4, DDB1- and CUL4-associated factor 7, Ran-specific GTPase-activating protein, and Actin cytoplasmic 1 proteins were up-regulated, elongation factor 1-delta, Rho GDP-dissociation inhibitor 1, Transitional endoplasmic reticulum ATPase, Testis-specific protease-like protein 50, and cytoplasmic Tryptophanyl-tRNA synthetase were down-regulated in the V493F mutant FTO expressing cells. STRING analysis based on the changes in expression patterns in the WT expressing cells led us conclude that the proteins changed their abundance relate to DNA repair mechanisms. On the other hand, the proteins changed their abundance upon the mutant FTO expression erased the FTO-repair mechanisms connection indicating that the mutant FTO may negatively affect DNA replication and repair system.

*This study was supported by TUBITAK project numbered 113S965*

## POSTER PRESENTATION – 151

### **PALLADIUM INCORPORATED MICELLE: A PROMISING MATERIAL FOR FUTURE NON-SMALL CELL LUNG CANCER**

Merve Erkisa<sup>1</sup>, Gülay Büyükköroğlu<sup>2</sup>, Behiye Senel<sup>2</sup>, Veysel T. Yılmaz<sup>3</sup>, Engin Ulukaya<sup>4</sup> Ferda Ari<sup>1</sup>

<sup>1</sup> Uludag University, Faculty of Arts and Sciences, Department of Biology, Bursa, Turkey,

<sup>2</sup> Anadolu University, Faculty of Pharmacy, Department of Pharmaceutical Biotechnology, Eskişehir, Turkey

<sup>3</sup> Uludag University, Faculty of Arts and Sciences, Department of Chemistry, Bursa, Turkey

<sup>4</sup> Istinye University, Faculty of Medicine, Department of Clinical Biochemistry, Istanbul, Turkey

One of the leading causes of cancer-associated deaths in most men and women in the world is lung cancer. Current standards of care for lung cancer includes surgery, radiation, and chemotherapy. However, systemic chemotherapy fails to elicit therapeutic responses and causes severe systemic toxicity due to limited concentration of drug reaching to tissue and blocking of drug penetration. Many important active agents such as anticancer active agents have poor solubility. Micelles have a core-shell structure which enables the system to incorporate poorly soluble drugs thus improve their bioavailability and protect from inactivation in biological media. The objective of this study is to investigate the solubilization of poorly water-soluble anticancer drug Palladium (II) in PEG–DSPE micelle formulation (PdNP) and enhances the efficacy of this formulation in vitro. The physicochemical characterizations of the formulation such as particle size, zeta potential, drug incorporation efficiency were examined followed by the investigation of their cytotoxicities on A549 cell lines.

The non-small cell lung cancer (NSLC) cell line A549 was treated with different concentration of Pd (II) nanoparticle (PdNP) (0.5-5µg/ml) effects on cell viability were detected by SRB and ATP assay at 48 h. To determine the mode of cell death (apoptosis/necrosis), fluorescent staining and M30 (for apoptosis) ELISA assays were carried out. The induction of apoptosis was confirmed by (Caspase 3/7 activity, Annexin-V, Mitochondria membrane potential (MMP), Bcl-2 activation, JC-1 dye, cell cycle and oxidative stress level) by Flow cytometry at the concentration (1 µg/ml) for 24h and 48h.

PdNP showed anti-growth effect against A549 cell in a dose dependent manner. Pyknotic nuclei, M30 level and sub-G<sub>1</sub> hypodiploid cells well-known markers for apoptosis, was observed after treatment with PdNP. However, PdNP induced a mitochondria-dependent apoptotic pathway via modulation of Bcl-2 expressions, resulting in the disruption of mitochondrial membrane potential ( $\Delta\psi_m$ ). Loss of  $\Delta\psi_m$  was followed by cytochrome c release from the mitochondria, resulting in the activation of caspases 3. PdNP induced reactive oxygen species (ROS) generation.

PdNP induce cytotoxicity and apoptosis in A549 cancer cells, and this effect is likely mediated through ROS generation and mitochondrial mechanism. Therefore, PdNP may be used for the treatment of non-small cell lung cancer that is extremely resistant to conventional therapy. Future investigations will focus on in vivo studies assessing the effects of PdNP in lung cells and elucidating their toxicity mechanism.

*Keywords: Palladium, Nanoparticles, Apoptosis, Lung Cancer*

*This study is supported by Uludag University with a project number of BUAP(F)-2014/3*



## POSTER PRESENTATION – 152

### **RALOXIFENE AND FLUOXETINE ALONE AND COMBINED EFFECTS ON BREAST TUMORS CAUSED BY 7,12-DIMETHYLBENZ ( $\alpha$ ) ANTHRACENE IN FEMALE RATS**

Oguzhan Tatar<sup>1</sup>, Necip Ilhan<sup>1</sup>, H. Fatih Gul<sup>1</sup>, Nevin Ilhan<sup>1</sup>, Solmaz Susam<sup>1</sup>

<sup>1</sup>Department of Medical Biochemistry, Faculty of Medicine, Firat University, Elazığ, Turkey

**Background / Aim:** Chemically induced rat mammary carcinogenesis models have been extensively used over the years to mimic human breast carcinogenesis. Hence, the current study was designed to analyze the therapeutic role of Raloxifene (RAL) and Fluoxetine (FLX) against 7,12-dimethylbenz [a] anthracene (DMBA)-induced breast cancer rat model.

**Materials and Methods:** *Thirty*-one healthy female Wistar Albino rats were assorted into four groups according to the following experimental regimen. DMBA (Group I), DMBA+ RAL (Group II), DMBA+FLX (Group III), DMBA+RAL+FLX, (Group IV). Tumors were induced in the rats using DMBA dissolved in olive oil (80 mg/kg body weight). Mammary tissue Cancer Antigen 15-3 (CA 15-3) was determined by Enzyme-Linked Immuno Sorbent Assay (ELISA) method. In order to evaluate the changes of the levels of malondialdehyde (MDA) as well as antioxidant enzyme activities superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT) were measured in the mammary tissues of rats.

**Results:** The level of tissue CA 15-3 level was found statistically significant higher in DMBA group and decreased significantly in all treatment groups ( $p < 0.001$ ). When the MDA levels were evaluated, it was observed a decrease in the whole treatment groups compared to the DMBA group, but it was not statistically significant. Mammary tissue SOD, GPx and CAT activities were found increased in Group II and Group IV respect to DMBA group. The most significant increase in GPx ( $p < 0.001$ ) and CAT activities ( $p < 0.05$ ) was observed in Grup IV.

**Discussion:** There are some clinical parameters such as tumor size and circulating marker such as CA 15-3 that have been used as predictive marker as well as for diagnosis and treatment of cancer patients. In our study, tissue CA 15-3 levels were higher in DMBA group but a significant decrease in CA 15-3 was observed following therapy in all treatment groups. During cancerous condition tumor cells have abnormal activities of antioxidant enzymes. Several reports have showed decreased enzymatic antioxidant activity in various cancer studies. Our study also in line with the findings, as decreased enzymatic antioxidant activities and increased MDA levels in DMBA group. However, the administration of the therapeutic agents to breast cancer rats restored the antiperoxidative enzyme (SOD, CAT and GPx) activities which may be due to their antioxidant potency against breast cancer-induced free radical generation.

**Conclusion:** Based on the scientific appraisal, we suggest that the combination of RAL and FLX was more effective than either agent alone.

*Keywords:* DMBA, breast cancer, CA 15-3, oxidant, antioxidant enzymes

*All experimental procedures were approved by the Clinical Ethics Committee and the Animal Care Committee of Firat University (Protocol No: 2016/57).*

*This study was funded by the Firat University Scientific Research Projects Unit under project TF.16.24*

## POSTER PRESENTATION – 153

### THE ANTIOXIDANT EFFECTS OF THE SELECTED THERAPEUTIC AGENTS ON BREAST CANCER IN FEMALE RATS INDUCED BY 7,12 DIMETHYLBENZ( $\alpha$ )ANTHRACENE

Oguzhan Tatar<sup>1</sup>, Necip Ilhan<sup>1</sup>, Nevin Ilhan<sup>1</sup>, H. Fatih Gul<sup>1</sup>, Solmaz Susam<sup>1</sup>

<sup>1</sup>Department of Medical Biochemistry, Faculty of Medicine, Firat University, Elazığ, Turkey

**Background / Aim:** The development of new breast cancer therapeutic drugs with acceptable efficacy and toxicity that are suitable for use is needed because the rates of breast cancer are continuously increasing. In this study, it was investigated the effects of raloxifene and fluoxetine alone and in combination on antioxidant enzyme activities in 7,12-dimethylbenz [a] anthracene (DMBA) -induced breast cancer rat model.

**Materials and Methods:** Female Wistar Albino rats were divided into four groups. Experimental animal design was as follows: Group I (DMBA group); administered with DMBA dissolved in olive oil (80 mg/kg body weight), Group II (DMBA+RAL Group); administered with DMBA as group 1 and then the rats were treated with RAL, Group III (DMBA+FLX Group); administered with DMBA as group I, then rats were treated FLX. Group IV (DMBA+RAL+FLX Group); FLX plus RAL were administered to the rats as mentioned above. Plasma Cancer Antigen 15-3 (CA 15-3) concentrations were measured using ELISA. Malondialdehyde (MDA) levels and antioxidant enzyme activities of superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT) in the plasma, were determined using spectrophotometry.

**Results:** Plasma CA 15-3 level was statistically significant higher in DMBA group ( $p < 0.05$ ). When cancer bearing rats were treated with FLX and RAL, it was found a statistically significant decreased in plasma CA 15-3 and MDA levels in whole therapeutic groups ( $p < 0.05$ ). GPx activities were higher in Group 4 than DMBA group ( $p < 0.05$ ). Plasma SOD activities were lower and the CAT activities were higher in all treatment groups but no statistically significance.

**Discussion:** Increased MDA levels in plasma have long been known to cause functional degradation; therefore, the degradation of vital tissue causing complications may be indirectly due to increased oxidative stress. In our study, the administration therapeutic agents caused significant decreases in plasma MDA and CA 15-3 levels compared to the DMBA group. The increase of plasma CAT activity in therapeutic groups can be explained as the response to high levels of H<sub>2</sub>O<sub>2</sub>. It has been also reported that an increase in GPx activity shows that the antioxidant system can be stimulated, due to excess generation of peroxides. However; unexpectedly SOD levels were decreased in all therapeutic groups, this situation may be due to SOD is the first antioxidant enzyme in the defense against oxidant molecules.

**Conclusion:** This study shows that selected therapeutic agents may be useful against on oxidative damage in the DMBA-induced breast cancer rat model.

*Keywords: DMBA, CA 15-3 MDA, CAT, SOD, GPx, breast cancer*

*All experimental procedures were approved by the Clinical Ethics Committee and the Animal Care Committee of Firat University (Protocol No: 2016/57).*

*This study was funded by the Firat University Scientific Research Projects Unit under project TF.16.24*

## POSTER PRESENTATION – 154

### THE PDL-1 GENE EXPRESSION LEVELS AND HISTOPATHOLOGICAL CHARACTERISTICS OF NON-SMALL LUNG CARCINOMAS WITH EGFR GENE MUTATIONS

Akif Turna<sup>1</sup>, Cem Horozoğlu<sup>2</sup>, Şeyda Ercan<sup>3</sup>, Öncü Koç Erbaşoğlu<sup>3</sup>, Özlem Küçük Hüseyin<sup>3</sup>, Saime Turan<sup>3</sup>, Mehmet Tolgahan Hakan<sup>3,4</sup>, Hasan Volkan Kara<sup>1</sup>, Ümit Zeybek<sup>3</sup>, İlhan Yaylım<sup>3</sup>

<sup>1</sup> Department of Thoracic Surgery, Cerrahpaşa Medical Faculty, İstanbul University, İstanbul

<sup>2</sup> Medical Services and Techniques Department, Vocational School of Health Services, İstanbul Gelişim University, İstanbul

<sup>3</sup> Department of Molecular Medicine, Aziz Sancar Institute of Experimental Medicine, İstanbul University, İstanbul

<sup>4</sup> Department of Biology, Hitit University, Art and Science Faculty, Çorum, Turkey.

**Background / Aim:** The lung cancer is the most common cancer causes mortality on the worldwide. Mutations of the EGFR gene or its downstream effectors may cause constitutive activations leading metastasis and inhibition of apoptosis. Apoptosis related gene programmed cell death 1 (PDL-1) which is also known as a vital immune checkpoint receptor attracts attention in lung cancer recently expressed in the activated T-cells and in certain tumors like NSCLC. The aim of our study was determination of possible relationships between EGFR gene mutations which are known to be clinically important in Exons 18, Exon 19, Exon 20 and Exon 21; serum EGFR levels; PDL gene expression levels and the risks of non-small cell lung cancer in Turkish cases. We also aimed to investigate concurrently the relationship between mutation results and histopathological findings.

**Materials and Methods:** DNA isolation was performed from peripheral blood sample and tumor tissues. PDL-1 gene expression levels examined pathologically and histopathologically following the tissue tracing of the 21 NSCLC-diagnosed cases. The mutation analysis was performed in the DNA samples with the INFINITI<sup>®</sup> EGFR Assay (Autogenomic, USA) kit used with Biofilmchip. Moreover, PD-L1 gene expression levels were investigated by using SYBR green at RT-PCR. Data evaluation was carried out with SPSS v20 package software (SPSS, Chicago, IL, US).

**Results:** In EGFR mutation detected patients, PDL-1 gene expression levels was determined to be associated with lymph node metastasis. EGFR mutation was determined in 6 patients exons as a results of mutation analysis in 21 patients. Although EGFR mutations was not found statistically significant according to histopathological examination; Exon 20 (c.2303G>T) mutation have demonstrated perineural invasion, the cases carrying, Exon20ins and c.2303G>T showed lymphatic invasion, and lymph node metastasis was observed positively in cases carrying Exon20ins. However, no gene pathology was detected in Exon 18. We observed that Exon19ins was found in all mutated cases in early tumor stage (T1-T2).

**Discussion:** EGFR is known as an important genetic marker plays a role in the diagnosis, follow-up, treatment and prognosis of NSCLC. Significant relationship between high PDL-1 gene expression levels and lymph node metastasis in EGFR mutation carrying patients supports a small number of clinical study in the literature. Despite not being statistically important, histopathological differences were observed in the cases carrying Exon 18 and Exon 20 mutations, on the other hand, EGFR mutation might be relevant in histopathologic studies performed with more cases.

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**Conclusion:** PDL-1 gene expression and EGFR mutation might have a combined effect on NSCLC. PDL-1 gene expression in tumor pathology may also be significant for tumor progression and tumorigenesis.

*Keywords: EGFR, PDL-1, Histopathology of Tumors, NSCLC*

*"Clinical Investigations Ethics Committee of Cerrahpaşa Medical Faculty of Istanbul University" was approved by ethics committee with the number 02-223166 dated 7 July 2017*

*The present work was supported by the Research Fund of Istanbul University. Project No. 20783 and 14516*

## POSTER PRESENTATION – 155

### EFFECT OF VITAMIN D ON CELL GROWTH IN GASTRIC CANCER CELL LINE

İlhan Yaylim<sup>1</sup>, Özlem Küçüküseyin<sup>1</sup>, Onur Temoçin<sup>2</sup>, Mediha Süleymanoğlu<sup>3</sup>, Damla Çelik<sup>3</sup>, Ammad Ahmad Farooqi<sup>4</sup>, Ceylan Hepokur<sup>5</sup>, Güneş Özen<sup>1</sup>, Ebru Nur Ay<sup>1</sup>, Emine Bilge<sup>6</sup>, Serap Kuruca<sup>3</sup>

<sup>1</sup>Istanbul University, The Institute of Experimental Medicine, Department of Molecular Medicine, Istanbul, Turkey,

<sup>2</sup>VU University Amsterdam, Faculty of Earth and Life Sciences (FALW), Biomolecular Sciences, Amsterdam, Netherlands,

<sup>3</sup>Istanbul University, Istanbul Medical Faculty, Department of Physiology, Istanbul, Turkey,

<sup>4</sup>Laboratory for Translational Oncology and Personalized Medicine, Rashid Latif Medical College, Lahore, Pakistan

<sup>5</sup>Cumhuriyet University, Faculty of Pharmacy, Department of Basic Pharmaceutical Sciences, Division of Biochemistry, Sivas, Turkey

<sup>6</sup>Istanbul University, The Institute of Experimental Medicine, Department of Neuroscience, Istanbul Turkey

Vitamin D, which is a hormone-like fat-soluble molecule, is a widely studied vitamin in today's research. Despite the fact that there are studies on effects of Vitamin D on cell growth of different cell lines *in vitro*, there is a lack of information about the selective effects of different doses of Vitamin D on different cell lines. In addition, the mechanisms how this vitamin influences cell proliferation and cell viability are not fully identified. In this study, we aimed to investigate effects of Vitamin D on cell growth and cell viability in AGS gastric cancer cell line. We used different doses of Calcitriol, the most active form of Vitamin D for *in vitro* treatment of this cell line and investigated its effects on cell growth by MTT (Methyl-Thiazol Tetrazolium) assays and cell viability by Trypan Blue staining. Calcitriol treatment clearly inhibited AGS cell growth after 120 hours. Higher doses inhibited the cell growth much higher. Interestingly, there was a sudden decrease in viability from 80% to 60% when 200 nM of Calcitriol was used, compared to that of 100 nM. As an outcome of our study, we observed that Vitamin D inhibited cell growth in AGS gastric cancer cell line.

This study was supported with Scientific Research Projects Coordination Unit of Istanbul University with TYO-2016-20407 project number.

*Keywords: Vitamin D, Calcitriol, cell growth, gastric cancer*

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## POSTER PRESENTATION – 156

### ***DROSOPHILA MELANOGASTER* AS A MODEL ORGANISM FOR UNDERSTANDING TO MOLECULAR MECHANISMS OF DISEASES**

Serkan Sugeçti<sup>1</sup>, Volkan Keleş<sup>2</sup>, Kemal Büyükgüzel<sup>3</sup>

<sup>1</sup> Istanbul Kemerburgaz University, Vocational School of Health Services, Istanbul, Turkey

<sup>2</sup> Faculty of Science and Arts, Department of Molecular Biology and Genetics, Bülent Ecevit University, Zonguldak, Turkey

<sup>3</sup> Faculty of Science and Arts, Department of Biology, Bülent Ecevit University, Zonguldak, Turkey

**Background/Aim:** Non-mammalian model organisms have become the most important model organisms to understand the molecular basis of health and disease in human and to serve as suitable animal models for human disease. They thus have an important role in the development of new therapeutic approaches to human and also animal diseases. Most of genetic and biological organisation is the same among a great range of invertebrates and vertebrates animals. It was possible to learn more about humans by studying any one of animals. Invertebrate animals, insects, including *Galleria mellonella* and *Drosophila melanogaster* have been frequently used as a model organism for researching responsive genes of diseases, toxicology, pharmacology besides their agricultural purpose.

**Materials and Methods:** We reared *D. melanogaster* larvae on artificial diet in our laboratory at  $25 \pm 2$  °C, 60-70% of relative humidity and in a photoperiod of 12 h day light. Around %75 of the human disease genes has conserved in this fruit flies. Thus, *Drosophila* system has been widely used as a model to understand molecular mechanisms of human disease including cancers, infection diseases, neurodegenerative diseases such as huntington disease, parkinson diseases and metabolic diseases such as diabetes, obesity. Because of the reason is that most of basic metabolic mechanisms such as lipid storage and mobilizing, sugar hemostasis and food intake in response to nutritional status have conserved between flies and mammals.

**Results:** *Drosophila* is useful model organism for study lipid metabolism and energy homeostasis. Obesity has been reached alarming levels due to its association with numerous life-threatening diseases including diabetes, heart diseases, hypertension, and cancer and its increased prevalence in both children and adults. Homologs of human neurodegenerative disease genes can be identified in the *Drosophila* genome. The function of these genes can then be studied by generating mutations in the *Drosophila* homolog and then studying the resulting phenotypes.

**Discussion:** *D. melanogaster*, has been used as a useful model organism due to its short generation time, available for genetic tools and completed genome in molecular sciences. We are maintaining the cultures of *D. melanogaster* and also *G. mellonella* as artificial mass-rearing in our laboratory to provide nonmammalian model organisms for basic and molecular researches.

**Conclusion :** It will be focused on *D. melanogaster* as a model organism to identify of obesity and related diseases and recognize their molecular mechanisms besides its commonly used as agricultural purposes.

*Keywords:* *Drosophila melanogaster*, Obesity, lipid metabolism, artificial mass-rearing

## POSTER PRESENTATION – 157

### REVERSAL OF UNRESPONSIVE LUNG CANCER CASES TREATED ON THE BASIS OF AN EX VIVO TUMOR CHEMOSENSITIVITY ASSAY (ONKOGRAM<sup>®</sup>)

Engin Ulukaya<sup>1</sup>, Pınar Alper<sup>2</sup>, Didem Karakaş<sup>2</sup>, Merve Erkisa<sup>2</sup>, Adem Deligönül<sup>3</sup>, Erdem Çubukçu<sup>3</sup>, Sami Bayram<sup>4</sup>, Ferda Arı<sup>2</sup>, Ender Kurt<sup>3</sup>

<sup>1</sup> Istinye University, Faculty of Medicine, Department of Clinical Biochemistry, Istanbul, Turkey

<sup>2</sup> Uludag University, Faculty of Arts and Sciences, Department of Biology, Bursa, Turkey,

<sup>3</sup> Uludag University, Faculty of Medicine, Department of Oncology, Bursa, Turkey

<sup>4</sup> Uludag University, Faculty of Medicine, Department of Thoracic Surgery, Bursa, Turkey

Lung cancer is the most common cause of cancer-related death in men. In order to improve the response-rate and thereby to increase the life-span, tailored/personalized-chemotherapy (patient-specific therapy) is essential. In the study presented, we aimed to investigate if the outcome of unresponsive lung cancer patients is reversed when their treatment is decided on the basis of the assay (onkogram) results. In the study, 2 male patients with advanced stage lung adenocarcinoma were included. Both patients, at 59 years of age, had progressive disease after three (pt #1) and two (pt #2) lines of various chemotherapy regimens. Tumor biopsy samples obtained by videothoracoscopy were studied and the tumor cells were exposed to the drugs of physician's choice. The best drug (the most sensitive one) was decided on the basis of index value (a value that is a special calculation taking all the doses into consideration). The first patient's tumor, progressive after three lines of chemotherapy, was the most sensitive to cisplatin, less but still substantially responsive to docetaxel. Due to high urinary creatinine level and low GFR (glomerular filtration rate) as suggestive for nephrosensitivity, this patient received docetaxel treatment as fourth line treatment and remained stable for the next 11 months without any progression. Second patient's tumor showed high sensitivity to gemcitabine. Therefore, gemcitabine was selected as third line treatment and PET-CT scan results showed 50% reduction in tumor volume. Taken together, onkogram seems to be a promising assay for the design of personalized chemotherapy.

*Keywords: Chemosensitivity, Onkogram, Lung Cancer, Ex Vivo, Chemotherapy*

## POSTER PRESENTATION – 158

### PCA 3 SUPPRESSION ENHANCES THE EFFECT OF ANDROGEN RECEPTOR INHIBITION IN PROSTATE CANCER CELLS

Emre Ozgur, Ugur Gezer

Istanbul University, Oncology Institute, Department of Basic Oncology, Istanbul, Turkey

Prostate cancer is an androgen-dependent disease. The Androgen receptor (AR), which exhibits its effect through androgens, is expressed at different stages of prostate carcinogenesis. The non-coding RNA, termed 'Prostate cancer antigen 3' (PCA3), is one of the molecules gaining importance in prostate cancer. PCA3 is a prostate cancer specific molecule that is overexpressed in prostate cancer cell lines and primary prostate cancer tumor tissues. In view of the importance of PCA3 in prostate cancer, we think that it may be one of the target molecules in prostate cancer treatment. In our study, we investigated following the PCA3 suppression with siRNA how the androgen receptor antagonist enzalutamide affects the efficacy of androgen receptor inhibition or radiotherapy. It is also aimed to investigate the effect of PCA3 suppression and receptor inhibition on androgen target genes and molecules.

PCA3 gene suppression was performed by siPCA3 or scrambled control siRNA (siScr) transfection in prostate cancer cell lines (LNCaP, LNCaP-AR +, VCaP). Enzalutamide (500 nM) and / or radiotherapy (5 Gy) were performed following PCA3 gene suppression. Cell death levels were determined by ELISA. Trypan blue and crystal violet staining were used to determine the effect of PCA3 gene suppression and treatment modalities on cell viability and survival. Expression changes of the target genes were examined by real-time PCR method.

It was determined that PCA3 gene suppression caused to decreased cell viability and colony forming capacity of cells. When apoptosis levels were compared in cell lines, a significant increase in the group treated with enzalutamide in all three cell lines compared to the control group and enzalutamide was given to PCA3 gene expression suppressed cells, apoptosis levels were slightly increased relative to the control group. The apoptosis levels of the radiotherapy-treated (5 Gy) cell groups were also more limited than those of enzalutamide. When enzalutamide and radiotherapy were administered together, there was a higher increase in cell death than in the control group in all three PCA3 suppressed cell lines. PSA expression in all three cell lines, in which PCA3 suppressed and androgen receptor inhibition was performed, a similar decrease was observed according to the control group, whereas AR expression levels in LNCaP and LNCaP-AR + cells showed more decrease than VCaP cells. The PRNCR1 gene expression decreased in LNCaP-AR + cells while no significant change was observed in the other two cell lines. PCGEM1 gene expression decreased in all three cell lines.

Findings suggest that PCA3 suppression promotes androgen receptor inhibition and radiotherapy effects. It has been found that the PCA3 molecule is one of the target molecules of androgen receptor, regulates AR target genes and stimulates the proliferation of prostate cells.

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## POSTER PRESENTATION – 159 ARE TERC GENE MUTATIONS RELATED TO GENDER AND HYPERTENSION IN CORONARY ARTERY DISEASE?

Cem Horozoğlu<sup>1</sup>, Cem Başaran<sup>2</sup>, Ümit Zeybek<sup>3</sup>

<sup>1</sup> Department of Medical Services and Techniques, Vocational School of Health Services, İstanbul Gelişim University, İstanbul

<sup>2</sup> Clinic of Cardiology, Medicana Bahçelievler Hospital, İstanbul-Turkey.

<sup>3</sup> Department of Molecular Medicine, Institute for Aziz Sancar Experimental Medicine Research, İstanbul University, İstanbul

**Background / Aim:** Coronary artery disease (CAD) occurs in a result of narrowing or obstruction of coronary artery with partial or total limitation of acute blood flow. Coronary artery disease is the most common disease for mortality in among coronary and ischemic cardiovascular disease. Relations between telomere, telomerase, telomere associated genes and several diseases have been demonstrated that telomere and shelterin complex genes are associated with CAD. The TERC gene provides instructions for making one component of an enzyme called telomerase. Telomerase maintains structures called telomeres, which are composed of repeated segments of DNA found at the ends of chromosomes.

**Materials and Methods:** In our study, DNA was extracted from peripheral blood samples of total 100 male and female hypertensive and non-hypertensive CAD patients. TERC gene region was amplified by PCR. TERC sequences were analyzed via Sanger sequencing method for all cases.

**Results:** Sequence analysis of TERC gene have demonstrated that male non-hypertensive cases had g.3:169765152delG (4 cases), g.3:169765148delC (10 cases) and g.3:1697655156delG (1 case) mutations. In male hypertensive patients, g.3:169765148delC (7 cases) and g.3:169765152delG (4 cases) have been detected. g.3:169765152delG (7 cases), g.3:169765148delC (4 cases) and g.3:169765081delA (1 case) mutations were determined in female non-hypertensive CAD cases. g.169765124delG (2 cases), both g.3:169764894delA (1 case) and 169764850delC (1 case) mutations were found respectively in intron and exon region in female hypertensive CAD patients.

**Discussion:** Mutations detected in hypertensive and non-hypertensive CAD male cases was found to be common, on the other hand, in hypertensive and non-hypertensive CAD female cases was determined different mutations. However, all mutations in this study were found 5' upstream of exon except hypertensive CAD female. Studies in the literature have been limited in this regard. As a consequence of this study suggest that gender differences might be significant to assembly of telomeric complexity in the pathogenesis of coronary artery disease.

**Conclusion:** As a conclusion of our study, it was demonstrated that deletions have been found in TERC gene sequence for CAD. However, TERC mutations effects may act differently for gender and hypertensive in the pathogenesis of coronary artery disease.

*Clinical Investigations Ethics Committee of Cerrahpaşa Medical Faculty of İstanbul University" was approved by ethics committee with the number 134 dated 17/03/2015*

*The present work was supported by the Research Fund of İstanbul University. Project No: 57392*

## POSTER PRESENTATION – 160 FREQUENCY OF BRCA1 AND BRCA2 MUTATIONS IN PATIENTS WITH UNSELECTED TRIPLE-NEGATIVE BREAST CANCER

Avsar M<sup>1</sup>, Tuncer SB<sup>1,2</sup>, Saip P<sup>2</sup>, Yazici H.<sup>1</sup>

Istanbul University, Oncology Institute, <sup>1</sup>Cancer Genetics Department and  
<sup>2</sup>Medical Oncology Department, Istanbul, Turkey.

**Aim of the study:** Patients with triple-negative breast cancers (TNBC) lack expression of estrogen, progesterone and HER2(erbB2) receptors. Triple negative breast cancer (TNBC) is the most aggressive and poorly understood subclass of breast cancer (BC). According to NCCN guidelines, BRCA gene testing recommended for patients with Triple-negative breast cancers (TNBC) aged under 60 years. The aim of the study was to evaluate frequency of BRCA mutations in unselected TNBC Turkish population. Mutation rates in the literature that it was showed 20% of TNBC patients harbour BRCA mutations. However, the frequency of BRCA mutations in TNBC patients have variety in different populations.

**Material and Methods:** In the study, 189 Turkish women with triple negative breast cancer were evaluated for BRCA mutation frequency and clinicopathologic features. One hundred eighty nine TNBC patients were recruited in the study. All patients were investigated for both small indels and rearrangements of BRCA genes using DNA sequencing and multiplex ligation-dependent probe amplification (MLPA)/CNV analysis using NGS and Sanger Sequencing Analysis.

**Results:** The mean ages at diagnosis were 41.9±9.9 years for BRCA non-carriers and 40.6±9.7 years for carriers with BRCA. The rate of BRCA mutations was also high in patients with triple-negative breast cancer. We identified *BRCA1* and *BRCA2* mutations in 51 of 189 (26.98%) in Turkish triple-negative patients with breast cancer. In our study, 8 patients of higher aged 60 with triple negative histology were not found any BRCA mutations. All mutated patients were in premenopausal status. Although half of the mutated patients had a breast cancer history in their family (28/51), eleven triple negative patients had an ovarian cancer history in their family (11/51). There was not any differences for overall survival between mutation carriers and non-carriers in the study.

**Discussion:** BRCA mutation rate was found 26.98% in patients with triple negative breast cancer in the study group. It was not found any BRCA mutations for patients in older than aged 60 and post menopausal status. The survival analysis was not statistically significant between BRCA non carriers and BRCA carries in the study.

**Conclusions:** The results were suggested that premenopausal women with triple-negative breast cancer should be candidates for BRCA testing in Turkish population. There was not found any statistical significance for overall survival between BRCA carriers and BRCA non-carriers in the our group of study.

*Keywords: Triple negative Breast cancer, BRCA mutation, Survival analysis, Turkish population.*

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*The study was approved by the Ethics Committee of Istanbul Medical Faculty at Istanbul University (Ethics Approval No:2011/1425-681).*

## POSTER PRESENTATION – 161 THE COMPARISON OF WHOLE GENOME MIRNA EXPRESSION LEVELS IN BRCA1 MUTATION CARRIERS

Tuncer SB<sup>1</sup>, Çelik B<sup>1</sup>, Avsar M<sup>1</sup>, Yazici H<sup>1</sup>.

<sup>1</sup>Istanbul University, Oncology Institute, Cancer Genetics Department Istanbul, Turkey

**Aim of the study:** In recent years, it is very important to compare expression patterns between cancer and normal cells of all known miRNAs in cancer research. In this study, the whole genome expression levels of miRNA was investigated between carriers and non-carriers of *BRCA1* mutation in the member of a high-risk ovarian cancer family for ovarian cancer etiology.

**Material Methods:** In our study, it was investigated the high-risk ovarian cancer family that were 6 members known BRCA mutation status. The lymphocytes were isolated from peripheral bloods of ovarian cancer patient and the healthy monozygotic twin sister, 2 older sisters, 1 niece, 1 brother and 1 daughter of patient. Following this process, total RNA and miRNAs were extracted from pellets of lymphocytes for miRNA screening. miRNA materials of patients were examined by using the 'Agilent miRNA array Kit'.

**Results:** Family members were included in the study that were firstly searched for *BRCA1* and *BRCA2* gene testing. A monozygotic twin patient diagnosed with early-onset cancer, a healthy monozygotic twin sister, three healthy sisters, and 1 niece had mutations in *BRCA1* gene. The mutation was found in the family that it was c.5266 dupC p.Gln1756Profs\*74 rs397507247 in the exon 20 of *BRCA1* gene.

Whole genome miRNAs expression profiles were evaluated at 5 different groups in the study. The our results represent that the high level of expression of 12 miRNAs, miR-320a, miR-320b, miR-320c, miR-320d, miR-320e, miR-324-3p, miR-4284, miR-4653-3p, miR-484, miR-6165, miR-874-3p, were observed in BRCA1 mutation carriers compared to non-carriers of BRCA1 mutation. However, the level of 9 miRNAs: miR-3656, miR-4281, miR-4516, miR-4741, miR-6089, miR-6869-5p, miR-6891-5p, miR-7107-5p, miR-7847-3p were highly decreased in the group.

The expression levels of 4 miRNAs: miR-1260a, miR-1260b, miR-4286, miR-5100 were statistically increased between cases of healthy and diagnosed with ovarian cancer in BRCA1 gene mutation carriers. Although the 6 miRNAs expression levels: let-7i-5p, miR-3653-3p, miR-451a, miR-6127, miR-664b-5p, miR-7641 were increased in patient with ovarian cancer, the level of 3 miRNAs: miR-4787-5p, miR-6800-5p, miR-8063 were decreased in the group.

The 17 miRNAs: miR-125a-5p, miR-15b-5p, miR-181a-5p, miR-197-3p, miR-22-3p, miR-223-3p, miR-23a-3p, miR-26a-5p, miR-27a-3p, miR-328-3p, miR-342-3p, miR-425-5p, miR-4430, miR-4697-5p, miR-766-3p, miR-92a-3p, were decreased when miRNA expression levels were compared in between patient with ovarian cancer and healthy cases in rest of family.

**Discussion:** miRNA expression levels were different in BRCA1 mutation carriers and also patients with ovarian cancer. It was suggested that the miRNAs can be used as a biomarker after more detailed studies. And also the miRNAs could be important for the etiology of ovarian cancer.

**Conclusions:** All the molecules found in the study should be examined in different population and large cohorts of ovarian cancer for further investigation.

*Keywords:* miRNAs, Ovarian Cancer, BRCA1 mutation carriers

*Istanbul University, Scientific Research Projects Number;20140; Ethics Committee's approval number:17*

## POSTER PRESENTATION – 162

### IDENTIFICATION OF NOVEL EPIGENETIC BIOMARKERS IN ORAL SQUAMOUS CELL CARCINOMA BY GENE EXPRESSION PROFILING

Semra DEMOKAN<sup>1</sup>, Sevde Comert<sup>1</sup>, Sena Sen<sup>1</sup>, Onder Eryilmaz<sup>1</sup>, Murat Ulusan<sup>2</sup>, Gulsum Ak<sup>3</sup>, Canan Alatli<sup>4</sup>, Nejat Dalay<sup>1</sup>

<sup>1</sup>Department of Basic Oncology, Oncology Institute, Istanbul University; <sup>2</sup>Department of Otorhinolaryngology, Faculty of Medicine, Istanbul University;

<sup>3</sup>Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Istanbul University; <sup>4</sup>Department of Tumor Pathology and Oncology Cytology, Istanbul University, Istanbul, Turkey

**Aim:** Oral squamous cell carcinoma (OSCC) has high morbidity and mortality; therefore 5-year survival is around 51% in patients. Both genetic and environmental factors play a role in the carcinogenesis of malignant lesions. Etiological factors predisposing to OSCC are smoking, alcohol and tobacco consumption, snuffuse, viral factors, chronic irritation, iron and various vitamin deficiencies, poor oral hygiene and diseases such as syphilis. Although the lesions occur in the visible region of oral cavity, it was only detected in late stage during clinical examinations and no progress has been made in the OSCC to make a meaningful contribution to the life span. There may be a chance for the cure of disease, if potential molecular biomarkers are identified for the early stage diagnosis. There are no reliable biomarkers to distinguish patients who are at risk of poor prognosis or early recurrence and to use personalized therapies. In our study, we investigated the differences in expression levels of tumor and matched normal tissue of OSCC determined by gene expression profiling method. In addition to, we were investigated downregulated genes possessing biomarker potency for diagnosis, screening and/or prognosis of the disease.

**Materials and Methods:** Synthesis of cDNA/cRNA was performed after isolation of total RNA from tissue samples. When the expression array study was completed, the raw data of the 9 OSCC patients' tumor and normal matched tissue samples were taken from Illumina iScan, and then bioinformatics analysis was performed by using the Illumina Genome Studio program.

**Results:** Tumor and corresponding normal tissue samples of OSCC patients were compared and results showed that 35 newly identified genes were downregulated at a significant level ( $p < 0.05$ ) at the end of the analysis.

**Discussion and Conclusion:** New potential genes found as downregulated in tumor samples are thought to play an important role in the development of malignancy as tumor suppressors and may be potential biological markers. The resulting candidate genes will be further validated in a larger group of patients.

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*The ethical approval of this study was given by Istanbul University, Istanbul Faculty of Medicine, Ethical Committee (File Number:2013/1470).*

## POSTER PRESENTATION – 163

### IDENTIFICATION OF NEW EPIGENETIC BIOMARKERS IN ORAL PREMALIGNANT LESIONS BY GENE EXPRESSION PROFILING

Semra DEMOKAN<sup>1</sup>, Sevde Comert<sup>1</sup>, Sena Sen<sup>1</sup>, Onder Eryilmaz<sup>1</sup>, Murat Uluşan<sup>2</sup>, Gulsum Ak<sup>3</sup>, Canan Alatlı<sup>4</sup>, Nejat Dalay<sup>1</sup>.

<sup>1</sup>Department of Basic Oncology, Oncology Institute, Istanbul University

<sup>2</sup>Department of Otorhinolaryngology, Faculty of Medicine, Istanbul University;

<sup>3</sup>Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Istanbul University

<sup>4</sup>Department of Tumor Pathology and Oncology Cytology, Istanbul University, Istanbul, Turkey

**Aim:** Oral premalignant lesions (OPML) which are a group of precancerous lesions in oral cavity, may have the potential malignancy risk. Some etiologic factors such as tobacco smoking and alcohol use play an important role in development of OPML. It is important to understand the molecular mechanisms underlying neoplastic progression for biologic markers determining malignant transformation (MT) risk and to identify potential therapeutic targets. In literature, it is urgently needed for the biomarkers that can predict both the development of dysplasia and the risk of conversion to malignancy, as well as potential drug targets in treatment. For this purpose, we identified the downregulated genes in tumor samples by determining expression profiles of premalignant lesions.

**Materials and Methods:** Synthesis of cDNA/cRNA was performed after isolation of total RNA from tissue samples. When the expression array study was completed, the raw data of the 12 OPML patients' tumor and normal matched tissue samples were taken from Illumina iScan, and then bioinformatics analysis was performed by using the Illumina Genome Studio program.

**Results:** Tumor and corresponding normal tissue samples of OPML patients were compared and results showed that 42 newly identified genes were downregulated at a significant level ( $p < 0.05$ ) at the end of the analysis.

**Conclusion:** New potential genes found as downregulated in tumor samples are thought to play an important role in the development of premalignancy as tumor suppressors and may be potential biological markers. These potential candidate genes will be further validated in a larger group of patients.

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*The ethical approval of this study was given by Istanbul University, Istanbul Faculty of Medicine, Ethical Committee (File Number:2013/1470).*

## POSTER PRESENTATION – 164 INVESTIGATION OF CTLA4 GENE VARIATION IN PATIENTS WITH BRAIN TUMORS

Sinem Demirbağ<sup>1</sup>, Roya Mesediyeve<sup>1</sup>, Ozlem Kucukhuseyin<sup>1</sup>, Ali Metin Kafadar<sup>2</sup>, Didem Kafadar<sup>3</sup>, Ilhan Yaylım<sup>1</sup>

<sup>1</sup>Istanbul University, Aziz Sancar Institute of Experimental Medicine, Department of Molecular Medicine, Istanbul University, Turkey

<sup>2</sup>Istanbul University Cerrahpaşa Faculty of Medicine, Department of Neurosurgery, Istanbul, Turkey.

<sup>3</sup>Bağcılar Education and Research Hospital, Istanbul, Turkey

**Background / Aim:** Primary brain tumors constitute a small percent of all malignant cancers, however, the aggressive nature of some types of these tumors have still unexplained molecular mechanisms, they may be related the disturbance of immune system. In this study, we focused on the importance of the immune system in the etiology of brain cancer by investigating critical polymorphism (CTLA4 +49 A>G) of cytotoxic T-lymphocyte-associated protein 4(CTLA4).

**Materials and Methods:** A total of 116 patients with primary brain tumours and 73 healthy controls were enrolled. Molecular assessment of CTLA4 49A>G variants were determined with polymerase chain reaction restriction fragment length polymorphism techniques.

**Results:** There was significant difference in the distribution of CTLA4 49A>G variants between patients with primary brain tumours and healthy controls (p=0.05). The frequency of CTLA4 +49AA /GG genotype was increased in patients with primary brain tumours than those with healthy controls (OR: 1,33; 95 % CI: 1,065- 1,667;p=0,015). We didn't find any correlation between CTLA4 49A>G variants and obtained clinico-pathological parameters such as tumor localization, the presence of necrosis in patients with primary brain tumours.

**Conclusion:** We can state that CTLA4 49A>G polymorphism might be associated with the risk for brain cancer but this data should be reevaluated in further studies with larger patients.

*Keywords: Cancer, brain tumor, polymorphism, CTLA4*

*The present work was supported by the Research Fund of Istanbul University. Project No. 57288*

## POSTER PRESENTATION – 165

### 5'HTTLPR IS NOT RESPONSIBLE FOR THE PATHOGENESIS OF SCHIZOPHRENIA IN TURKISH PATIENTS

Pinar Çetinay Aydın<sup>1</sup>, Mustafa Pehlivan<sup>2</sup>, Nazan Aydın<sup>1</sup>, Selin Kurnaz<sup>3</sup>, Hazal Yavuzlar<sup>1</sup>, Fatih Kaasım Yavuz<sup>1</sup>, Suna Uysal<sup>2</sup>, Sacide Pehlivan<sup>3</sup>

<sup>1</sup>Department of Psychiatry, Bakirkoy Research and Training Hospital for Psychiatry, Neurology and Neurosurgery, Istanbul, Turkey

<sup>2</sup>Department of Haematology, Gaziantep University, Faculty of Medicine, Gaziantep, Turkey

<sup>3</sup>Department of Medical Biology, Istanbul University, Istanbul Faculty of Medicine, Istanbul, Turkey

**Aims and Scopes:** Recent studies show that schizophrenia is a group of heritable disorders caused by a moderate number of separate genotyping networks associated with several distinct clinical syndromes. The serotonin system plays an important role in schizophrenia. The present study was examined to investigate the associations between 5'HTTLPR VNTR variant and the risk of schizophrenia + nicotine dependence (SND).

**Materials and Methods:** We included 47 (33F-Female/14M-Male) patients with SND, 66 (41F/25M) healthy controls (HC). DNA isolated from peripheral blood cells. The genotypes of the study variant were determined using the PCR-based methods. The results were statistically analyzed by calculating the odds ratios (OR) and 95% confidence intervals (CI) using the  $\chi^2$  test.

**Results and Discussion:** The distributions of genotypes and allele frequencies were compared among the groups. The LL, LS and SS genotypes were observed in 11 (24%), 23 (48%), and 13 (28%) patients with Schizophrenia + nicotine dependence and in 14 (21%), 32 (47%), and 22 (32%) healthy controls. The L and S alleles were observed in 45 (47%) and 49 (52%) patients with SND and in 60 (44%) and 76 (55%) HC. We found that no significant difference between SND patients and HC both genotypes and alleles. In the literature, there are approximately 15 studies have been examined. We compared our study with all literature; most of the studies similar to our results except two from South Indian and Japanese population patients.

*Keywords: 5'HTTLPR, Schizophrenia, VNTR*

## POSTER PRESENTATION – 166 CAN VNTR VARIANTS IN ENOS AND XRCC4 GENES CONTRIBUTE TO FORMATION OF RHEUMATOID ARTHRITIS?

Sacide Pehlivan<sup>1</sup>, Ali Aydeniz, Rüştü Oguz, Mustafa Pehlivan, Tuğçe Sever, Savaş Gürsoy

<sup>1</sup>Department of Medical Biology, Istanbul University, İstanbul Faculty of Medicine, Istanbul, Turkey

In recent years, evidence has been accumulated for the involvement of VNTRs in the formation of predisposition to a wide spectrum of pathologic states. In intronic region, VNTRs is probably linked with another one that is functionally significant and localized in a coding region. Endothelial Nitric Oxide Synthetase (eNOS) involves mainly the endothelium, continuously producing NO in inflammatory conditions. A VNTR (27 nt) in intron 4 of eNOS gene is responsible for production of more than 25% of basal plasma NO. It is established that this VNTR produces a small RNA (sirRNA from "short intronic repeat small RNA") inhibiting eNOS expression on the transcriptional level. DNA double-strand breaks (DSBs) are capable of destroying the integrity of the DNA molecule. The gene encoding X-ray repair cross-complementation group 4 (XRCC4) play a role in repair of DSBs. A VNTR variant exists in intron 3 of the XRCC4 gene. In present study, we aimed to investigate whether the VNTR variants in eNOS and XRCC4 genes play a role in rheumatoid arthritis (RA) etiopathogenesis. Sixty-five patients with RA and 70 healthy controls (HCs) were examined for the VNTR variants in eNOS and XRCC4 genes. All variants were genotyped by PCR. The intron 3 VNTR variant in the XRCC4 gene showed an association with RA patients while no association was identified between the intron 4 VNTR in the eNOS and RA. In conclusion, we suggested that the intron 3 VNTR variant in the XRCC4 gene may be associated with the etiopathogenesis of RA as a marker of immune aging.

*This review paper is a an overall findings rheumatoid arthritis patients, genetic variants and functional status in Turkish population.*



## POSTER PRESENTATION – 167

### TRAIL IS ASSOCIATED WITH TUMOR PROGRESSION ON NON-SMALL CELL LUNG CANCER

Öncü Koç Erbaşoğlu<sup>1</sup>, Cem Horozoğlu<sup>2</sup>, Şeyda Ercan<sup>1</sup>, Hasan Volkan Kara<sup>3</sup>, Akif Turna<sup>3</sup>, İlhan Yaylım<sup>1</sup>

<sup>1</sup> Department of Molecular Medicine, Aziz Sancar Institute of Experimental Medicine, İstanbul University, İstanbul

<sup>2</sup> Department of Medical Services and Techniques, Vocational School of Health Services, İstanbul Gelişim University, İstanbul

<sup>3</sup> Department of Thoracic Surgery, Cerrahpaşa Medical School, İstanbul University, İstanbul

**Background / Aim:** Lung cancer is the leading cause of cancer deaths all over the world. Non-small cell lung cancer (NSCLC) accounts 80-85% of all lung cancers. The 5-year survival rate of patients with lung cancer is only 15%. It is known that disorders in apoptosis function play an important role in the pathogenesis of many types of cancer such as lung cancer. Tumor necrosis factor related apoptosis inducing ligand (TRAIL), type II transmembrane protein, is a death ligand capable of inducing apoptosis by activating distinctive death receptor. It selectively triggers apoptosis in cancer cells, while TRAIL does not affect normal cells. TRAIL-induced apoptosis has been reported in variety of human tumors such as colon cancer, breast carcinoma, renal cell carcinoma, multiple myeloma, glioblastoma, pancreatic adenocarcinoma. Our purpose in this study is to investigate TRAIL gene expression levels in non-small cell lung cancer patients and to clarify whether the effect on the pathogenesis and prognosis of disease of TRAIL gene expression levels.

**Materials and Methods:** The tumor and surrounding tissue samples of the 48 NSCLC cases were used to demonstrate TRAIL gene expression, and after tumor tissue and surrounding tissue were dissected, Non-invasive surrounding tissue was used as an internal control in the study. TRAIL gene expression in control and tumor tissue samples was examined using real time polymerase chain reaction. Data were statistically evaluated using the Chi-square and Mann-Withney U tests with SPSS Pack 7 and GraphPad Prism programs.

**Results:** In our study, we found that tumor tissue showed lower expression in terms of TRAIL gene expression compared to control tissue (P=0.026).

**Discussion:** Despite the existence of data related to TRAIL gene variants and mutations in relation to NSCLCs, there is very little data in the literature on TRAIL gene expression. In immunohistochemical studies performed, it has been reported data in relation to that tumors showing high positive expression of TRAIL have a longer survival than TRAIL low positive tumors, but it has not found significant statistically. In our study, high expression of TRAIL gene according to tumor tissue in control tissues is supporting this data in terms of tumor progression.

**Conclusion:** The TRAIL gene expression level may be thought to play a role in tumor progression in the pathogenesis of NSCLC.

*Keywords: TRAIL, Apoptosis, Gene Expression, Lung Cancer, NSCLC*

*Clinical Investigations Ethics Committee of Cerrahpaşa Medical Faculty of İstanbul University" was approved by ethics committee with the number 219543 dated 09.07.2015.*

*The present work was supported by the Research Fund of İstanbul University. Project No. 56384 and 29008*

## POSTER PRESENTATION – 168

### IS THERE ANY RELATIONSHIP BETWEEN THE ICAM-1 +469 A/G POLYMORPHISM AND LARYNX CANCER IN A TURKISH POPULATION

Şeyda Ercan<sup>1</sup>, Roya Mesediyeva<sup>1</sup>, Faruk Çelik<sup>1</sup>, Dilara Sönmez<sup>1</sup>, Selin Baltacı<sup>2</sup>, Bilsay Metin Ekiz<sup>2</sup>, Aysegul Verim<sup>3</sup>, Gulbu Isitmangil<sup>4</sup>, Ümit Zeybek<sup>1</sup>, İlhan Yaylım<sup>1</sup>

<sup>1</sup> Department of Molecular Medicine, Istanbul University, Aziz Sancar Institute of Experimental Medicine.

<sup>2</sup> Department of Biology, İstanbul University

<sup>3</sup> Department of Otorhinolaryngology/Head and Neck Surgery, Haydarpasa Numune Education and Research Hospital.

**Background / Aim:** Intercellular adhesion molecule-1 (ICAM-1) is implicated to play a role in cancer metastasis, and may serve as a diagnostic tool for tumor prognosis and progression as well as a target for therapeutic intervention. Intercellular adhesion molecule-1 (ICAM-1), a cell adhesion molecule with a key role in inflammation and immune surveillance, has been implicated in carcinogenesis by facilitating instability of the tumor environment. A number of studies have investigated the association between ICAM-1 +469 A/G polymorphism and cancer risks. The aim of this study was to investigate the association between the ICAM-1 +469 A/G polymorphism and larynx cancer.

**Materials and Methods:** 110 patients with laryngeal cancer and 90 healthy subjects were enrolled to the study. In the present study, ICAM-1 +469 A/G genotypes were determined by using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP).

**Results:** There were no significant differences in the distribution of ICAM-1 +469 A/G genotypes and frequencies of the alleles between laryngeal cancer patients and controls. We found that the laryngeal patients with ICAM-1 +469 A/G GG genotype who had advanced tumour stage were higher than those of patients with early tumor, but it was not significant.

**Conclusion:** Our findings have suggested that ICAM-1 +469 A/G genotypes might be associated with the progression, but not on risk of laryngeal cancer in Turkish population.

*Keywords: ICAM-1 +469 A/G, laryngeal cancer, risk, progression, polymorphism*

*"Clinical Investigations Ethics Committee of Haydarpasa Numune Hospital" was approved by ethics committee.*

## POSTER PRESENTATION – 169

### INVESTIGATION OF *PD-1* GENE POLYMORPHISM (PD-1.5 C/T) IN TURKISH PATIENTS WITH COLORECTAL CANCER

Yosra Lamami<sup>1,2</sup>, Roya Mesediyeva<sup>3</sup>, Soykan Arıkan<sup>4</sup>, Hilal Fındık<sup>3</sup>, İlhan Yaylım<sup>3</sup>, Cihat Tatar<sup>4</sup>, Ali Emre Naycı<sup>4</sup>, Bayram Kiran<sup>1</sup>

<sup>1</sup> Genetic and Bioengineering Department, Institute of Science / Faculty of Science at Kastamonu University, Kastamonu, Turkey.

<sup>2</sup> Cell Biology Research Group, Human Tissue Culture Department, Biotechnology Research Centre, Tripoli, Libya

<sup>3</sup> Molecular Medicine Department, Aziz Sancar Institute of Experimental Medicine / Istanbul Medical Faculty at Istanbul University, Istanbul, Turkey.

<sup>4</sup> General Surgery Clinics, Haydarpaşa Numune Training and Research Hospital, Istanbul, Turkey

**Background / Aim:** Programmed death-1 (PD-1), expressed by activated T cells, is an inhibitory cell surface receptor concerned in the regulation of T cell task during immunity and tolerance. The associations of the immune response-related genes with cancer have been established. This study investigates PD-1.5 (C/T) polymorphism in patients with colorectal cancer (CRC).

**Materials and Methods:** PD-1.5 (C/T) polymorphism was investigated in 249 Turkish subjects (99 patients with CRC and 150 healthy individuals as controls) by using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP).

**Results:** The distribution of PD-1.5 (C/T) genotypes between the patients with CRC and healthy controls were significantly different ( $p=0.003$ ). The patients who have distant metastasis have increased C allele and, CT genotypes than those with negative metastatic ( $p=0.016$ , odds ratio (OR), 1.248; %95 confidence interval (CI), 1.063-1.465;  $p<0.001$ , odds ratio (OR), 1.732; %95 confidence interval (CI), 1.291-2.322).

Moreover, the patients who have angiolymphatic invasion have increased frequency of C allele than those with the absence of angiolymphatic invasion ( $p=0.006$ , odds ratio (OR), 2.077; 95% confidence interval (CI), 1.318-3.274} metastasis have increased. The patients who have mucinous component have increased frequency of T allele than those with the absence of mucinous component ( $p=0.023$ , OR: 1.284, 95% CI:1.066-1.546). Our results have shown significant associations between PD-1.5 (C/T) polymorphism and CRC susceptibility and progression of the disease.

**Conclusion:** Further researches comprising more patients are required to clarify whether a particular genotype of the PD-1.5 polymorphism is associated with colorectal cancer and clarify the association of PD-1.5(C/T) polymorphism and clinicopathological characteristics.

*Keywords: PD-1.5 (C/T), polymorphism, colorectal cancer*

*"Clinical Investigations Ethics Committee of Istanbul Education and Research Hospital" was approved by ethics committee "*

## POSTER PRESENTATION – 170

### INVESTIGATION OF THE CYTOTOXIC EFFECTS OF *ARUM CONOPHALLOIDES* EXTRACT

Ceylan HEPOKUR<sup>1</sup>, Sema MISIR<sup>1</sup>, Ebru Nur AY<sup>2</sup>, Mehmet Tolgahan HAKAN<sup>2-3</sup>, İlhan YAYLIM<sup>2</sup>

<sup>1</sup>Cumhuriyet University, Faculty of Pharmacy, Department of Basic Pharmaceutical Sciences, Division of Biochemistry, Sivas, Turkey

<sup>2</sup>Istanbul University, Department of Molecular Medicine, Aziz Sancar Institute of Experimental Medicine, İstanbul, Turkey

<sup>3</sup> Department of Biology, Hitit University, Art and Science Faculty, Çorum, Turkey.

**Aim:** The uncontrolled division of cancer cells. Cancer has become an important health problem for the world, and as a result it has increased the economic burden in world countries. In our country, it is estimated that 150000 people are caught each year, and in 2020 this number is estimated to be 300,000. Cancer is the second leading cause of cardiovascular disease. For this reason, studies in the field of health have shifted to new methods of treatment for cancer. Economic and therapeutic efficacy has become the most important target to develop more agents. In this study, it is aimed to study the antiproliferative effects of *Arum conophalloides*.

In this study, it was aimed to investigate the cytotoxic effects of *Arum Conophalloides* extracts on the human glioma (C6) cancer, human bone cancer (MG-63), and mouse fibroblast (L929) cell lines.

**Material and Method:** The cell lines were treated with the different concentrations of *Arum Conophalloides* extract in 24 hours and the analysis of cytotoxicity was performed with XTT. The IC50 values were calculated.

**Results:** The IC50 values of *Arum Conophalloides* extracts in the human glioma cancer (C6), human bone cancer (MG-63), and mouse fibroblast were found as 15.29; 20.24; 30.13  $\mu\text{gml}^{-1}$ , respectively.

**Conclusion:** It was shown that the nontoxic doses of *Arum Conophalloides* extracts with inhibit the cellular proliferation.

## POSTER PRESENTATION – 171

### THE RELATIONSHIP BETWEEN 5-HTT GENE AND NEUROPSYCHIATRIC DISORDERS IN ATHLETES

<sup>1</sup>Kahraman-Timirci O, <sup>2</sup>Comert-Tari I, <sup>3</sup>Aydın M, <sup>1</sup>Tunoglu S, <sup>1</sup>Zeybek U, <sup>4</sup>Bayraktar B, <sup>5</sup>Kurtoglu M

<sup>1</sup>Istanbul University, Aziz Sancar Institute of Experimental Medicine, Department of Molecular Medicine, Istanbul, TURKEY

<sup>2</sup>Fatih Sultan Mehmet Vakif University, Department of Psychology, Istanbul, TURKEY

<sup>3</sup>Galatasaray Football Academy, Istanbul, TURKEY

<sup>4</sup>Istanbul University, Istanbul Faculty of Medicine, Department of Sports Medicine, Istanbul, TURKEY

<sup>5</sup>Istanbul University, Istanbul Faculty of Medicine, Department of General Surgery, Istanbul, TURKEY

**Background:** Most studies on mental health of active athletes have investigated attention deficit, depressive and anxiety symptoms. However, the genetic mechanisms leading to both depression and anxiety disorders among athletes are mostly unknown. The aim of the present study was to investigate the influence of serotonin transporter (5-HTT) gene associated with prevalence of neuropsychiatric disorders, including attention deficit, depressive and anxiety syndromes on the sports performance.

**Materials and Methods:** Quantitative real-time polymerase chain reaction (qRT-PCR) analysis was used to determine the expression patterns of 5-HTT gene in 61 athlete. We selected > 0,66 cut-off values for gene expression fold changes. Furthermore, depression, anxiety and stress scale (DASO) was used as data collection tool.

**Results:** We observed significant correlation between attention deficit and depressive symptoms in athletes with low level of 5-HTT gene expression. Additionally, those with low 5-HTT gene expression showed significant correlation between anxiety and attention deficit ( $p < 0,005$ ).

**Conclusion:** These results suggest a significant interaction between 5-HTT gene and neuropsychiatric symptoms in athletes. Identification of homogeneous groups of athletes having predispositions to attention deficit, depression and anxiety may help to apply early prevention programs.

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## POSTER PRESENTATION – 172

### ASSOCIATION BETWEEN CPT1A/CROT GENE VARIATIONS AND DYSLIPIDEMIA PHENOTYPE IN PATIENTS WITH CORONARY ARTERY DISEASE

Aslıhan Demircan<sup>1</sup>, Ender Coşkunpınar<sup>1</sup>, Deniz Kanca<sup>1</sup>, Gülçin Özkara<sup>1</sup>, Zehra Buğra<sup>2</sup>, Oğuz Öztürk<sup>1</sup>, Hülya Yılmaz Aydoğan<sup>1</sup>

<sup>1</sup> Istanbul University, Aziz Sancar Institute of Experimental Medicine, Department of Molecular Medicine, Istanbul; <sup>2</sup> Istanbul University, Istanbul Medical Faculty, Cardiology Department, Istanbul

**Background.** Continuous and high energy demand of heart to maintain its uninterrupted contraction activity is provided principally by beta oxidation of long chain fatty acids. Therefore, fatty acid beta oxidation defects are supposed to cause cardiovascular problems at covering energy requirement of heart. Carnitine palmitoyltransferase-I (CPT-I) which is the responsible enzyme of long chain fatty acids to be transferred from cytosol to mitochondria by carnitine shuttle for energy production at lipid metabolism via beta oxidation, catalyses separation of acyl from thiol group at acyl-CoA and transfer to OH group at intermembrane space. Carnitine octanoyltransferase (CROT) is a kind of carnitine acyltransferase enzyme which catalyses reversible transfer of fatty acyl groups between carnitine and CoA. Previous studies showed the importance of CPT1A and CROT gene variations at beta oxidation. Aim of this study is to assess CPT1A rs3019613-G>A and CROT rs2214930-T>C variations in individuals with coronary artery disease (CAD) and define the effects of these variations to serum lipid profile and CAD risk.

**Material and Method.** 104 patients with coronary heart disease and 76 healthy controls were included to this study. CPT1A rs3019613-G>A and CROT rs2214930-T>C SNPs were assessed by real time PCR. SPSS 20.0 was used for statistical analysis.

**Results.** CPT1A rs3019613-G>A and CROT rs2214930-T>C distribution was similar between patient and control groups ( $p>0.05$ ). CROT rs2214930-TT genotype was found to be associated with high Total-Cholesterol ( $p=0.045$ ), LDL-Cholesterol ( $p=0.009$ ), while it was prone to have decreased HDL-Cholesterol levels ( $p=0.054$ ). Also, CROT rs2214930-T allele was found to have association with high systolic blood pressure ( $p=0.039$ ). Body mass index values were found higher in patients with CPT1A rs3019613-A allele comparing to ones with GG genotype at CAD group ( $p=0.004$ ), however HDL-Cholesterol threshold value ( $HDL-K\leq 0.90$  mmol/l) was found lower ( $p=0.017$ ).

**Conclusion.** Our findings support possible important effects of CPT1A rs3019613 and CROT rs2214930 variations on serum lipid profile, body mass index and blood pressure at CAD etiopathology.

*Keywords: CPT1A, CROT, gene, lipid metabolism, coronary artery disease*

*This study was funded by Scientific Research Project Coordination Union of Istanbul University. Project Number: 36173*

## POSTER PRESENTATION – 173

### EVALUATION OF LATS2 TUMOR SUPPRESSOR PROTEIN EXPRESSION IN CHRONIC LYMPHOCYTIC LEUKEMIA

Esra Nazligul-Sert<sup>1,2</sup>, Ender Coskunpinar<sup>3</sup>, Derya Ozturk<sup>4</sup>, Mustafa Nuri Yenerel<sup>2</sup>, Melih Aktan<sup>2</sup>, Oguz Ozturk<sup>1</sup>, Hulya Yilmaz-Aydogan<sup>1</sup>

<sup>1</sup>Department of Molecular Medicine, Aziz Sancar Institute of Experimental Medicine, Istanbul University Istanbul, Turkey

<sup>2</sup> Department of Hematology, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey

<sup>3</sup> Department of Medical Biology, Faculty of Medicine, University of Health Sciences, Istanbul, Turkey

<sup>4</sup>Department of Medical Genetics, Division of Internal Medicine, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey.

**Background.** Chronic lymphocytic leukemia (CLL) is characterized by the accumulation of the malign lymphocytes in the bone marrow and blood. CLL exhibits remarkable clinical heterogeneity likely reflecting the underlying biological heterogeneity. LATS2 (Large Tumor Suppressor Homolog 2) is an important component of the Hippo pathway. This tumor suppressor pathway is considered as the control pathway, which organizes the apoptosis, proliferation and cell growth. Although the recent studies have revealed the importance of LATS2 in the pathogenesis of various cancers, its potential impact on CLL has not been studied. The current study was designed to explore the effect of interactions between LATS2 mRNA levels and immunophenotype on the CLL risk in hospital-based subjects.

**Materials and Methods.** LATS2 mRNA levels were measured with the Real-Time PCR method in 20 healthy subjects and 28 patients diagnosed with CLL. Measurements were done from the peripheral blood, which was taken from the treated, non-treated patient groups and healthy control group for RNA isolation and immunophenotyping. The Beta-Actin gene was used as reference for normalization of the gene expression levels. The gene expression levels analysed  $\Delta\Delta C_t$  method.

**Results.** It was found that the LATS2 mRNA expression was down-regulated in the CLL group compared to the control group. We observed that the percentage of CD20 was significantly higher in CLL subjects with the LATS2 mRNA Fold Change  $\leq 0.1$  than those with the LATS2 mRNA Fold Change  $> 0.1$  ( $p < 0.05$ ). However, CD3 and CD8 percentages were significantly lower in CLL subjects with the LATS2 mRNA Fold Change  $\leq 0.1$  than those with the LATS2 mRNA Fold Change  $> 0.1$  ( $p = 0.004$  and  $p = 0.008$ , respectively).

**Conclusion.** As a conclusion, the results of this study indicate that LATS2 mRNA expression downregulated in the CLL patient group in comparison to the control group. Moreover, the inverse relationship between the immunophenotypically determined B-cell marker CD20 and LATS2 mRNA levels may suggest a diagnostic value of LATS2 in CLL.

*Keywords:* LATS2, expression, CLL, Immunphenotype, RT-PCR

*The present work was supported by a grant from the Scientific Research Projects Coordination Unit of Istanbul University (Project No: 28845).*

## POSTER PRESENTATION – 174

### MELATONIN'S IMPACT ON LUNG TISSUE OF RATS WITH LPS INDUCED ENDOXEMIA

Hatice YORULMAZ<sup>1</sup>, Gülten ATEŞ ULUÇAY<sup>2,3</sup>, Elif ÖZKÖK<sup>4</sup>, Sevcihan MUTLU<sup>5</sup> GÜNER, Vakur OLGAC<sup>5</sup>, Şule TAMER<sup>3</sup>

1. Halic University, Medical Faculty, Istanbul, Turkey

2. Istanbul Yeni Yuzyil University, Faculty of Medicine, Department of Physiology, Istanbul, Turkey

3 Istanbul University, Istanbul Medical Faculty, Department of Physiology, Istanbul, Turkey

4 Istanbul University, Institute of Experimental Medicine, Department of Neuroscience, Istanbul, Turkey

5 Istanbul University, Institute of Oncology, Department of Basic Oncology, Istanbul, Turkey

6 Istanbul University, Institute of Oncology, Department of Pathology, Istanbul, Turkey

**Background:** There are studies about reactive oxygen species (ROS) are involved in the pathogenesis of multiple organ failure following sepsis, which often cause to death. Lipopolysaccharide (LPS) is an endotoxin in the cell membrane of gram negative bacteria, causes an inflammatory response. The lung is frequently the first organ to be involved during the development of multiple organ dysfunction in sepsis. In the literature, few studies have investigated the effects of Melatonin on oxidative stress in lung tissue inducing endoxemia. We aimed to evaluate the effects of melatonin on lung tissue structure and antioxidant-oxidant level in Wistar albino rats with endoxemia.

**Material-Methods:** We divided rats into 4 groups, Control, LPS (20 mg/kg, i.p, single dose), Melatonin (10 mg/kg, i.p. three times), and Melatonin + LPS. Melatonin was injected i.p. 30 min before and after the 2<sup>nd</sup> and 4<sup>th</sup> hours of LPS injection. Blood glutathione (GSH) levels were determined using Ellman method using spectrophotometry in 412 nm. The levels of lung TBARS were measured by the thiobarbituric acid assay (TBA) spectrophotometrically at 532 nm. Four-micron thick tissue sections were obtained and stained with H&E to evaluate the inflammation, and were then examined by light microscopy.

**Results:** In the LPS group, there were found to increase Serum creatinine kinase, aspartate aminotransferase, alanine aminotransferase and blood leukocyte values when we compared the other groups ( $p < 0.05$ ). While blood GSH were found to decrease significantly in the LPS group, it was increased in the melatonin treated LPS group ( $p < 0.01$ ). TBARS levels were increased in the LPS group compared to that of controls ( $p < 0.01$ ) but its level was found to decrease in melatonin treated LPS group compared to that of LPS group ( $p < 0.05$ ). Microscopy of representative rat lung tissue shows intense lung inflammation, congestion in vessels and extravation of erythrocytes caused by LPS. Moreover there was severe damage in the lung alveoli in LPS group. In Melatonin+LPSgroup, it was observed to decrease the injury of lung and also inflammatory infiltration was disappeared.

**Conclusion:** Our findings showed to prevent lung damage in Melatonin treatment in rats with LPS induced endoxemia.

*Keywords: Endotoxemia, Lung, Oxidative Stress, Rat*



## POSTER PRESENTATION – 175

### **SURVIVIN GENE PROMOTER POLYMORPHISM -31G/C AS A RISK FACTOR FOR COLORECTAL CARCINOMAS WITH SIGNET RING CELL COMPONENT TUMOR DEVELOPMENT**

Serap Yalcin<sup>1</sup>, Mükerrerem Sefali<sup>2</sup>, Önder Öngürü<sup>2</sup>

<sup>1</sup>Department of Molecular Biology and Genetics, Faculty of Art and Sciences, Ahi Evran University, Kırşehir, Turkey

<sup>2</sup>Department of Pathology, Gulhane School of Medicine, Health Sciences University, Ankara, Turkey

Signet ring cell carcinoma is a rare subtype of colorectal carcinomas with an association of *Survivin*(*BIRC5*) gene -31G/C polymorphism. We investigated the frequency of -31G/C in 28 colorectal carcinomas containing variable signet ring cell component and its relation with clinicopathologic parameters. According to the presence of signet ring cell component, the tumors were categorized into the groups of 0-9%, 10-24%, 25-49% and >50%. Genomic DNA was isolated from paraffin-embedded tissue blocks and analyzed for *Survivin* gene by polymerase chain reaction- restriction fragment length polymorphism. The multiple 4-micron sections were obtained from the most representative blocks of each case. Genomic DNA was manually isolated by using a DNA extraction kit, following the manufacturer's protocol. In order to scan *BIRC5*(*Survivin*) -31G/C mutation, a 341-bp fragment of 5' UTR region of the *survivin* gene was amplified PCR products was also confirmed a DNA direct sequencing. Single-pass sequencing was performed on each template using the forward primer. Regarding the genotypes, a total of 6 cases were homozygote-typical (GG), 20 were heterozygote (GC) and 1 were homozygote-atypical (CC) for the *Survivin* gene -31G/C polymorphism. The observed frequencies for the G and C alleles were 59,3 % and 40,7%, respectively. The genotype and allele frequencies were consistent with Hardy–Weinberg equilibrium ( $p < 0.05$ ). The statistically significant differences were found in clinicopathologic parameters between *Survivin* gene -31G/C homozygote-typical, heterozygote and homozygote-atypical SR-CRC ( $p < 0.05$ ). On the other hand, when we adjusted age, gender, percentage of signet ring component and stage, we found a statistically significant increased risk in *Survivin* gene -31G/C polymorphic group compared to homozygote-typical in Cox regression analysis (HR=199,66; 95% CI=5,85-6819,69;  $p=0,003$ ). *Survivin* gene polymorphisms are frequent in CRC-SRCs. This finding may support its diverse molecular pathogenesis and could have important therapeutic implications for those patients. To clarify the relation of *Survivin* gene polymorphisms with clinicopathologic parameters and prognosis in SR-CRC, studies with multi-institutional larger series are needed.

*Keywords: Colorectal Carcinomas with Signet Ring Cell Component, Survivin, polymorphism*

POSTER PRESENTATION – 176  
**EXPRESSION OF METALLOTHIONEIN 2A (MT-2A) IN CADMIUM-INDUCED  
BREAST CANCER CELLS**

Serap Yalçın

Department of Molecular Biology and Genetics, Faculty of Art and Sciences, Ahi Evran University, Kırşehir, Turkey

Metallothionein (MT) is a small protein with a high affinity for divalent heavy metals such as Cadmium(Cd). Cadmium has estrogenic properties (metallo-estrogen) known to activate the estrogen receptor and encourage breast cancer cell growth. The purpose of this study was to assess the MT2A gene expression in cadmium-induced breast cancer cell lines. In this study, MCF-7 (breast adenocarcinoma, estrogen receptor positive) and MCF-10A (non-tumorigenic breast epithelial cell line) cell lines were established and maintained in RPMI and MEGM Kit medium, respectively. Total RNA isolated from cadmium treated and untreated cell lines and cDNA was synthesized from 1 ug total RNA by using Random Hexamer. Changes in the expression levels of MT-2A were determined by using qPCR method in cadmium treated and untreated MCF-7 and MCF-10A cell lines. MT-2A gene that was up or downregulated more than two folds were considered as significant. Using competitive RT-PCR, cadmium treated cells showed 8 fold increases in expression of MT-2A compared to untreated cells in normal media. Increased expression of MT-2A, protects against metal toxicity in cancer cells.

*Keywords: MT-2A, Cadmium, Cancer*

*This work was supported by the Ahi Evran University Scientific Research Projects Coordination Unit. Project Number: MMF.A2.16.001.*

## POSTER PRESENTATION – 177

### IMPORTANCE OF DETECTION OF ALK GENE REARRANGEMENT WITH FISH METHOD IN NON-SMALL CELL LUNG CARCINOMA PATIENTS

Pelin Nimet Seymen

Department of Medical Genetic, University of Kocaeli, Kocaeli, Turkey

**Background / aims:** Lung cancer, the most common type of carcinoma, due to long-term tobacco usage is the leading cause of cancer deaths in the World. Genetic factors that cause lung cancer are the oncogenes and tumor suppressor genes underlying carcinogenesis. The anaplastic lymphoma kinase (ALK) gene is a transmembrane protein with tyrosine kinase activity. The anaplastic lymphoma kinase (ALK) gene is a transmembrane protein with tyrosine kinase activity. As a result of inversion of ALK gene with EML4 gene, EML4-ALK complex occurs. EML4-ALK complex is continuously active which results in continuous cell proliferation. FISH is known as ‘gold standard’ method in detection of EML4-ALK fusion gene, which mostly seen in adenocarcinoma. Success rates of treatment with tyrosine kinase inhibitors after detection of this complex is high. In our study we aimed to underly the outcomes of detection of EML4-ALK gene rearrangement in our clinics.

**Material and Method:** In our study, we selected and analysed 50 cases (48 males, 2 females) with FISH method which are diagnosed as non-small cell lung carcinoma after pathologic evaluation between 2014 and 2016 at Kocaeli University Hospital. The denaturation and hybridization of this test were performed with the Euro-Lone Hychrome instrument and the results were analyzed with the Olympus BX-51 microscope.

**Results:** As a result of the study, EML4-ALK rearrangement was detected in 8 (%16) cases. Positive cases are between 48 and 74 years old. The positivity among the cases was seen in 50% of the smokers (4 cases) for 40 years, in 12.5% of the smokers (1 case) for 20 and 30 years and in 25% of the cases (2 cases) never smokers. %75 of positive cases have metastasis and %50 has positive familial history. All of the positive patients was started to have ALK inhibitors as a treatment after approval of positive results.

**Discussion:** ALK inhibitors are recognized as new treatment modalities for NSCLC patients and have prominent clinical efficacy. Appropriate selection for this treatment is critical in clinical practice. In patients with EML4-ALK positivity as a result of FISH, the success rate of tumor-targeted therapies administered with ALK kinase inhibitors is 3-4 times higher than chemotherapy.

**Conclusion:** In our study we aimed to take attention to importance of detection of ALK rearrangement in our region.

*Keywords: Non-small cell lung cancer, adenocarcinoma, ALK, EML4-ALK, FISH*

## POSTER PRESENTATION – 178

### DOSE DEPENDENT EFFECTS OF VITAMIN 1,25(OH)<sub>2</sub>D<sub>3</sub> ON OXIDATIVE STRESS AND APOPTOSIS

<sup>1</sup>Cagri Cakici, <sup>1</sup>Turkan Yigitbasi, <sup>2</sup>Sule Ayla, <sup>1</sup>Hadi Karimkhani, <sup>1</sup>Feyza Bayramoglu, <sup>3</sup>Pakize Yigit, <sup>4</sup>Ertugrul Kilic, <sup>1</sup>Nesrin Emekli

<sup>1</sup>Istanbul Medipol University, Faculty of Medicine, Biochemistry Department

<sup>2</sup>Istanbul Medipol University, Faculty of Medicine, Histology and Embryology Department

<sup>3</sup>Istanbul Medipol University, Faculty of Medicine, Biostatistics and Medical Informatics Department

<sup>4</sup>Istanbul Medipol University, Faculty of Medicine, Physiology Department

**Aim:** The purpose of this study is to examine the dose-dependent effects of vitamin 1,25(OH)<sub>2</sub>D<sub>3</sub> on apoptosis and oxidative stress.

**Material and Methods:** In the study, 50 male Balb/c mice were used as control and experiment groups. The mice were divided into 5 groups each consisting of 10 mice. Vitamin 1,25(OH)<sub>2</sub>D<sub>3</sub> was intraperitoneally administered to the low dose, medium dose, medium-high dose and high dose vitamin D groups (at 0.5 µg/kg, 1 µg/kg, 5 µg/kg and 10 µg/kg, respectively), for three times a week during 14 days. At the end of the study, Annexin V were measured by Elisa method, and total antioxidant capacity (TAC) and total oxidant status (TOS) values were measured by colorimetric method in serum. Hematoxylin Eosin (HE) staining was performed in liver tissues and periodic Acid Schiff (PAS) staining was performed in kidney tissues.

**Results:** Comparing the results of medium-high dose (5 µg/kg) and high dose (10 µg/kg) D vitamin administration to that of the control group, it was observed that serum TAC and Annexin V levels decreased and glomerular mesenchial matrix ratio increased in kidney (p<0.05). In addition to these findings, in the group receiving high dose D vitamins (10 µg/kg), it was observed that the damage to the liver increased together with the the oxidative stress index (OSI) values (p<0.05).

**Discussion:** High-dose vitamin D (10 µg / kg) results in oxidant effect, and causes severe histopathological toxicity in the liver and kidney.

**Conclusion:** As a result; this study was the first in the literature to report that use of high-dose vitamin D results in oxidant effect.

*Keywords:* 1,25(OH)<sub>2</sub>D<sub>3</sub>, apoptosis, oxidative stress, TAC, TOS.

*This work was funded by a grant from the Istanbul Medipol University (Grant no. BAP 2016/17).*

## POSTER PRESENTATION – 179

### PUTRESCINE LEVEL AND ITS RELATIONSHIP WITH OXIDATIVE STRESS IN OBESITY

<sup>1</sup>Hicret Tetik, <sup>2</sup>Türkan Yigitbasi, <sup>2</sup>Cagri Cakici, <sup>3</sup>Nihal Büyüksulu, <sup>4</sup>Orhan Çakan; <sup>5</sup>Pakize Yiğit, <sup>4</sup>Cüneyd Parlayan <sup>2</sup>Nesrin Emekli

<sup>1</sup>Istanbul Medipol University, Institute of Health Sciences

<sup>2</sup>Istanbul Medipol University, Faculty of Medicine, Biochemistry Department

<sup>3</sup>Istanbul Medipol University, Faculty of Health Sciences

<sup>4</sup>Istanbul Medipol University, Regenerative And Restorative Medicine Research Center

<sup>5</sup>Istanbul Medipol University, Faculty of Medicine, Biostatistics and Medical Informatics Department

**Aim:** The aim of the study is to investigate putrescine levels and the relationship between putrescine and oxidative stress in obese individuals and a control group.

**Material and Methods:** Within the scope of the study, 85 obese individuals, aged 18-70, and 29 healthy individuals constituted the control group. Exclusion criteria were; being younger than 18 years, being older than 70 years, smoking, presence of kidney dysfunctions, hypertension, cardiac diseases, osteoarthritis, cancer, polycystic ovary disease and inflammatory and infectious diseases. Blood was taken from patients who applied to Medipol Mega Hospital for routine surveys and analyses, after 12 hours of fasting. The levels of starvation blood glucose, HbA1c, urea, uric acid, hemogram, C-Reactive Protein, total antioxidant capacity and putrescine levels were measured. Starvation blood glucose, HbA1c, urea, uric acid, hemogram, C-Reactive Protein levels were determined at Medipol Mega Hospital using the immunoturbidimetric method, while total antioxidant capacity was spectrophotometrically determined at REMER and putrescine levels were measured using the HPLC method.

**Results:** Putrescine levels were found to be lower in the case group ( $0.25 \pm 0.13$ ) at a statistically significant level, compared to the control group ( $0.39 \pm 0.08$ ) ( $p < 0.05$ ). In subgroup analysis, putrescine levels were found to increase in a statistically significant trend ( $p < 0.05$ ) compared to the obese subgroup, but not differently from control group ( $p > 0.05$ ) in diabetic obese individuals. When the control group was compared with the obese group, there was no statistical difference in TAK values, whereas TOS values were found statistically higher in the obese group ( $p < 0.05$ ).

**Discussion:** Putrescine values were found to be lower in the obese group than in the control group, but it was also observed that putrescine levels also increased with increasing oxidative stress in diabetic obese individuals. The positive correlation between OSI and putrescine indicates that putrescine plays an important role in oxidative stress in cases of obesity.

**Conclusion:** As a result, our study is the first in the literature to measure putrescine levels in obese adults. This study indicates that putrescine plays an important role in oxidative stress in cases of obesity.

*Keywords: obesity, putrescine, oxidative stress, TAK, TOS, OSI*

## POSTER PRESENTATION – 180 SPERMIDINE AND SPERMINE LEVELS AND THEIR RELATIONSHIP WITH OXIDATIVE STRESS IN OBESITY

<sup>1</sup>Nurcan Göktürk, <sup>2</sup>Türkan Yigitbasi, <sup>2</sup>Cagri Cakici, <sup>3</sup>Nihal Büyüksulu, <sup>4</sup>Orhan Çakan, <sup>5</sup>Pakize Yiğit, <sup>4</sup>Cüneyd Parlayan <sup>2</sup>Nesrin Emekli

<sup>1</sup>Istanbul Medipol University, Institute of Health Sciences

<sup>2</sup>Istanbul Medipol University, Faculty of Medicine, Biochemistry Department

<sup>3</sup>Istanbul Medipol University, Faculty of Health Sciences

<sup>4</sup>Istanbul Medipol University, Regenerative And Restorative Medicine Research Center

<sup>5</sup>Istanbul Medipol University, Faculty of Medicine, Biostatistics and Medical Informatics Department

**Aim:** In this study, we aimed to investigate spermidine and spermine levels and their relationship with oxidative stress in obesity.

**Materials and Methods:** Sera obtained from routine blood sampling of patients, who applied to Medipol University Mega Medipol Hospital Laboratories, was used in the study. A total of 114 individuals participated in the study. 85 of these individuals were obese, while 29 were normal. Patients were divided into groups according to BMI values, taking into account the exclusion criteria. From the sera obtained, glucose, HbA1c, CRP, urea and uric acid were examined quantitatively in the Cobas Roche 6000 autoanalyser using the immunochemiluminescence method, and hemogram was performed in the Symex 2000i device using the Flow cytometric method, in Mega Medipol Hospital. TOS and TAS values were examined spectrophotometrically using the method developed by Erel, while spermidine and spermine levels were examined using the HPLC method.

**Results:** Spermidine levels were found to be lower in the case group ( $1.80 \pm 0.68$ ) at a statistically significant level, compared to the control group ( $2.29 \pm 0.79$ ) ( $p < 0.05$ ). In subgroup analysis, spermidine levels were found to increase in a statistically significant trend ( $p < 0.05$ ) compared to the obese subgroup, but not differently from control group ( $p > 0.05$ ) in diabetic obese individuals. No statistically significant difference was found between the spermine levels in the case group (6.73) and the control group (6.59) ( $p > 0.05$ ). In the subgroup analysis, spermine levels in the obese subgroup were found numerally lower compared to those of the control and diabetic obese groups. However, no statistical difference was observed among the groups ( $p > 0.05$ ). When the control group was compared with the obese group, there was no statistical difference in TAK values, whereas TOS values were found statistically higher in the obese group ( $p < 0.05$ ).

**Discussion:** Spermidine and spermine values were found to be lower in the obese group than in the control group, but it was also observed that spermine and spermidine levels also increased with increasing oxidative stress in diabetic obese individuals. The negative correlation between the BMI and spermidine suggests that low spermidine levels increase obesity.

**Conclusion:** As a result, our study is the first in the literature to measure spermidine and spermine levels in obese adults. In order to investigate the cause of the differences in spermidine and spermine levels, new studies should be carried out in which enzymes involved in the synthesis, production and degradation of polyamines are examined.

*Keywords: obesity, spermidine, spermine, oxidative stress, TAK, TOS, OSI*

## POSTER PRESENTATION – 181 EFFECT OF LIPIDS IN TISSUE FACTOR ACTIVITY ISOLATED FROM SHEEP AND LAMB LUNG

Aslıhan TENKEKİGİL<sup>1</sup>, Halil ŞENOL<sup>2,3</sup>, A.Merve ŞENOL<sup>2,3</sup>, Nesrin EMEKLİ<sup>4</sup>

<sup>1</sup>T.C. Ministry of Health, Health Sciences University, Bağcilar Education and Research Hospital, Medical Biochemistry Laboratory, Istanbul;

<sup>2</sup>Bezmialem Vakıf University, Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Istanbul

<sup>3</sup>Ataturk University, Faculty of Science, Department of Chemistry, Erzurum

<sup>4</sup>Medipol University, Institute of Health Sciences, Medical Biochemistry Department, Istanbul.

**Introduction:** The Tissue factor (TF), also known as thromboplastin, Factor III and CD 142 is a membrane glycoprotein responsible for initiating the clotting system. Phospholipids that activate the activation of the coagulation system in the molecular structure are important. TF is used has always been an important tool in the monitoring of the coagulation system. In parallel with the advancing technology, it is known that TF is also effective in the pathogenesis of many diseases. TF is the active ingredient in thromboplastin reagents used to perform prothrombin time (PT) clotting tests. Thromboplastins are complex mixtures prepared from extracts of lung, brain, placenta, although newer generation thromboplastins contain recombinant human tissue factor incorporated into phospholipid vesicles. Differences in the content of TF produced affect the outcome of the prothrombin time test. A calibration system, the International Sensitivity Index (ISI) and International Normalized Ratio (INR) have compensated for this. The most promising developments in TF are the use of these receptors for treatment of cancer.

**Aim of the study:** In this study, it was aimed to investigate the effect of lipids and phospholipids on the activity of TF isolated from sheep and lamb lung.

**Materials and Methods:** TF extract and purified TF were prepared and lipids were extracted. TF activity was determined by prothrombin time test. The TF extract was lyophilized (nitrogenous and without nitrogen) for later use. Total lipid was determined by gravimetric method. Phospholipids were identified by thin layer chromatography (TLC) and major phospholipids such as phosphatidylcholine (PC), phosphatidylethanolamine (PE), phosphatidylserine (PS) and sphingomyelin (SM) were determined by using phospholipid standards. To determine the amounts of phospholipids in the TF extract, phosphors assignment have been done spectrophotometrically for each sample.

**Results:** By the procedure we used, 65 mg of purified lung thromboplastin (lamb) was obtained from 100 grams of starting tissue. Thromboplastin powdered with liquid nitrogen was lyophilized more quickly. The TF extract from lamb lung found more active than sheep lung. The TF activity was observed in the lipid fraction separated by extraction, but not in the protein fraction. The two fractions together had the highest activity. Purification decreased activity. The amount of lipid in the sheep's lung was found to be higher than the lamb's lung. Sequence of phospholipids in the TF obtained from lamb lung was determined as PE> PC> PS> SM.

**Conclusion:** The results of this study have shown that lipid profile is important both in the pathogenesis of diseases and in TF activity used as test material in the laboratory. This study also emphasized the importance of the lipid profile of TF that can be produced for use in laboratory tests.

*Keywords:* tissue factor, prothrombin time, phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine, sphingomyelin

## POSTER PRESENTATION – 182 COMPARISON OF DIFFERENT METHODS IN URINE PROTEOM PROFILE

<sup>1</sup>Feyza Bayramoglu, <sup>2</sup>Cuneyd Parlayan, <sup>1</sup>Cagri Cakici, <sup>1</sup>Turkan Yigitbasi, <sup>1</sup>Nesrin Emekli

<sup>1</sup>Istanbul Medipol University, Faculty of Medicine, Biochemistry Department

<sup>2</sup>Department of Biomedical Engineering School of Engineering and Natural Science

**Aim:** The aim of this study is to perform proteomic analysis in the urine of patients with prostate cancer (PCa) with our control group, to try different techniques, to detect possible protein differences, and to provide a basis for our biomarker studies to be performed.

**Materials and Methods:** The sample preparation stage is a very important step in the study of urine proteomics. Therefore, two different peptide separation methods have been used in a healthy person urine which is FASP and In-solution protocols in order to determine the best method for our study.

**Results:** While 152 proteins have been identified with the FASP kit, 26 proteins have been identified in the sampling study according to the in-sol protocol. The protein concentration of a normal person urine is very low and the salt concentration blocking the proteomic analysis is quite high. For this reason, urine specimens were subjected to the acetone precipitation and dialysis during the sample preparation phase for the purposes of finding the most efficient method of removing the salts. 52 and 10 proteins were identified, respectively. Acetone precipitation and FASP were applied in accordance with these results obtained from our preliminary studies to the patients with prostate cancer and urine samples of our control group, which form our main experiment set. 10 proteins are identified.

**Discussion:** The relative efficacy of these different methods in terms of quality and recovery yield is still not sufficient. Each method has both its advantages and disadvantages when compared to each other. We know there is not a single perfect protocol to analyse all urine proteomics.

**Conclusion:** As a result of this study, at least two different sample preparation methods must be used together to obtain the largest amount and quality of data.

*Keywords: Proteomics, acetone precipitation, dialysis, FASP, in-solution.*



## POSTER PRESENTATION – 183

### CREATING AN IOT DEVICE TO MONITOR VITAL SIGNS OF INFANTS

Serkan Türkeli<sup>1,5</sup>, Kenan Kaan Kurt<sup>2</sup>, Hüseyin Tanzer Atay<sup>3,5</sup>, Remzi Yalın Sönmez<sup>4</sup>

<sup>1</sup> Istanbul Technical University - Control and Automation Engineering Department

<sup>2</sup> Boğaziçi University – Biomedical Engineering MSc Program

<sup>3</sup> Istanbul Technical University - Biomedical Engineering MSc Program

<sup>4</sup> Istanbul Technical University – Electrical Engineering MSc Program

<sup>5</sup> Tesodev, İstanbul

According to U.S. Census Bureau, worldwide average of infant mortality rate is 90, meaning that 90 infants die per 1000 live births within one-year period after birth. The leading causes are stated as birth defects, preterm birth, maternal complications of pregnancy, sudden infant death syndrome (SIDS) and injuries (e.g. Suffocation). Considering SIDS and injuries, the rate increases because of uneducated or/and unobservant parents in such cases, infant chokes on vomit or due to misplacement infant suffocate. This study aims to reduce death rates of infants by monitoring them continuously. We created a wristband for infants to monitor SpO2 and heart rate, which is cloud integrated, to share patients' status with their doctor. By this way, doctor can lead parents to take required actions in a controlled manner. Moreover, the device also has the ability to create audible alarms to warn the parents in case of a complication.

## POSTER PRESENTATION – 184

### EVALUATION OF CIRCULATING LEVELS OF MIR-205, LET-7F, MIR-221, MIR-21 AND MIR-92 AS NON-INVASIVE BIOMARKERS IN DIAGNOSIS AND PROGNOSIS OF OVARY CANCER

Veysel Sal<sup>1</sup>, Sinem Durmus<sup>2</sup>, Pinar Atukeren<sup>2</sup>, Remise Gelisgen<sup>2</sup>, Fuat Demirkiran<sup>3</sup>, Tugan Bese<sup>3</sup>, Macit Arvas<sup>3</sup>, Ayse Ender Yumru<sup>1</sup>, Hafize Uzun<sup>2</sup>

<sup>1</sup>Department of Obstetrics and Gynecology, Sisli Etfal Hamidiye Education and Research Hospital, Istanbul, Turkey

<sup>2</sup>Department of Biochemistry, <sup>3</sup>Department of Obstetrics and Gynecology, Division of Gynecologic Oncology, and Istanbul University Cerrahpasa Faculty of Medicine, Istanbul, Turkey

**Objective:** To determine miR-205, let-7f, miR-221, miR-21 and miR-92 levels of circulating non-invasive biomarkers in diagnosis and prognosis of ovarian cancer. Thus, it is aimed that new markers with high specificity and sensitivity are used at early diagnosis, follow-up and determination of prognosis.

**Method:** In Cerrahpaşa Medical Faculty, Department of Obstetrics and Gynecology, Division of Gynecologic Oncology, 43 patients with malignant epithelial ovarian tumor and 51 patients with benign ovarian pathology who were operated for adnexal mass between 2015-2016 were included in the study. Pre-operative peripheral blood samples were obtained from the Department of Biochemistry and were studied for miR-205, let-7f, miR-221, miR-21 and miR-92 as rNu44 miRNAs.

**Results:** Mean age of malignant and benign groups were  $57.1 \pm 13.5$  and  $38.7 \pm 12.6$ , respectively ( $p < 0.001$ ). miR21(1.28 fold) and miR-221 (1.7 fold) in the malignant group were down-regulated in let-7f (0.81 fold), miR-92a (0.51 fold) and miR-205(0.91 fold) Was found to be up-regulated. Only the let-7f was statistically significant ( $p = 0.019$ ), whereas the other mirRNAs were not statistically significant in the evaluation according to tumor histological subtypes. Let-7f showed the most increase in endometrioid type tumors. When we evaluate the relationship between stage, grade, residual disease and acid and miRNA levels; It was observed that miR-221 increased significantly in advanced disease (stage 3-4) compared with early stage disease ( $p = 0.004$ ).

**Conclusion:** miRNA-221 may be a prognostic factor in malignant epithelial ovarian cancer as it is detected in advanced stage malignant epithelial ovarian cancer at higher levels than early stage cases.

## POSTER PRESENTATION – 185 SUCCINIC ACID EFFECTS ON LEUKEMIA CELL LINES

Baris Ertugrul<sup>1</sup>, Elif Sinem Bireller<sup>2</sup>, Bedia Cakmakoglu<sup>1</sup>

<sup>1</sup>Istanbul University, Institute for Aziz Sancar Experimental Medicine Research, Department of Molecular Medicine, Istanbul, Turkey.

<sup>2</sup>Department of Pharmaceutical Microbiology, Faculty of Pharmacy, Istanbul Yeni Yuzyil University, Istanbul, Turkey

Acute lymphoblastic leukemia is characterized by proliferation of white blood cells (B or T cell origin) in bone marrow. Even though, there are many successful options for the treatments of leukemia, there are still a number of problems such as highly effective side effects for patients. From this point, herbal product and additional food supplies are become a new area for cancer treatment. Succinic acid is a dicarboxylic acid that naturally found in plants, animals and human metabolisms. It is also used in daily life such as food and cosmetic fields by supplying from bacterias.

In our study, possible antiproliferative effect of succinic acid on T-ALL cell lines were investigated by using CCRF-CEM and MOLT-4 cell lines. WST-1, Caspase 3 / BCA and Annexin V were determined by time and dose dependent manner of succinic acid.

Succinic acid showed most cytotoxic effects on MOLT-4 and CCRF-CEM for 25  $\mu$ M and 50  $\mu$ M during 48 h of incubation period. Succinic acid interaction with MOLT-4 line 48 hours and in 25  $\mu$ M, caspase showed a 2.5-fold increase in response to 7.5% increasing level in apoptosis, in 50  $\mu$ M caspase showed a 1.33-fold increase in response to 9.7% increasing level in apoptosis. CCRF-CEM showed 1,98 decreasing results on caspase level in response to 6,7% level in apoptosis by 25  $\mu$ M succinic acid and 0,97 decreasing results on caspase and 5,8% level in apoptosis by 50  $\mu$ M succinic acid.

As a result of our study, the apoptotic effect of succinic acid was observed on T-ALL cell lines CCRF-CEM and MOLT-4 has been observed during the incubation time depended on dosage and time. On the MRC-5 cell line, where we work as healthy control, succinic acid, a natural metabolite intermediate, is an important data feature for potential use in treatment, and it promises for further cancer research.

*Keywords: T-acute lymphoblastic leukemia, succinic acid, apoptosis.*

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## POSTER PRESENTATION – 186

### THE EFFECT OF DOXORUBICINE LOADED MICROBUBBLES ON BREAST CANCER IN IN VIVO EXPERIMENTAL ANIMAL MODEL

Efe Özgür Serinan<sup>1</sup>, Mustafa Barış<sup>2</sup>, Gülşah Kürkcü<sup>3</sup>, Meryem Çalışır<sup>4</sup>, Melek Aydın<sup>1</sup>, Cansu Önercan<sup>3</sup>, Safiye Aktaş<sup>1</sup>, Zekiye Altun<sup>1</sup>, Sevgi Kılıç Özdemir<sup>3</sup>, Osman Yılmaz<sup>4</sup>, Ekrem Özdemir<sup>3</sup>

<sup>1</sup>Department of Basic Oncology, Dokuz Eylül University School Of Medicine, Izmir, Turkey

<sup>2</sup>Department of Radiology, Dokuz Eylül University School Of Medicine, Izmir, Turkey

<sup>3</sup>Department of Chemical Engineering, Izmir Institute of Technology, Izmir, Turkey

<sup>4</sup>Department of Laboratory of Animal Science, Dokuz Eylül University School of Medicine, Izmir, Turkey

In-vitro effects of doxorubicin (DOX) and Doxorubicin confined to liposomes (Lipo- DOX) on 4T1 breast cancer cells were examined. MB images were displayed under ultrasound and demonstrated to be detonated under ultrasound in a controlled manner.

Approximately 6 weeks of female athymic nude mice were used for the animal model. 5 experimental groups were formed. The number of animals in each group was determined as 7.

When 4T1 cells were subcutaneously injected and the tumors reached 1cm in diameter, nude mice underwent 3-dimensional tumor volume measurement under ultrasound followed by drug administration. The drug-treated mice were sacrificed on the 4th day of the study, again following a 3-dimensional tumor volume measurement under ultrasonication. The tissues (lung, liver, kidney, brain, tumor) were stained with hematoxylin-eosin in sections after formalin fixation and histopathologically evaluated. The animals were also treated with 5 mg / kg DOX, which is a well-documented LD50 dose, in the breast cancer 4T1 cells. Lung, liver, kidney, brain and tumor tissues were examined histopathologically from tissues taken during sacrifice of athymic nude mice. Normal histology was observed in all groups in the lung, kidney and brain. In the liver, in the DOX and Lipo-DOX groups, the damage in the spotty necrosis style was observed mildly in the parenchyma of 7 cases in each group. Necrosis rate, apoptosis rate, cell viability and liver damage were statistically significant when the tumor size difference did not give statistical significance between the groups (p = 0,145).

As a result of our study, it has been shown that ultrasound contrast agent microtubules can be contrasted and controlled in vitro under in vivo conditions under ultrasound imaging. Doses of LD50 of DOX and LIPODOX have been shown to induce tumor necrosis in nude mice.

In future studies, it is proposed to perform experiments with Doxorubicin loading at high doses of microbubbles, prolongation of microbubbles until sacrifice to see if the microbubbles are detonated more than once under ultrasound and statistically significant decrease in tumor size.

Keywords: Breast Cancer, Liposome, Doxorubicin, Microbubble, Ultrasonography

#### DECLARATIONS

*The manuscript is new and is not being considered elsewhere. Authors have no any commercial association and conflict of interest. All the experiments were done following the principles of Dokuz Eylul University Animal Ethical Committee's approval (Protocol No: 29/2015).*

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## POSTER PRESENTATION – 187

### EFFECT OF TACROLIMUS ON TRIPLE NEGATIVE BREAST CANCER ANIMAL MODEL

Safiye Aktaş<sup>1</sup>, Pinar Erçetin<sup>1</sup>, Efsun Kolatan<sup>2</sup>, Osman Yılmaz<sup>2</sup>

<sup>1</sup>Department of Basic Oncology, Dokuz Eylül University, Institute of Oncology, Izmir, Turkey

<sup>2</sup>Department of Laboratory of Animal Science, Dokuz Eylül University School of Medicine, Izmir, Turkey

The subtype of breast cancer which is triple negative (estrogen receptor (ER) negative, progesterone receptor (PR) negative and HER2 negative) does not response to therapeutic agents that target these three receptors. New combination therapies and agents are needed for this breast cancer type with poor prognosis. Constantly active receptor tyrosine kinases involved in cancer cells use PI3K/AKT/mTOR signalling pathway to modulate the functions of cancer cells. The anti-proliferative effect of calcineurin inhibitor tacrolimus which structurally resembles to the most well known mTOR inhibitor rapamycin and modulates mTOR in the absence of rapamycin, was found in such cancers as, glioblastoma multiforme, hepatocellular carcinoma and lymphoma. Our aim was to evaluate the in vitro and in vivo effect of tacrolimus on triple negative breast cancer cells.

In this study, After 4T1 triple negative breast cancer cell line was cultivated in RPMI-1640 medium under 37°C and 5% CO<sub>2</sub> conditions, cells were incubated with tacrolimus (1, 10, 20, 30, 40, 50, 100 µM) for 24, 48 and 72 hours. Cell proliferation percentages were evaluated by WST-1 analysis. To evaluate the in vitro effective dose of tacrolimus on experimental animals, 4T1 cells were inoculated subcutaneously to 5-7 weeks old, averagely 25 grams weighted 7 female athymic nude mice. When tumor volume had become 150 cm<sup>3</sup>, test groups were randomized as normal saline was given control group and tacrolimus (10 mg/kg tacrolimus at the 1st and 8th days, intraperitoneously, 0,5 cc) treated group. In the 14th day, animals were sacrificed and tumor tissues were evaluated histopathologically and fresh cell suspensions were prepared for apoptosis analysis with annexin V and propidium iodide (PI) by flow cytometry.

According to the in vitro evaluation, tacrolimus decreased cell viability in a dose dependent manner and this cytotoxic effect did not change dependent to time. LD<sub>50</sub> dose of tacrolimus was found as 30 µM. In experimental animal model, tumor growths were observed after 12- 14 days. After once a week exposure to tacrolimus did not cause any side effects. In the 14th day, after sacrifice significant necrosis, necrobiosis and apoptosis were observed in histopathological evaluation of tumor tissues. At the annexin V- PI staining for flow cytometric analysis of apoptosis, early apoptotic effect of tacrolimus was found to be more than late apoptosis and necrosis.

Tacrolimus was found to be both in vitro and in vivo effective on triple negative breast cancer cells. This effect was occurred by inducing apoptosis as well as necrosis. Tacrolimus is suggested as a promising therapeutic agent for triple negative breast cancer.

#### Declarations

*The manuscript is new and is not being considered elsewhere. Authors have no any commercial association and conflict of interest. All the experiments were done following the principles of Dokuz Eylül University Animal Ethical Committee's approval (Protocol No: 25/2014).*

**Keywords:** Triple negative breast cancer, tacrolimus

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## POSTER PRESENTATION – 188

### THE PLACE OF SCANNING ANOMALIES IN ALL CHROMOSOMES WITH COMPARATIVE GENOMIC HYBRIDISATION WITH THE MICROSEQUENCING SYSTEM IN PAEDIATRIC CANCERS WITH DIFFICULTIES IN DIFFERENTIAL DIAGNOSIS

Safiye Aktas<sup>1</sup>, Gulden Diniz<sup>2</sup>, Hulya Tosun Yildirim<sup>3</sup>, Ragip Ortac<sup>4</sup>, Yesim Oymak<sup>5</sup>, Canan Vergin<sup>5</sup>, Nur Olgun<sup>1</sup>

<sup>1</sup>Basic Oncology Department, Dokuz Eylul University, Izmir ( Make presentation)

<sup>2</sup>Pathology Department, Tepecik Hospital, Izmir

<sup>3</sup>Pathology Department, Antalya Hospital, Izmir

<sup>4</sup>Pathology Department, Izmir University Medical Park Hospital, Izmir

<sup>5</sup>Hematology Department, Dr. Behçet Uz Children's Hospital, Izmir

**Introduction- Aim:** Despite conventional histopathology and immunohistochemical methods, difficulties may be experienced in the differential diagnosis of paediatric cancers, especially in small, round-cell tumour morphology and sometimes in spindle-cell tumour morphology. In these cases, determination of chromosomal abnormalities can be helpful. Examination of a single translocation or deletion with the FISH method in a sample with a single probe may not always give a definitive response as the chromosomal abnormality in question may not be a single type. Variations may be found and therefore, it may be necessary to examine more than one area for diagnosis. For example, for the Ewing sarcoma (ES) tumour family, specific chromosomal translocation is at a high rate in the t (11;22) (q24;q12) region and t (11;22) (q12;q12), t (7;22) (q22;q12), t (17;22) (q12;q12) variants may be observed. The aim of this study was to evaluate the place of the whole genome comparative genomic hybridisation method in paediatric cancers where difficulty is experienced in differential diagnosis.

**Material and Method:** In Comparative Genomic Hybridisation (CGH), 135,000 probes were scanned as 3 probes per gene in all genomes. It was possible to work from paraffin block tissues. From the archive of the Pathology Laboratory of Dr Behçet Uz Paediatric Hospital, DNA extraction was made from the paraffin blocks of 20 cases where difficulty had been experienced in the differential diagnosis and for each case, control comparisons were made of anomalies in all the chromosomes with array technology. The chromosomal anomalies determined were compared with the clinicopathological findings.

**Results:** Together with the typically observed chromosomal anomalies observed in the cases, additional impairments could be determined, the importance of which required discussion. In the whole genome CGH study from paraffin tissue, difficulties were experienced compared to fresh tissue.

**Conclusion:** The whole genome CGH method may be useful in paediatric cancers where difficulties are experienced in the differential diagnosis. \*However, there are technical difficulties in the examination of paraffin tissue. The possibility of storing fresh tissue from each tumour would be helpful for genetic and molecular examinations. \* A limitation of the method is that although chromosomal anomalies can be determined, translocation such as in situ hybridisation cannot be reported.

*Key Words: Comparative Genomic Hybridisation, Uncommon Paediatric Cancers, Differential Diagnosis*

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