Moleküler Biyoloji Derneği

İZMİR BİYOTIP VE GENOM MERKEZİ

DOKUZ EYLÜL ÜNİVERSİTESİ
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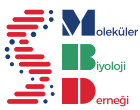
MOLBİYOKON'18

5 - 8 September 2018

6th International Congress of the Molecular Biology Association of Turkey

ABSTRACT BOOK

Izmir Biomedicine and Genome Center



The Book of Abstracts
MolBiyoKon'18
6th International Congress of the
Molecular Biology Association of Turkey
5 - 8 September 2018
Izmir Biomedicine and Genome Center

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Dear Friends and Colleagues

It is a great pleasure to welcome you in Izmir at the 6th International Congress of the Molecular Biology Association of Turkey, MolBiyoKon'18. We sincerely hope that you will enjoy four days of excellent science in the area located just few hundred meters away from Turkey's beautiful Aegean Coast. Being one of the oldest cities of the Mediterranean World, Izmir has been of continuous historical importance during the last 5,000 years. It emerged as one of the principal cities of Anatolia and was later the center of a civil diocese in the Roman province of Asia, vying with Ephesus and Pergamum for the title "first city of Asia." Roman emperors visited there, and it was celebrated for its wealth, beauty, library, school of medicine, and rhetorical tradition.

MolBiyoKon'18 is hosted by Izmir Biomedicine and Genome Center (IBG). IBG was established on 16 August 2017 within the scope of law no. 6550 as the first Thematic Research Center of Turkey in the healthcare industry. Located within the Dokuz Eylül University health campus, IBG houses 23 independent research groups working on biomedicine and genome sciences and 10 core facilities that are open for the use of all public and private sector institutions in Turkey. IBG is proud to host the 6th annual congress of Molecular Biology Association of Turkey.

Founded in 2011, the Molecular Biology Association of Turkey aims to bring together the community of molecular biologists from Turkey and abroad to support the development of molecular biology, a relatively young field of science in Turkey. The annual MolBiyoKon is one of the primary and noteworthy international conferences in the field of molecular biology in Turkey. The congress aims to bring together researchers from all around the world to exchange research results, scientific observations and ideas, as well as to motivate and inspire students to pursue their career and education in life sciences.

We would like to especially thank to all our sponsors and European Molecular Biology Organization (EMBO) for their financial support. We very much appreciate the help of our volunteer graduate students and administrative staff who took big part in the congress organization.

We wish all participants an exciting and fruitful meeting, many interesting discussions and new scientific interactions. Have a great time in Izmir!

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Nesrin Özören, Umut Şahin, Şerif Şentürk

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Şevin TURCAN, University of Heidelberg

Sezai TÜRKEL, Uludağ University

Gerhard WINGENDER, Izmir Biomedicine and Genome Center

Congress Program

DAY 1 - September 05 2018 | Wednesday

IBG Tour & Registration 13:00 -15:00

IBG Tour is Optional
Registration will be taken at “Kurucu Ögretim Üyeleri” Conference Hall

Panel 15:00 -17:00

Türkiye’de Moleküler Biyoloji ve Genetik’in Bugünü ve Geleceği; Problemler ve Çözüm Önerileri
Chair: **Yusuf BARAN**

Opening / Welcome Address 17:00 -17:15

Mehmet ÖZTÜRK *(IBG Director)*
Nesrin ÖZÖREN *(President MBD)*
Güneş ÖZHAN *(Conference Chair – MolBiyoKon 2018)*

Keynote Lecture I (Moderator Güneş ÖZHAN) 17:15 -18:00

Eithan GALUN
MicroRNAs are also hormones

Keynote Lecture II (Moderator: Nesrin ÖZÖREN) 18:00 -18:45

Jonathan M. SCHOLEY
Motor Proteins in the Assembly of Eukaryotic Cilia and Prokaryotic Flagella

Welcome Reception 19:00 - 21:30

DAY 2- September 06 2018 | Thursday

Keynote Lecture III (Moderator: Erdinç SEZGİN) 09:15 -10:00

Simon DAVIS
Signaling by Immune Receptors

Plenary Session I (Moderator: Şerif ŞENTÜRK) 10:00 -10:25

Serkan Göktuna
Identifying IKKepsilon Specific Roles in Gastrointestinal Cancers

Coffee Break 10:25 -10:55

Mazhar ADLI **10:55 -11:20**
Editing, Imaging and Screening Genome with CRISPR Technology

Elif ERSON BENSAN **11:20 -11:45**
Deciphering the Cancer Transcriptom through 3'UTRs

İlhan SATMAN **11:45-12:30**
Türkiye Sağlık Enstitüleri Başkanlığı'nın' (TÜSEB) Çalışmaları

Bilge YAYLAK **12:30-12:45**
Genomewide Analysis of Circular RNA Expression in Apoptotic HeLa Cells

Burcu AKMAN **12:45-13:00**
CD25 is a direct transcriptional target of PRDM1 in activated human natural killer cells

Lunch Break 13:00 -13:45

Poster Session I 13:45 -15:00

Award Ceremony 15:00 -15:05

Nesrin ÖZÖREN *(President of the Molecular Biology Association)*

2017 MBD PhD Award 15:05-15:30

Plenary Session II (Moderator: Esra ERDAL) 15:05-15:30

Onur BAŞAK
Reconstructing Neural Hierarchies Cell by Cell *15:30-15:55*

Ayşe KOCA ÇAYDAŞI
Centrosomes as Signaling Platforms for the Spindle Position Checkpoint *15:55-16:20*

Uygar TAZEBAY
Coiled-coil domain containing protein 124 is involved in formation of cellular phase-separated biocondensates *16:20-16:35*

Cihangir YANDIM
Expression Profiling of Repetitive DNA in Early Human Development *15:35-16:50*

Coffee Break 16:50 -17:20

Plenary Session III (Moderator: Ralph MEUWISSEN)

Erdinç SEZGİN
Biomimetics Systems to Investigate Cell Membrane Dynamics and Structure *17:20 - 17:45*

Ezgi KARACA
Integrative Modeling of Biomolecular Interactions *17:45 - 18:10*

Sofia PIEPOLI
Function from structure: PATZ1 BTB domain *18:10 - 18:25*

Ecem Kural MANGIT
THE TALE OF TWO PROTEINS: Interaction Between Desmin and Lamin B *17:45 - 18:10*

Workshop: Imaging Technologies in Life Sciences 16:50 -17:20

Erdinç SEZGİN

DAY 3 - September 07 2018 | Friday

Keynote Lecture IV (Moderator: Neşe ATABEY) 09:15 -10:00

Aslıhan TOLUN
What We Learned in Disease Gene Search

Şermin GENÇ 10:00 -10:30

Bilim ve Bilim Akademileri

Coffee Break 10:30 -11:00

Plenary Session IV (Moderator: Tolga SÜTLÜ)

Uğur SEZERMAN ***11:00-11:25***
Integration of Omics Data in a Pathway Related Context Reveals Individualized Disease Aetiology in Complex Diseases

Rengül ÇETİN ATALAY ***11:25-11:50***
Personalized Medicine in Liver Cancer Through Bioinformatics

Evren ALICI ***11:50-12:15***
Prediction of Response to NK Cell Based Adoptive Immunotherapies in Cancer: Lessons from Three Phase I/II Clinical Trials

Bilge GÜVENÇ TUNA ***12:15-12:30***
Roles of Epigenetics in the Preventive Effects of Calorie Restriction in Breast Cancer Development

Sema Elif ESKİ ***12:30-12:45***
Wnt/β-catenin signaling affects two modes of neurogenesis in the zebrafish olfactory epithelium

Tayfun Hilmi AKBABA ***12:45-13:00***
Analysis of genetic background in Turkish early onset Parkinson's disease patients

Lunch Break 13:00 - 13:45

Poster Session II 13:45 - 15:00

Plenary Session V (Moderator: Yavuz OKTAY)

Damla OR CEYHAN
TÜBİTAK Horizon 2020 Supports and Awards - TÜBİTAK Directorate for International Cooperation **15:00-15:30**

Jale ŞAHİN
International Cooperation Opportunities and Mobility Programmes in Life Sciences **15:30-16:00**

Şevin TURCAN **16:00-16:25**
Deciphering the Role of IDH Mutations in Gliomas

Serap ERKEK **16:25-16:50**
Interplay between SWI/SNF and Polycomb in Atypical Teratoid Rhabdoid Tumors

Coffee Break 16:50 - 17:20

Plenary Session VI (Moderator: Umut ŞAHİN)

Sibel KALYONCU **17:20-17:45**
Antibody Fragments for Therapeutic Applications

Nurhan ÖZLÜ **17:45-18:10**
Proteomics in Cell Division

Said TİRYAKİ **18:10-18:25**
Expression profiling and co-culture studies of miR-376a-3p and cholinergic receptor subunit CHRNA5

Gözde ÖZÇELİK **18:25-18:40**
BioID as proximity labeling for studying of protein-protein interactions in Drosophila Cells

Poster Award Ceremony 18:40 - 18:50

Gala Dinner 19:30 - 22:00

DAY 4 - September 08 2018 | Saturday

Plenary Session VII (Moderator: Zeynep A. KOÇER)

Nuri ÖZTÜRK
Early Events in Photic Resetting of the Circadian Clock ***09:15-09:40***

Halil KAVAKLI ***09:40-10:05***
Discovery of Small Molecules that Regulate Cryptchrome Half-life and Circadian Rhythm

Elmasnur YILMAZ ***10:05-10:20***
Better Call RoH: What a 11Mb homozygous haplotype block can tell us about a possible founder mutation in the Turkish population

Nebibe MUTLU ***10:20-10:35***
The yeast kinase Ksp1 regulates cellular stress response

Yakup Berkay YILMAZ ***10:35-10:50***
Nitrobenzamide derivatives as iNOS inhibitors also promotes Nrf2 mediated cytoprotective response: in vitro and in silico approaches

Müge Anıl INEVI ***10:50-11:05***
Biphasic assembly of bone marrow stem cells in distinct lineages by magnetic levitation

Coffee Break 11:05 - 11:30

Career Opportunities for Young Scientists

Chair: ***Yavuz OKTAY***
Panelists: Simon Davis, Uğur Sezerman, Saliha Durmuş ***11:30 - 13:15***

Closing Ceremony 13:15 - 13:30

KEYNOTE LECTURES

Keynote Lecture I

Eithan GALUN

Goldyne Savad Institute of Gene Therapy
Hadassah Hebrew University Hospital

MicroRNAs are also hormones

Eithan Galun

Goldyne Savad Institute of Gene Therapy; Hadassah Hebrew University Hospital; Jerusalem; Israel

In single cell organisms gene regulation although complex is defined within the cell walls. However, in multicellular and multi-organ organisms gene regulation is also tightly controlled by neighboring or distant cells or neighboring or distant organs. Cell-to-cell and organ-to-organ communication is crucial in development, homeostatic physiological and under stress conditions. Evolution has enabled the generation of “kingdoms” of gene regulators which are cross-talking also among themselves and each other. Most gene expression regulators are by themselves regulated and are under either a positive or a negative feedback regulatory system. MicroRNAs are becoming apparent as major players in the field of gene expression. However, is there enough evidence also to think of microRNAs as hormones? Hormone come from the Greek word of “activation”. Hormones are chemical compositions produced by cells of one organ that affects distant cells and tissues. Hormones usually are transported by blood, and there they usually are in low concentration. Negative and positive feedback loops sometimes control their own levels and effects. These could be either small molecules like amines, steroids, peptides and proteins. Hormones are produced and secreted from glands, but also from “non-professional” glands as the gastrointestinal track or adipose tissues. From the data reported during the last twenty years and more, I wish to present information which could suggest that microRNAs meet the criteria of hormones. Intense investigation was devoted to microRNA biogenesis, and this aspect in microRNA physiology is reviewed by others. But an interesting question which was less investigated is what regulates the regulator - microRNA expression. Interestingly we find that a number of microRNAs are tissue specific. One of the most investigated in this regard is microRNA 122 (miR-122). It is specifically expressed in the liver, in hepatocytes. This teaches that tissue/cell specific regulators as tissue specific transcription factors are potentially involved in tissue specific expression of microRNA. Tissue specificity is a hallmark of hormonal production and secretion. I’ll show evidence that microRNAs are produced in one cell type and affect a remote cell in other organs in the same organism. Furthermore, the effect of the microRNA also induces a feedback effect on the production of the same microRNA. I’ll show evidence that microRNA 122 regulates, in a hormonal manner hemoglobin production and triglyceride – free fatty acids metabolism.

Keynote Lecture II

Jonathan M. SCHOLEY

University of California

Motor Proteins in the Assembly of Eukaryotic Cilia and Prokaryotic Flagella.

Jonathan M Scholey
Department of Molecular and Cell Biology, University of California, Davis

Eukaryotic cilia function in motility and sensory reception and their assembly requires kinesin-2-driven intraflagellar transport (IFT) of ciliary building blocks along microtubule tracks to their site of incorporation. Heterotrimeric kinesin-2 is generally the core ciliogenesis motor e.g in motile cilia of sea urchin embryos. In many cases e.g. sensory cilia in Caenorhabditis elegans, ciliogenesis requires functional cooperation between two forms of kinesin-2, heterotrimeric kinesin-II and homodimeric OSM-3. Using time-lapse fluorescence microscopy to visualize IFT in living wild-type and motor-mutant C.elegans, we found that kinesin-II serves to import the IFT-machinery into the cilium and OSM-3 drives its transport to the distal tip, thereby enhancing cargo transport for ciliogenesis. Bacteria and archaea use protruding flagella and archaella, respectively, to drive cell motility. These organelles differ from each other and from cilia with respect to their motor machinery and assembly mechanisms, revealing a striking example of convergent evolution among life's three domains.

Keynote Lecture III

Simon DAVIS

University of Oxford
Weatherall Institute of Molecular Medicine

The T-cell receptor (TCR) has no intrinsic enzymatic activity and is instead phosphorylated by the Src tyrosine kinase, Lck. There are three main explanations for how this occurs, including the kinetic-segregation (KS) model. The KS model postulates that the state of TCR phosphorylation is maintained by an equilibrium between kinases and phosphatases. This equilibrium is disturbed locally in favour of kinases when TCRs engage their ligands, owing to the exclusion of large receptor-type tyrosine phosphatases such as CD45 from the regions of contact. Importantly, the KS model predicts that TCR signaling is not strictly ligand dependent. I will discuss evidence offering strong support for the KS model, based on the crystal structure of the extracellular region of CD45, and the behaviour of the phosphatase at new structures we call “close-contacts”. We also propose that signaling by the TCR co-stimulatory receptor CD28 induced by superagonistic antibodies is also explained, at least in part, by the physical segregation of the receptor from large phosphatases. Antibody superagonism could, in principle, be harnessed clinically to dampen immune responses by activating inhibitory receptors.

Keynote Lecture IV

Aslıhan TOLUN

Boğaziçi University

What We Learned while Hunting for Disease Genes

Disease gene discovery is an important area in research in genetics, as identification of a novel disease gene can uncover the function of the gene and even a new cellular mechanism. Functions of most of our genes are still not known. In disease gene hunt, it is best that first the disease locus is mapped, because all genomes carry numerous deleterious mutations even in homozygous state, and determining which of them underlies the disease is a challenge. Even when there is only one candidate gene variant at a locus identified for a disease, it is essential that the variant is related to the pathology in patients. Although the strategy of disease gene hunt seems straightforward, locus identification, mutation detection and mutation evaluation can be all very tricky and/or difficult. Surprises and pitfalls encountered during the experience of almost two decades will be shared together with some of the interesting findings.

INVITED SPEAKERS

Ayşe KOCA ÇAYDAŞI
Koç University

Centrosomes as Signaling Platforms for the Spindle Position Checkpoint

In addition to their fundamental role in microtubule nucleation and organization, centrosomes play key roles as signaling centers in modulating eukaryotic cell division. Budding yeast Spindle Pole Body (SPB; functional equivalent of the centrosome in yeast) is associated with components of two mitotic signaling pathways: the mitotic exit network (MEN) and the spindle position checkpoint (SPOC). The MEN drives M-G1 transition whereas the SPOC halts this transition in response to spindle positioning errors. Thus, mitotic exit in budding yeast is under the control of spindle orientation. SPOC and MEN proteins associate with the cytoplasmic side (outer plaque) of the SPBs, where astral microtubules that position the spindle are nucleated. Here, I present the molecular mechanisms of how checkpoint protein-SPB interactions are regulated by the spindle orientation.

Elif ERSON BENSAN
Middle East Technical University

Deciphering the cancer transcriptome through 3'UTRs

Despite the flow of new information provided by genome and transcriptome sequencing studies, certain aspects of diagnosis, prognosis, and treatment of cancer patients are still important challenges to be addressed. Therefore, a better understanding of the complexity of cancer necessitates characterization of "less obvious but potentially important" changes that we generally fail to detect or consider to be noise in conventional experimental setups. From this perspective, gene expression studies face a key bottleneck; conventional methods are generally not tailored to detect nor quantify 3′ isoforms generated by alternative polyadenylation (APA). This may negatively impact our ability to discover cancer-related genes and comprehensively understand critical molecular mechanisms underlying disease progression. Our laboratory is focused on identifying alternatively polyadenylated mRNA isoforms that generally have different length 3'UTRs. This talk will summarize our work on the discovery and characterization of such isoforms with potential implications in better understanding cancer mechanisms.

Erdinç SEZGİN
University of Oxford

In Vitro Reconstitution of Immune Signalling

The spatiotemporal regulation of signalling proteins at the immune cell-cell contacts determines how and when immune responses begin and end. Therapeutic control of immune responses will therefore rely on thorough elucidation of the molecular processes occurring at these interfaces. However, the detailed investigation of each component's contribution to the formation and regulation of the contact is hampered by the complexities of cell composition and architecture. Moreover, the transient nature of these interactions creates additional challenges. One approach to circumventing these problems is to establish in vitro systems that faithfully mimic immune cell interactions, but allow complexity to be 'dialled-in' as needed. Here, I present in vitro systems making use of synthetic vesicles that mimic important aspects of immune cell surfaces. Using this system we explore the spatial distribution of signalling molecules and how this changes during the initiation of signalling.

Evren ALICI

Karolinska Institutet

Despite substantial progress in the last decades, mortality in most malignant diseases remains high representing a major threat to the European population and health care system. Many efforts are undertaken to develop innovative therapies especially in the field of immunotherapy. Approaches based on boosting CAR T lymphocytes have recently yielded promising clinical results.However, supplementary therapeutic strategies are urgently needed since tumors often escape from T cell-based therapies. Autologous CAR T cells are partly limited in both, viability and cell numbers, which led to failure in several patients. In addition, the application of allogeneic CAR T cell therapies with downregulation of MHC still has been associated with off-target toxicities and severe side effects including graft-versus-host-disease. Thus, there are now great hopes on the application of donor NK cells, because of their efficient direct cytotoxic anti-tumour activity and their potential to bridge the innate to the adaptive immune response. According to our experience, haploidentical and even allogeneic NK cell-based therapy is generally well tolerated at high doses and no severe adverse effects have been observed to date. Ljunggren & Alici labs at Karolinska Institutet and Karolinska University Hospital in Sweden have been working on NK cell based immunotherapies during the last 2 decades. Our groups have completed two clinical trials which utilized ex vivo expanded natural killer cells for both allogeneic and autologous uses. The most recent clinical trial on the use of autologous ex vivo expanded NK cells in patients with Multiple Myeloma lead to an approval for orphan drug designation by European medicines agency during 2017. This expansion protocol and autologous NK product is now being developed by CellProtect Nordic pharmaceuticals, a Swedish small enterprise. The rapidly developing knowledge on molecular regulation of the innate immune system and its complex interplay with adaptive immunity has spurred interest in exploring its potential in cancer therapy. NK cells have been first described 40 years ago as a separate, heterogeneous group of innate lymphocytes capable to kill transformed and infected cells without prior sensitization. Small- scale clinical trials using polyclonal allogeneic or autologous NK cells for infusion have demonstrated promising results in leukaemia, significantly increasing 5-year survival rates of Acute Myeloid Leukaemia (AML) patients. However, only a fraction of AML patients responded and moderate response rates were observed with other malignancies. Thus, the anti-tumor efficacy of NK cells needs to be enhanced. Furthermore, the cost-/labour-intensive semi-automated Good Manufacturing Practice (GMP)-compatible manufacturing process limits the number of patients that can benefit from NK cell therapies. There is an urgent need to develop GMP-compliant expansion strategies for manufacturing optimized NK cell products and an automated pipeline for advanced cell manipulation. This is essential to improve treatment success and decrease production costs to make therapies available to higher numbers of patients, thereby overcoming a key bottleneck in clinical NK cell therapy. In this talk, I will discuss the bottleneck and our strategies to overcome them with reference to 2 completed and one ongoing NK cell based adoptive immunotherapy clinical trials.

Ezgi KARACA

Izmir Biomedicine and Genome Center

Towards Characterizing the Factors Tuning the Specificity of Biomolecular Complexes

The interplay between specificity and affinity is a significant drive in biomolecular recognition. Since the experimental determination of both has been a challenge for many systems, there is a growing interest in their computational prediction. There are numerous algorithms present, which are poised to determine the binding affinity of biomolecular complexes. On the other hand, we have only a handful of tools tuned to predict the specificity of binding. To that end, we have developed novel and simple specificity-related metrics through structural and dynamical analysis of two model systems. The complementarity metric used in our first model system has delivered the factors guiding the selective binding of transmembrane receptor tyrosine kinase TAM (Tyro3, Axl, Mer) proteins to different ligands. Structural investigation of our second system has pinpointed the distance-based measures explaining the specificity of de novo DNA methyltransferase 3 towards its non-CpG DNA binding site(s). Expanding on these findings, our short-term goal is to probe the generic applicability of our metrics in dissecting the specificity of different types of biomolecular systems.

İ. Halil KAVAKLI

Koç University

Identification of Small Molecules Regulate CLOCK Activity

Several physiological variables require a robust clock for their proper functions. Therefore, any disturbances of clock result in different types diseases and accelerated aging as well. It is, therefore, essential to small molecules modulates the activity of the core clock proteins and, in turn, alleviate disease related with disturbed clock. In this study, we applied a structure-based design to find small molecules that regulate the activity of CLOCK. After the identifications of the molecules by virtual screening, experimental studies enable us to discover a compound (CLK8) that specifically binds to CLOCK and regulates CLOCK and BMAL1 Interaction and its stability. Further studies indicated CLK8 enhances the amplitude of circadian rhythm in at cellular level. Studies in this work suggested that CLK8 can be used as tool to understand the role CLOCK in amplitude and has potential to be used a therapeutic agent in health problems associated with dampened rhythms that is observed in aging.

Mazhar ADLI

University of Virginia

Manipulating, Imaging and Screening Genome with CRISPR

While endonuclease activities of WT CRISPR/ Cas9 system has been repurposed as efficient and robust genetic tool, the catalytically dead Cas9 has it own unique application areas. In this talk, I will discuss major CRISPR/Cas9 tools focusing on applications areas beyond gene editing. I will present some published and unpublished results from our recent efforts using CRISPR technology for locus specific epigenetic editing, live cell chromatin imaging and whole genome gene KO screenings.

Nurhan ÖZLÜ

Koç University

Proteomics Analysis of Cell Division in Mammalian Cells

Cell division is a fundamental process by which all living things propagate. Mistakes during the cell division can decrease the viability and cause complex diseases such as cancer. Throughout the cell division different cellular complexes undergo dramatic re-organization in a coordinated manner. The major questions that we aim to understand are how cell cycle dependent changes are regulated and how the changes on the cell membrane are coordinated with cell's interior to drive cell division. Towards this goal, we apply quantitative proteomic and phosphoproteomic techniques to examine the biochemical profile of different cellular compartments as mammalian cells progress at different cell cycle stages. Our proteomic analysis provides basic information on cell cycle progression mechanisms as well as potential pharmacodynamic biomarkers for anti-mitotic cancer chemotherapy.

Nuri ÖZTÜRK

Gebze Technical University

Early Events in Photic Resetting of the Circadian Clock

In the early morning, circadian clock is reset by sunlight. During photoreception in fruit fly, light causes a conformational change in the cofactor of Cryptochrome (CRY), which triggers CRY to open its C-terminal tail. This conformational change provides docking sites for Timeless (TIM) and E3 ligases (JET and BRWD3). Binding of CRY to JET and TIM leads to the degradation of TIM, which resets the molecular clock. Additionally, the binding of CRY to BWRD3 leads to the degradation of CRY, which ensures that the clock is reset only once a day. I will discuss how light signal is transformed into the clock resetting and about the flexibility of this mechanism. I will also talk about the identification of new light-dependent protein interactions in the photoreceptor complex. Finally, I will explain how our findings can be harnessed to develop novel optogenetic tools.

This study was supported by TUBITAK 215Z278.

Onur BAŞAK

University of Medical Center Utrecht

Reconstructing Neural Hierarchies Cell by Cell

The adult mouse subependymal zone (SEZ) provides a niche for mammalian neural stem cells (NSCs). However, the molecular signature, self-renewal potential and fate behavior of NSCs remain poorly defined. Here we propose a model in which the fate of active NSCs is coupled to the total number of neighboring NSCs in a shared niche. Using knock-in reporter alleles and single-cell RNA sequencing, we show that the Wnt target Tnfrsf19/Troy identifies both active and quiescent NSCs. Quantitative analysis of genetic lineage tracing of individual NSCs under homeostasis or in response to injury reveals rapid expansion of stem cell number before some return to quiescence. Fate-mapping proliferating cells using a novel Ki67 iresCreER allele confirms that active NSCs reversibly return to quiescence, achieving long-term self-renewal. Our findings suggest a novel niche-based mechanism for the regulation of NSC fate and number.

Rengül Çetin ATALAY
Middle East Technical University

Cancer is a complex disease which is defined by uncontrolled proliferation and spreading of abnormal cells. Cancer tissue includes cell groups that have different characteristics – so-called side population which includes cancer stem cells. In current cancer treatment, "personalized therapies" present improved prognosis and survival rates. Our group has been working on the discovery of novel anticancer candidate molecules for epithelial cancers focusing on liver cancer. This talk will focus on the importance of PI3K/AKT/mTOR network for targeted cancer drug discovery, particularly for liver cancer stem cells. I will present molecules inducing oxidative stress and alter PI3K/AKT/mTOR network as well as other kinase inhibitors for synergistic therapeutic strategies. Finally, a novel method in the field of computational drug discovery and its experimental validation on the PI3K/AKT signalling pathway in liver cancer cells will be presented.

Serap ERKEK

Izmir Biomedicine and Genome Center

Interplay Between SWI/SNF and Polycomb in Atypical Teratoid Rhabdoid Tumors

Biallelic inactivation of SMARCB1, a member of the SWI/SNF chromatin remodeling complex, is the hallmark of atypical teratoid rhabdoid tumor (ATRT). We describe how loss of SMARCB1 affects the epigenome in these tumors. Using ChIP-sequencing on primary tumors for selected histone marks, we determined the chromatin states differentially represented in ATRTs compared to other brain tumors and non-neoplastic brain. We identified repressive H3K27me3, strongly correlated with binding of EZH2 and REST, to localize to SMARCB1 binding sites, resulting in repression of neuronal differentiation genes. A substantial fraction of SMARCB1 binding sites in ATRTs is bound by EZH2 but lacks H3K27me3. Residual SWI/SNF complex binding, measured by SMARCA4 ChIP-seq, maintains these genes in an active state, even in the presence of Polycomb and REST. This divergent interplay between SWI/SNF and Polycomb hints at potential vulnerabilities in this disease, but also provides new insights into fine-tuned regulatory networks relevant beyond ATRT biology.

Serkan GÖKTUNA

Bilkent University

Identifying "IKKepsilon Specific Roles in Gastrointestinal Cancers"

Previously, we showed that genetic ablation of IKKε reduced tumor incidence and extended survival in mice with Wnt-driven intestinal tumor models. Mechanistically, tumor-promoting effects of IKKε was attributed to limited TNF-dependent apoptosis in transformed intestinal epithelial cells. Further studies to identify upstream factors revealed that inflammatory IL17A, synergized with commensal bacteria-derived LPS to trigger IKKε phospho-activation intransformed intestinal epithelia establish a positive feedback loop to sustain an inflammatory microenvironment support tumor development. Currently, we want to extend these observations to other potential tumor models in colorectal or hepatocellular carcinogenesis. For this purpose, we have developed cellular and animal models of tumorigenesis Surprisingly, we observed that not all of our previous assumptions on IKKe involvement in tumorigenesis can be extended to later stages of cancer. Hence, we reason that IKKε may have diverse roles during the course of tumorigenesis and these roles may differ depending on the stage of the cancer.

Şevin TURCAN

University of Heidelberg

"Majority of lower grade gliomas harbor mutations in the isocitrate dehydrogenase gene 1 (IDH1). Mutated IDH1 produces the oncometabolite, 2-hydroxyglutarate (2-HG), which inhibits histone demethylation and leads to global DNA hypermethylation. Yet, small molecule inhibition of 2-HG is not uniformly effective in controlling tumor growth in preclinical models. While the mutation leads to an aberrant epigenome, its exact contribution to glioma pathogenesis is incompletely defined. We recently generated a large-scale atlas of mutant IDH1 induced epigenetic changes and demonstrated that a subset of these alterations are not completely reversible. This talk will highlight our efforts in characterizing the mutant IDH induced epigenetic and transcriptional changes and provide insights into mechanisms that can be targeted to provide therapeutic benefit for glioma patients"

Sibel KALYONCU

Izmir Biomedicine and Genome Center

Antibody fragments for therapeutic applications

Antibodies currently represent more than half of the total sales of allbiopharmaceutical products and their market size has been growing steadily. There are many advantages of antibodies for use as biopharmaceuticals: (i) high specificity and affinity for its target (ii) low immunogenicity (iii) longer half-life (days to weeks) (iv) higher approval rate than other biopharmaceutical products. Currently, there are more than 50 antibodies approved on the market to treat a variety of diseases and there are even more on phase II and III clinical trials.

Most of therapeutic antibodies are discovered with in vivo techniques but antibodies produced with in vitro techniques such as phage display and yeast surface display becomes more common than before. The most important advantage of in vitro technologies is having full control of antibody library, sequence and screening. Even though most antibodies are discovered in vivo, their properties are usually further optimized with in vitro screening techniques. It is challenging to screen full-length (IgG) antibodies because of their large size (~150 kDa) and glycosylation sites on constant regions. Antibody fragments where all or some parts of constant regions are eliminated are commonly used in many biotechnological applications. It is very well-known that antibody fragments usually show similar binding properties as their full-length versions with even better biophysical properties. The most commonly used antibody fragments are Fab, single chain antibody fragment (scFv) and V H. In this talk, I will discuss antibody fragments as next-generation biopharmaceuticals.

Uğur SEZERMAN
Acibadem University

Integration of Omics Data in a Pathway Related Context Reveals Individualized Disease Aetiology in Complex Diseases

Advancements in omics technologies facilitated a deeper look into cellular mechanisms involved in complex disease aetiology. They all reveal different aspects of the aetiology. The main challenge is the integration of these data to understand the whole picture and reveal individualized disease mechanisms involved. The data has to be integrated in a pathway related context to understand set of interactions targeted by the changes in the diseased individuals.We have developed a new methodology for identification and ranking of disease related sub paths.

In this talk I will go over system biology approaches used in identification of disease relatedpathways and focus on how these methods can be exploited to determine individualized disease aetiology and therapy targets.

SELECTED ABSTRACTS FOR ORAL PRESENTATION

Genomewide Analysis of Circular RNA Expression in Apoptotic HeLa Cells

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Apoptosis is a major type of regulated cell death in human body. Numerous non-coding transcripts, such as miRNAs and lncRNAs, have been reported to regulate apoptosis. However, circular RNA involvement in regulation of apoptosis remains unknown. In this research, we performed a genomewide transcriptomics study to identify differentially expressed circular RNAs in apoptotic HeLa cells. Apoptosis was triggered in HeLa cells in three biological replicates through two different drugs (cisplatin and doxorubicin) and two ligands (TNF-alpha and FAS). circular RNAs were enriched by eliminating linear RNAs through RNAse R treatment and subjected to deep RNA-sequencing to identify dys-regulated circular RNAs. Interestingly, some circRNAs were originated from well-known protein coding genes involved in apoptosis. Then, a number of candidate circRNAs were validated with qPCR. Bioinformatical analyses revealed that our candidates harbor putative miRNA response elements. These results suggest that circRNAs potentially regulate apoptosis by sponging pro-/anti-apoptotic regulatory miRNAs.

Keywords: Circular RNA, Apoptosis

CD25 is a Direct Transcriptional Target of PRDM1 in Activated Human Natural Killer cells

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PRDM1 is a transcription factor that is involved in regulating differentiation or homeostasis of lymphocytes. There is little insight into genes directly targeted by PRDM1 in natural killer (NK) cells. IL2 receptor signaling is crucial for many features of NK cell activation. Here we evaluated whether CD25 (IL2Rα) is regulated by PRDM1 in normal NK cells. We observed that CD25 was progressively upregulated in response to IL2 in normal NK cells. ChIP-Seq revealed PRDM1 occupancy on an intronic site of CD25 in activated NK cells. Two PRDM1α-transduced PRDM1-nonexpressing NK cell lines showed significant transcriptional repression of CD25 by DNA microarray and RNA-Seq. Knock-down of CD25 inhibited growth of two NK cell lines. By contrast, ectopic expression of CD25 resulted in positive selection of primary NK cells. Altogether these results establish CD25 as a direct transcriptional target of PRDM1 in human NK cells. These observations show that PRDM1 may play a role in termination of NK-cell activation and growth, with implications on neoplastic transformation or autoimmunity

Keywords: CD25 (IL2Rα), NK cell growth, Termination of NK-cell activation Neoplastic transformation

Coiled-coil Domain Containing Protein 124 is Involved in Formation of Cellular Phase-Separated Biocondensates

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Membraneless organelle formation by phase-separated liquid/gel droplets is a new concept in cytoplasmic and nuclear organization. Coiled-coil domain-containing protein 124 (Ccdc124) is an intrinsically disordered conserved eukaryote protein. It contains a putative RNA binding domain, and several possible RNA interactors of Ccdc124 were identified in silico. Bio-ID based LC-MS/MS analysis were performed in order to find proteins interacting with Ccdc124, and lists of Co-IP validated interactors were mainly composed of proteins previously identified either in nuclear or cytoplasmic phase separated complexes. By using immunofluorescence confocal microscopy analysis, we characterized Ccdc124 protein mainly in centrosome, but also in multiple phase separated complexes such as p-bodies, stress-granules, nuclear speckles, as well as in midbody during cytokinetic abscission. Furthermore, we have generated putative phosphosite mutants that lead to aberrant cytoplasmic droplet-like particles. We propose Ccdc124 as a novel component of cellular phase-separated droplet organelles.

Keywords: membraneless organelles, Coiled-coil domain-containing protein 124, Cellular organization, Cellular phase-separation

Expression Profiling of Repetitive DNA in Early Human Development

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Human pre-implantation development provides a key window to study the regulation of our genome. Indeed, this is the period during which a de novo chromatin architecture is built. In mouse, it was shown that a key regulatory player within this context is the expression of repeat elements nearby centromeric regions. However, such elements were not identified yet in human development. In our study, we analysed the expression of all repetitive DNA elements in human pre-implantation embryos. Our holistic analysis included all tandem repeats (e.g. centromeric and pericentromeric satellites) as well as interspersed repeats (LINEs, SINEs and LTRs etc.). We revealed that human repeatome exhibits distinct expression patterns across stages of development with stage specific expressions for subsets out of more than a thousand repeat elements. In addition, we identified stage-specific genes whose promoters are enriched by certain interspersed repeats and whose expressions showed correlation with the expression of these elements; highlighting the significance of repetitive DNA.

Keywords: Repetitive DNA, Human Development, Bioinformatics, Epigenetics

Roles of Epigenetics in the Preventive Effects of Calorie Restriction in Breast Cancer Development

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Beneficial effects of calorie restriction (CR) has been shown in many pathophysiological conditions such as ageing, cancer and cardiovascular diseases. However, molecular mechanisms of the protective effect of CR remains to be unanswered. We aimed to understand the roles of epigenetic mechanisms specifically miRNA and DNA methylation in this process in MMTV-TGF-α mice. Mice were enrolled to ad libitum (AL), chronic CR (CCR) or intermittent CR (ICR) groups. Animals were sacrificed at weeks 10, 49/50 and 81/82 to collect tissue samples. Using Affymetrix GeneChipTM Array Strip, changes in 3195 miRNAs was analyzed. DNA methylation levels of adipokine related genes was measured by using Pyrosquencing. Mammary Tumor (MT) incidence rate was higher in AL and ICR group compared to CCR. Total of 81 miRNAs were differentially expressed in mice developed MT compared to MT free mice. DNA methylation results and changes in miRNA levels due to ageing will also be presented.

Keywords: Breast Cancer, Calorie Restriction, Epigenetics, DNA methylation

Wnt/β-catenin Signaling Affects Two Modes of Neurogenesis in The Zebrafish Olfactory Epithelium

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Olfactory sensory neurons undergo continuous turnover and the olfactory epithelium (OE) is capable of efficient regeneration following traumatic injury. We have identified distinct progenitor cell populations in the zebrafish OE that selectively contribute to maintenance and repair neurogenesis. Gene expression analysis during OE regeneration suggests that canonical Wnt/β-catenin signaling contributes to the regulation of OE neurogenesis. To test the contribution of Wnt signaling functionally, we pharmacologically manipulated the pathway in the intact OE and an experimental model of OE regeneration. Stimulation of the pathway resulted in an enhanced cell proliferation response that shares similarity with the pattern of neurogenesis that can be observed in the damaged OE. Inhibitors of Wnt signaling suppressed both, the base rate of maintenance neurogenesis and damage-induced proliferation. Our results suggest that Wnt/β-catenin signaling is both necessary and sufficient to induce repair and maintenance neurogenesis. Supported by Bogazici University BAP 17B01P8.

Keywords: Neurogenesis, Regeneration, Wnt, olfactory epithelium,

Biphasic Assembly of Bone Marrow Stem Cells in Distinct Lineages by Magnetic Levitation

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Gravity acts as a biomechanical factor with various implications on structure, function and relationship of cells. Removal of gravitational loads lead to novel cellular manipulation methods for scaffold free tissue engineering strategies. In this study, we performed label free magnetic levitation of cells in a microfluidic channel / neodymium magnet assembly platform that guide cells in suspension based on their densities. This is achieved via magnetic levitation, where diamagnetic objects (i.e. cells) move towards low magnetic field in a magnetic gradient. Using this method, we established a co-culture assembly model for bone marrow cells that are quiescent and lineage committed to adipogenesis. Establishing scaffold free assembly of biphasic structures may lead to novel tissue engineering applications for mechanobiology and drug testing studies.

Keywords: Bone marrow stem cells, Magnetic levitation

Function from Structure: PATZ1 BTB Domain

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PATZ1 transcription factor regulates gene expression during T-cell differentiation and is implicated in various cancer types. The protein belongs to the ZBTB structural family consisting of an N-terminal BTB domain and C-terminal DNA binding Zinc Finger motifs. The BTB domain can recruit co-repressors (NCOR/SMRT/BCOR) that are involved in chromatin remodelling. The PATZ1 protein (ZBTB19) shares the common predicted structures with the other 48 ZBTBs in the human genome but it contains a 30aa-long fragment (central loop) in the BTB domain that is absent in all other. The central loop is conserved in all vertebrates that express PATZ1 but is absent in fish. We solved the crystal structures of the PATZ1-BTB domain from mouse and zebrafish and show the two proteins can form homodimers and they only differ in the region of the central loop. Functional assays aim to compare the two proteins to understand the role of this unique feature. Furthermore, MD simulations have further characterized the protein dynamics of the available ZBTB structures.

Keywords: Transcription factors, Crystallography, Protein-protein interactions, MD simulations

BioID as Proximity Labeling for Studying of Protein-Protein Interactions in Drosophila Cells

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Proximity-dependent biotinylation (BioID) is a method to label proteins in close vicinity by a biotin ligase fused to interested protein, and capture labeled proteins by streptavidin-beads to identify by mass-spectrometry. We applied BioID technique to identify light-dependent and independent interactions in Drosophila circadian clock system. We want to detect weak and transient interactions by labeling proteins in proximity of photoreceptor complex by using BioID2 enzyme fused to CRY and its light-dependent interacting partner TIM which will be followed by identification of molecules in photoreceptor under dark and light conditions in comparison. We expressed CRY-BioID2 alone or photoreceptor complex containing TIM-BioID2, PER, CRY,JET to detect interactions in vivo in S2 cells. Light-dependent CRY/TIM and light-independent TIM/PER interactions were shown in pulldown assay as positive controls of this system. We also showed that more active mutant biotin ligase, miniTurbo, enabling labeling in much shorter time windows can be used in Drosophila cells

Keywords: BioID, Circadian clock, Drosophila, Protein-protein interactions

Expression Profiling and Co-Culture Studies of miR-376a 3p and Cholinergic Receptor Subunit CHRNA5

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Cholinergic receptor nicotinic alpha 5 (CHRNA5) is a ligand-gated ion channel and one of the subunits of nicotinic acetylcholine receptors. We have shown in our previous studies that CHRNA5 depletion in breast cancer cell line MCF7 is antiproliferative (TUBITAK 111T316). In present study, we investigated the effects of CHRNA5 depletion on miRNA expression profile and identified a significant three-fold decrease in the expression of hsa-miR-376a-3p. To test the synergism and/or antagonism of hsa-miR-376a-3p mimic with CHRNA5 siRNA treatment we performed a microarray study and identified the signaling pathways involved. Target genes were selected using miRNet tool and tested with RT-qPCR. We then employed a co-culture-based competition assay using MCF7 cell lines expressing different fluorescent molecules and assessed competition by both flow cytometer and fluorescent imaging. Our findings revealed decreased competitive potential of cells treated with the siRNA+mimic combination in comparison to controls. This study has been funded by TUBITAK (114S367).

Keywords: CHRNA5, co-culture, whole transcriptome analysis, miRNA

Analysis of Genetic Background in Turkish Early Onset Parkinson's Disease Patients

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About 10% of all Parkinson's disease(PD) cases consist of early onset Parkinson's Disease(EOPD), usually related to mutations of PRKN, PINK1 and DJ-1 genes.In EOPD cases, frequency of genomic rearrangements changes upon the ethnicity of the population.In this study, we aimed to investigate the frequency and phenotypical features in Turkish EOPD patients. 52 unrelated Turkish EOPD patients were screened for genomic rearrangements by using the multiplex ligation-dependent probe amplification (MLPA)method and sequencing. We identified exonic rearrangements in 22 patients(42%). PRKN gene of 39 patients with one mutated allele or none were sequenced and homozygous or heterozygous exonic variation are determined in 14 patients(35%). And then, DJ-1 and PINK-1 gene of 5 patients were sequenced and heterozygous exonic variation are determined in PINK-1 gene of one patient. To sum up, PRKN gene might be the most common reason for EOPD. Also, genomic rearrangements and point mutations in DJ-1 and PINK-1 are identified in Turkish EOPD cases.

Keywords: Parkinson's disease, PRKN, PINK-1, DJ-1

Better Call RoH: What a 11Mb Homozygous Haplotype Block can Tell us About a Possible Founder Mutation in the Turkish Population

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Introduction:The high prevalence of rare genetic disorders is usually a consequence of a high carrier frequency due to founder effect in specific populations. Runs of homozygosity (ROH) are contiguous regions of the genome that show identical alleles on both chromosomes. Here we present a possible founder mutation detected in exon 4 of SAMHD1 in two patients. Methods:In the scope of CONSEQUITUR study consisting of undiagnosed neuropediatric patients from consanguineous marriages in Turkey, WES was performed by Broad Institute. By using RD-Connect Platform and PLINK, the mutation and runs of homozygosity were detected. Results:We identified a 11Mb homozygous region harboring the SAMHD1 stop-gain (c.490C>T,p.Arg164Ter) mutation associated with Aicardi-Goutieres syndrome 5 (OMIM# 612952). Conclusion:Homozygosity mapping and the identification of the mutation using WES as a single source of data made possible to identify exactly the same rare (gnomAD AF=0.000004) mutation in two seemingly unrelated cases indicating possibly founder mutation for this region.

Keywords: Whole exome sequencing (WES), Runs of homozygosity (ROH) Consanguineous marriages, Founder mutation

The Yeast Kinase Ksp1 Regulates Cellular Stress Response

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Pseudoyphal growth is a cellular stress response where yeast cells form elongated multicellular filaments, similar to filamentous development required for virulence in pathogenic yeast. We have identified KSP1 as a gene required for yeast pseudohyphal growth, likely through its association with the Target of Rapamycin Complex (TORC1). We undertook an analysis of Ksp1 signaling through quantitative phosphoproteomics, identifying proteins differentially phosphorylated in a catalytically inactive kinase-defective Ksp1 mutant under conditions of nitrogen and glucose stress. Analysis of the proteins differentially phosphorylated upon loss of Ksp1 kinase activity identifies a statistically significant set of proteins associated with mRNA-protein (mRNP) granules. We further find that Ksp1 kinase activity regulates the localization of TORC1. We identified a putative interaction between Ksp1 and the cap binding translation initiation factor eIF4E. Collectively, these results suggest a function for Ksp1 in coordinating TORC1-signaling, translation and the regulation of mRNP dynamics.

Keywords: Yeast, Kinase signaling, mRNP granules, Stress response,

Nitrobenzamide Derivatives as iNOS Inhibitors Also Promotes Nrf2 Mediated Cytoprotective Response: in Vitro and in Silico Approaches

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Overproduction of NO induced by iNOS has been implicated in various pathological conditions including tissue damage, ER stress, obesity, and cancer. Previously, two nitrobenzamide derivatives with potent inhibitory activity against iNOS have been reported (Tumer et al., Int Immunopharmacol. 2017; 43:129-139.). Based on these results, herein we synthesized and evaluated iNOS inhibitory potential of eight novel molecules in LPS stimulated RAW264.7 macrophages and SIM-A9 microglia. Two compounds (1 and 3) exhibited potent and dose-dependent inhibitory activities against the production of NO in LPS induced macrophages (IC 50: 5.8 and 3.8 μM, respectively) and microglia (IC 50: 6.1 and 10.8 μM, respectively). The inhibition was regulated at mRNA and protein levels. Compounds 1 and 3 also induced the expression of phase II detoxifying enzymes which was mediated by Nrf2 activation. To understand their action mechanism, target-driven in silico approaches were performed. Pharmacokinetic profiles of these two promising molecules were studied using MetaCore/MetaDrug platform.

Keywords: iNOS, NQO1, Nrf-2, Computer-aided drug design

THE TALE OF TWO PROTEINS: Interaction Between Desmin and Lamin B

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Desmin is a muscle specific intermediate filament protein located in cytoplasm. Lamin B, on the other hand, is a nuclear intermediate filament protein. In this study the interaction between desmin and lamin B has been investigated. Proteins of interest were isolated from muscle tissue of wild type AB zebrafish and the interaction was determined via reciprocal co-immunoprecipitation (Co-IP). To confirm the results proximity ligation assay was used in skeletal muscle sections of zebrafish and a mass spectrometry (MS) analysis was performed on Co-IP lysates. The results of MS analysis also showed that there is an interaction between desmin and Nup153, a FG Nup located in the central channel of the nuclear pore complex that is responsible for controlling nucleocytoplasmic transport, which is known to interact with lamin B. Also the Co-IP results revealed an interaction between desmin and Nup214 -another FG Nup. All together this data suggests that desmin might enter the nucleus to regulate one or more cellular processes in muscle cells. Funded by TUBITAK (214S174).

Keywords: Protein-protein interaction, Co-immunoprecipitation, Zebrafish Intermediate filament,

POSTER PRESENTATIONS

PT 001

Effects of Estrogen Receptor Variants Alpha and Beta Genes on Severity of Breast Cancer

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Introduction: Reproductive factors pose a risk for sporadic breast cancer (BC) development owing to the lifetime exposure to estrogen. An objective of the present study was to determine the association of rs2228480 (ESR1) and rs4986938 (ESR2) variants in Pakistani BC patients. Methods: DNA of ninety randomly selected BC patients were genotyped by Pyrosequencing. Later on, they were analyzed for association with epidemiological, clinical, and reproductive factors. Results: We found a high frequency of rs2228480*GG genotype and rs4986938*GG with MAF 45% and 38%, respectively among ER+ tumors (OR=1.81) and little association with clinical stage 0 (OR=0.119). rs2228480*GA genotype associated with less ER expression, whereas rs2228480*GG associated with high expression of PR. The frequency of rs4986938*GG was high among women who breastfed (OR=2.1) and high association with clinical stage 0 (OR=3.383) whereas less association with the positive family history of breast cancer (OR=0.005) Conclusion: ESR1 and ESR2 variants did not alter sporadic BC risk, but they did modulate the BC severity.

Keywords: Breastcancer, variants, ESR 1, ESR 2

PT 002

Epigenetic Effect of Estrogen on the Differentiation of Mesenchymal Stem Cell

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Mesenchymal stem cells (MSCs) are a group of adult stem cells. MSCs are multipotent and in a specific condition, like the presence/absence of estrogen, tend to differentiate in one type of cell line including osteocytes and adipocytes. Estrogen deficiency is considered as major cause of osteoporosis, osteoarthritis and obesity in postmenopausal women. However, this estrogen-dependent switch mechanism between osteogenesis and adipogenesis are not epigenetically explained. Previously, we have shown estrogen treatment decreased the expression of major adipogenic transcription factors, C/EBPα, FABP4, PPARγ, Adipsin while increasing key osteogenic transcription factor RUNX2 in MSCs. Here, we report that, estrogen epigenetically regulate the adipogenic and osteogenic transcription factors via ERα. Using Co-IP assay, we indentified protein-protein interactions between ERα and histone methyltransferases, EZH2 and Set7/9, and H3K4me3 which is Set7/9 histone methyltransferase's modification, suggesting that ERα may promote the recruitment of H3K4me2/3 in order to modulate histone modifications on transcription factors involved in differentiation. Through this pathway, estrogen leads and regulates the MSC differentiation epigenetically

Keywords: Mesenchymal stem cell, Estrogen, Epigenetics, Osteogenesis

PT 003

Some Dwarf Gene Expression Profiles in Different Almond Species

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When evaluating from the view of the agricultural plants, it can be said that while the dwarfism are disadvantages like the breakage of the annual plants, tolerance of the stress and the decrease of the canopy and the photosynthesis product, it is generally preferred in terms of the variety/rootstock in the fruits included in this group, more crops each area, easy cultural processes, expansion of plantation areas for different climatic condition. In this study, the expression of the natural dwarf almond genotypes of gene candidates of different plant species originated from the pre-determined functionalities of the comparative genomic approaches were investigated at the gene expression level in comparison with the root-stem. Datas of study conducted with qPCR are of importance in dwarf and semi-dwarf species, root-stem comparisons and in revealing the differences in annual-perennial plants.

Keywords: dwarfism, almond, gene expression, qPCR

PT 004

Determination of the Biodiversity of Actinomycete Species in Human Blood Exposed Soil Samples Using 16S rRNA Analysis

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Scene of a crime can be forensically examined using a microbiological approach. Thepurpose of this study is to determine if exposing soil to human blood, will have any effecton the pre-existing Actinomycete's population of the soil. The scene of the crime waslocated at the garden of the Biology department of the Faculty of Science, in Ankara University Tandogan campus. Two samples were taken; control and blood contained.Bacteria was isolated followed by genomic DNA isolation using CTAB, then PCR was preformed to amplify the 16s rRNA gene region. No Actinomycete was present in the control however, blood exposed soil showed strong presence of bacteria that is morphological similarity to that of Actinomycete, or rare Actinomycete. Using 16s rRNA analysis we will then determine the species of bacteria present in the blood exposed soil sample. The results can then be used in future crime scene investigation of cases. The findings of this study nonetheless, require further research in order to develop a more comprehensive understanding of the effect of human blood on soil.

Keywords: Actinomycete, 16S rRNA, Forensic microbiology

PT 005

Comparative Analysis of Structural and Dynamic Properties of a Transforming (HRas-G12D), a Non-Transforming Mutant (HRAS-G12P) and the Wild Type HRas Protein

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Ras proteins are involved in various processes as proliferation, growth and survival. Any problem in this family leads to cancer; however, H-RASG12P mutant retains intrinsic-GTPase activity, and thus does not cause any transformation. Here, we report results obtained from atomistic molecular dynamics simulations of H-RASG12P, H-RASWT and H-RASG12D transforming mutant. According to them switch I-II regions have higher flexibility in H-RASG12D than the other two, whereas both regions are more stable in H-RASG12P which might explain intrinsic GTPase activity of the protein. Dynamic cross-correlation-analysis shows H-RASG12P has the lowest anti-correlation in functionally-relevant regions. Principal component analysis shows switch I-II regions represent the dominant motion in each system; however, the space spanned by the first and the second eigenvectors is more restricted in H-RASG12P which might be related to higher intrinsic-GTPase activity of the protein. Finally, understanding properties of HRASG12P might help prevent transformation in these oncogenic protein family.

Keywords: Molecular Dynamics, Structural and Dynamical Properties of H Ras, Point Mutations

PT 006

MGAT1 is a Novel Transcriptional Target of Wnt/β Catenin Signaling Pathway

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The Wnt/β-catenin signaling pathway is an evolutionary conserved pathway which has important functions in vertebrate early development, axis formation, morphogenesis, cellular proliferation, and it controls cancer progression. To date most of the identified targets are shown to harbour tumorigenic properties. We identified Mannosyl glycoprotein acetylglucosaminyl-transferase (MGAT1) enzyme, which is one among the Wnt/β-catenin signaling putative target genes in hepatocellular carcinoma cell lines (Huh7). The activation of Wnt/β-catenin pathway culminates in the upregulation of MGAT1 enzyme both at transcriptional and post-transcriptional levels. We also showed that overexpression of β-catenin gene increased the promoter activity of MGAT1 gene. Furthermore we showed that MGAT1 expressing Huh7 cells have greater proliferative and invasive capabilities and that it leads to a significant increase in tumor growth rate in SCID mice. Taken together, we showed for the first time that MGAT is a novel Wnt/β-catenin pathway target that has important implications for tumorigenesis.

Keywords: Wnt/beta Catenin Pathway, Tumorgenesis, MGAT I Enzyme

PT 007

Transcriptional Analysis of Amsacta Moorei Entomopoxvirus (AMEV) Genes Encode Entry Fusion Complex (EFC) Proteins in HeLa Cells

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Amsacta moorei entomopoxvirus (AMEV), type member of Betaentomopoxviruses that infect insects, has been suggested to be used as gene therapy vector. Its distant relative Vaccinia virus (VACV) has been used as vaccine for Pox disease that successfully eradicated by World Health Organisation. Studies with AMEV showed that they have ability to enter mammalian cells with no cytophatic effects but unable to produce new viruses similar to Baculoviruses. In this study, we aimed to investigate the transcription of entry fusion complex (EFC) genes of AMEV in human cervical cancer cells (HeLa ATCC). For this purpose HeLa cells were infected with AMEV and total RNA was isolated at 24 hourpost infection. DNAse treated RNA samples were then used as a template to generate cDNA and transcription of EFC members were determined with polymerase chain reaction (PCR). Results showed that four of ten genes encoding EFC proteins were transcribed in mammalian cells.

Keywords: Amsacta moorei entomopoxvirus, Viral entry, Entry fusion complex, Gene Expression,

PT 008

Multi-Functional Plant Capparis Ovata: Focusing on the Anti-Carcinogenic Effect

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The effect of 1H-indole-2-Hydroxy, 3-Carboxylic Acid (I2H3C) as a novel and natural compound isolated from Capparis ovata were investigated Caco-2 cell line. The cytotoxic effect of the compound was determined in Caco-2 using crystal violet staining. The impact of IHC at EC25 and EC50 doses on the expression of the selected genes related to cancer initiation, development and progression as well as tumor suppression, cell death and proliferation were studied. The EC25 and EC50 values of the I2H3C were found 11.1 µg/ml and 38.8 µg/ml respectively. The effect of I2H3C at EC25 and EC50 values in the relative mRNA levels of 17 genes related to different cellular pathways was determined. It was found out that I2H3C treatment significant changed the expression profiles in three different cellular pathways in Caco-2 cells. Genes promoting cell cycle is severely reduced along with the significant increases in genes associated with apoptosis. The mRNA levels of nuclear receptors that are important for tumor suppression were increased significantly with I2H3C.

Keywords: Caco cell line, Capparis ovata, Anti cancer

PT 009

Investigation of a Potential APA Regulated Gene in Cancer

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Alternative polyadenylation (APA) generates transcript isoforms with different 3'UTR lengths due to selection of one of several poly(A) signals on pre-mRNAs. Given that these isoforms may be differentially regulated by trans factors, consequences of deregulated APA could be important, especially in cancers. Earlier, we identified SNX3 (sorting nexin 3) as an APA regulated mRNA. SNX3 binds to endosomal phospholipids and has a role in receptor recycling. We hypothesized SNX3 proteins levels to be deregulated by APA and that might have consequences in receptor dynamics in cancers. We developed SNX3 silenced cell line models to examine the phenotypical consequences. We examined known receptor cargo molecules to test for their dependencies on SNX3 mediated receptor recycling. Our results suggest SNX3 to have a pivotal role in modulating receptor levels and that may have important consequences in cellular signaling pathways. Our future work will aim to better understand the consequences of regulated APA and how SNX3 might regulate neoplastic phenotypes.

Keywords: APA, Membrane Trafficking, mRNA, 3'UTR,

PT 010

Identification and Annotation of Putative lncRNAs Involved in Mesenchymal-Epithelial Transition

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Mesenchymal-epithelial transition (MET) is a key process of multicellular organisms, involved in development, wound healing, and metastasis. Recent studies indicate the regulation of MET is more complex than the removal or inhibition of epithelial-mesenchymal transition inducers, but the exact mechanisms are poorly studied so far. Long noncoding RNAs (lncRNAs) exhibit translation-independent functions and are involved in diverse biological events including cellular reprogramming. To better understand MET, we employed computational analysis to identify previously unannotated lncRNAs in MET transcriptome time course data, and predict their biological functions. Our analysis pipeline discovered 608 novel lncRNAs, and a majority of them exhibited stage specific expression, or upregulation during MET compared to mesenchymal cells. Using co-expression modules, we identified the biological niches of lncRNAs via enrichment analysis of annotated genes. We have found that these novel lncRNAs may have the potential to be involved in reprogramming events such as chromatin remodeling.

Keywords: lncRNA, Mesenchymal-epithelial transition, RNA-sequencing, Weighted gene co-expression network analysis

PT 011

Oxidative Stress and Mitochondrial Disruption Induced by Camphor in the Fission Yeast (S. pombe)

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Camphor is one of the most abundant bicyclic monoterpens. In this study, we used Sod1Δ mutant yeast (S. pombe) cells lacking most of the scavenging activity, particularly in the cytosol. S. pombe is known as a uni-cellular eukaryotic model organism, also known as micro-mammal. We analyzed oxidative stress levels using DCFDA staining and NBT reduction assay. DCFDA fluorescence gradually increased in parental cells, at least 1.5-fold, and in mutant cells at least 2-fold, in correlation with camphor concentrations (400-1200 mg/L) and the results were statistically significant ($p<0.05$). This data points out ROS production and accounting antioxidant system can be (de)regulated by camphor in the fission yeast (S. pombe). Besides, gradual decreasing trend of mitochondrial membrane potential showed by Rhodamine 123 fluorescence assay was consistent with the increasing amounts of ROS. In conclusion, camphor potentially caused cytotoxicity mediated by oxidative stress which also induces ROS production.

Keywords: Camphor, S. pombe, ROS, Mitochondrial Membrane Potential

PT 012

Apoptotic Cell Death Induced by Camphor in the Fission Yeast (S. pombe)

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Camphor is used in food and cosmetics industry in addition to its antimicrobial effects. The fission yeast (S. pombe) constitutes a valuable model organism with mitochondrial biogenesis and cell cycle regulation analogous to mammals and can be used as a unicellular model organism. We evaluated apoptotic effects of camphor in parental and Sod1 lacking cells (800-1200 mg/L). Cell proliferation and viability were assessed using hemocytometer and methylene blue staining. Nucleus was stained with DAPI and acridine orange/ethidium bromide (AO/EB) dual stain. The IC50 and LC50 were calculated as 760 mg/L and 1186 mg/L in parental cells and 356 mg/L and 898 mg/L in Sod1Δ mutant cells. DNA fragmentation and condensation were observed in all treatment groups, 20-90% of cells showed apoptotic nuclear morphology in correlation with increasing doses of camphor. The results were validated with AO/EB dual staining. The potential effects of camphor on apoptosis were shown in S. pombe.

Keywords: Camphor, S. pombe, Apoptosis, DNA fragmentation

PT 013

Genome-Wide Identification And Characterization of Whirly and ARR-B Genes in Common Bean (Phaseolus vulgaris L.) and Assessment of Their Possible Role in Biotic Stress Response at Gene Expression Level

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Biotic disease stress is one of the most important factors affecting bean productivity. Stress can be caused by fungi, bacteria or viruses. In this study, it was decided to use Sclerotinia sclerotiorum as a biotic stressor in the field. In this study, we selected a durable and sensitive bean varieties that were exposed to biotic stress, and then ARR-B and Whirly transcription factor family genes were analyzed to compare gene expression profiles of plants with biotic stress response with qrt-PCR. Experimental studies were conducted simultaneously with in silico analyzes. Bioinformatic tools and in silico analyzes were based on the identification of Whirly and ARR-B proteins in the bean genome, the identification of bean Whirly and ARR-B gene members, physical location, gene duplications and identification of conserved motifs, phylogenetic analysis and alignment of sequences, gene ontology analysis, micro-RNAs (miRNA) and targeted bean Whirly and ARR-B genes include expression analysis of bean Whirly and ARR-B genes in RNA-Seq.

Keywords: Whirly, ARR-B, Biotic stress, Transcription factors

PT 014

Identification of the Importin-Alpha Sub-Type that is Responsible for the Import of HNF1A Transcription Factor into the Nucleus and the Analysis of the Nuclear Localization Signal (NLS)

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Maturity-onset diabetes of the young (MODY) is a monogenic subtype of diabetes mellitus. MODY3 associated with HNF1A gene mutations is the most common form of MODY. The aim of the study is to analyze the nuclear transportation of HNF1A by different importin α proteins and to demonstrate the interaction between specific importin protein and mutant HNF1A proteins (R271W and S345Y). The protein interactions mentioned were evaluated by co-immunoprecipitation technique. The Co-IP results showed that importin α7 (mouse Kpna 6) is mainly responsible for the transport of wild-type HNF1A to the nucleus, while the mutated proteins showed no interaction. To confirm this interaction, specific importin α protein was knocked down by siRNA in mouse pancreatic cells (MIN6) and the location of HNF1A was analyzed by immunochemical staining techniques. Kpna6 knockdown in Min6 cells exhibited a deficiency in nuclear localization of HNF1A protein. The results clarify the molecular pathway of nuclear import of HNF1A protein and molecular pathogenesis of HNF1A mutations.

Keywords: MODY,Importin proteins,HNF1A, Co-immunoprecipitation

PT 015

Evaluation of Cytotoxic and Genotoxic Effects of Phthalates and Phthalic Acid Esters

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Phthalate esters are mainly used as plasticizers in a wide variety of products and applications such as gelling agents, cosmetics, adhesives, emulsifying agents, coated pharmaceutical tablets. However, phthalates are not covalently bound to the plastic material and leach into the environment. Numerous toxicity studies have been conducted on phthalates. They have shown that some of them can produce severe developmental toxic effects in rodents, and more particularly affect the male reproductive organs and sexual development. After absorption, phthalates are rapidly hydrolyzed by esterases in the gut and other tissues into a monoester. Their metabolites are constantly detected in plasma, urine, amniotic fluid or breast milk, therefore reflecting substantial and constant exposure. This presentation was also designed to evaluate cytotoxic and genotoxic effects of phthalates such as Butylcyclohexyl phthalate by Comet Assay and Ames Test. Additionally, it was assessed the basic toxicological properties of some phthalates which their usage limited by ECHA.

Keywords: Phthalates, Genotoxicity, Cytotoxicity

PT 016

Coagulation Proteases Regulate eNOS Uncoupling in Diabetic Nephropathy

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Diabetic nephropathy (dNP) is caused by extracellular matrix accumulation in mesangium after primary alterations in glomerulus and podocytes. Thrombomodulin related protein C activation (aPC) in intact endothelial cells inhibits coagulation, apoptosis, and inflammation. Two different mouse models were used in our study: wild type (WT) and transgenic mouses with high-level active protein C synthesis (APChigh). Diabetic models were formed in both mouse types by 30-week streptozotocin (STZ) administration as well as control groups. Blood urine nitrogen (BUN) levels were measured in all groups. In addition to this, eNOS, Arjinaz-2, Caveolin-1, Dihydrofolate reductase (DHFR), Akt (protein kinaz B) total protein levels were determined by immunoblotting. Periodic acid–Schiff (PAS) staining were also performed to indicate extracellular matrix accumulation as a histopathochemical marker. In conclusion, aPC which is an important element in coagulation cascade mediates eNOS activity and oxidative mechanism in dNP.

Keywords: Activated protein C, Arginase-2, Diabetic nephropathy, eNOS

PT 017

High Incidence of Mitochondrial Etiology of Neurogenetic Disorders in Consanguineous Turkish Families: The Power of NGS

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Mitochondrial diseases show great heterogeneity both clinically and genetically.They affect most-energy consuming organs.Differences in symptoms and their severity lead difficulties in clinical diagnosis. Here we describe four patients who were originally suspected of having primary disease of neurogenetic disorders.Patients were recruited from paediatric neurology clinics in Turkey.WES was performed using Illumina exome capture.Analysis of WES data to list medically interpretable genes was carried out on the RD-Connect Platform. We identified highly pathogenic homozygous frameshift variant in NDUFA12 and a homozygous missense variant in NDUFS3,both associated with mitochondrial complex I deficiency,and a homozygous nonsense variant in TACO1 and a homozygous splice site variant in COX6B1,both associated with mitochondrial complex IV deficiency.NGS has an advantage in diagnosis of a genetic diseases and appropriate clinical management of patients.These cases that had been initially diagnosed as neurogenetic disorder and WES resulted in the diagnoses of mitochondrial disorders.

Keywords: Mitochondrial disorders, Whole Exome Sequencing(WES), Neurogenetics

PT 018

Pro-Metastatic Functions of Notch Signaling is Mediated by CYR61 in Breast Cancer Cells

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Metastasis is the main reason of death in breast cancer, which is the most frequently diagnosed cancer type. Notch, an oncogenic signaling pathway involved in breast cancer, is known to induce EMT, migration and invasion, which are considered as initial steps of metastasis. CYR61 is associated with poor prognosis in breast cancer and its inhibition reduced lung metastasis in xenograft models. In this study, we aim to understand whether CYR61 is a downstream mediator of Notch signaling for its pro-metastatic functions. We show that CYR61 expression in regulated by Notch activity breast cancer and normal cell lines. In normal breast cells, Notch induced migration and invasion is partially abrogated by CYR61 silencing. Furthermore, silencing of CYR61 decreased EMT regulators, Snail-2 and Zeb-2 that were upregulated by Notch activation. Our results suggest that CYR61 is a mediator of Notch induced EMT, migration and invasion in breast cancer and Notch - CYR61 interaction could be a potential target for anti-metastatic therapy.

Keywords: Breast cancer, EMT, Notch signaling

PT 019

Expression and Regulation of Toxic Boron-Related Genes in a Model Plant and Screening of Striking Results in Wheat Cultivars

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Oxidative damage level, accumulation of non-enzymatic antioxidants, expression levels of antioxidant enzymes and their respective activities and expression levels of some related microRNAs were determined in Arabidopsis thaliana under 1 mM B (1B) and 3 mM B (3B). Increased in levels of flavonoids, anthocyanins, proline and superoxide dismutase (SOD) activity provoked B tolerance under 3B. The correlation was found between the expressions and activities of SOD and ascorbate peroxidase (APX). Rather than phi class glutathione S-transferase (GST) genes, ATGSTU19 and ATGSTZ1 can have role in dramatic increase of GST activity under 1B. Expression levels of microRNAs related to jasmonate and ethylene metabolisms were induced remarkably by 1B. B toxicity might not affect cell wall modification at post-transcriptional level due to stable levels of miR397 and miR408 expressions. Striking results from Arabidopsis thaliana were screened in B-sensitive and -tolerant wheat cultivars. Accordingly, miR172 and its target (TOE1) can have role in B tolerance mechanism in plants.

Keywords: Boron toxicity, Transcriptional regulations, Arabidopsis thaliana, Antioxidative mechanisms

PT 020

Transcription Elongation in Connection to 3'UTR Ends

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Transcription machinery is a coordinated and complex process, where various proteins have dynamic interactions. We are interested in better understanding how transcription related processes determine the end of 3'UTRs.3'UTRs harbor multiple polyadenylation signals that are selectively used by the polyadenylation machinery. While many factors may influence poly(A) signal selection, transcriptional initiation and/or elongation is expected to play a major role. To begin investigating this, we chose in silico approach to determine whether transcription elongation rates affect poly(A) signal selection by using an in-house algorithm called APADetect. APADetect reveals potential short and long 3'UTR isoforms, as an indication of differential poly(A) selection. Overall, while inhibition of transcription elongation is also linked to decreased mRNA levels, we detected several cases where target genes are upregulated with a shift in proximal/distal poly(A) site usage.We plan to further investigate whether these unexpected cases are due to indirect effects and/or mRNA stability issues.

Keywords: Alternative polyadenylation, Transcription, mRNA, 3'UTR

PT 021

WLS Expression in ER + Breast Cancers

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Wnt signaling is a developmentally important signaling pathway and is mutated and/or deregulated in various cancer types. We identified a retromer protein SNX3 that regulates recycling of WLS (Wntless) receptor that has a role in WNT ligand secretion. Secreted WNT ligands can then bind to Frizzled family receptors on that same cell or neighboring cells to activate the nuclear accumulation of β-catenin in the nucleus. We identified SNX3 in a transcriptomic screen where shorter 3'UTR isoforms were over represented in breast cancers. Given that SNX3 has been implicated in endocytic recycling of WLS, we hypothesized SNX3 to be a potential cancer related gene in breast cancers through regulating WLS. Therefore, here, we aimed to study SNX3 in ER+ breast cancers that are known not to be heavily dependent on Wnt signaling. We present evidence on SNX3 silencing in ER+ breast cancers and how WLS and Wnt signaling cascades are affected. Further studies will clarify the significance of SNX3/WLS connection and Wnt signaling in ER+ breast cancers.

Keywords: SNX3, WLS, Breast cancer, Endosomal recycling

PT 022

Inhibiting FoxM1 has Promising Effects on Metastasis in Triple Negative Breast Cancer

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FoxM1 transcription factor which is overexpressed in many cancers, has important roles in cell migration, invasion, angiogenesis and metastasis. In this study, we examined the effects of FoxM1 inhibitor (Thiostrepton) alone and in combination with MEK inhibitor (Selumetinib) on metastatic parameters in 4T1 allograft Balb/C triple negative breast cancer model. Protein expressions were analyzed by western blot and immunohistochemically. uPA activity was determined by enzymatically. Our in vivo results showed, Thiostrepton alone and in combination with Selumetinib had negative effects on metastasis related protein markers. Immunohistochemically, Thiostrepton alone and combination group with Selumetinib showed decreased expression intensity of FoxM1 expression in tumor. Plasma uPA expression decreased after 25 mg/kg Thiostrepton treatment. Even Thiostrepton alone offers promising potentials. This study should be considered as a model study for the inhibition of FoxM1. Also, this agent or its equivalents could be developed to be studied in vitro and in vivo cancer models.

Keywords: FoxM1, Thiostrepton, Triple negative breast cancer, Metastasis

PT 023

Use of a Split GFP System to Detect TIR Domain Interactions

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TIR domain interaction is a crucial control mechanism of TLR signaling pathway. Recently discovered bacterial TIR domain proteins were shown to manipulate TLR signaling pathway via targeting TIR domain interactomes. Therefore we are studying protein interactions in order to understand bacterial control on immune system. GFP-fragment reassembly is a method used to investigate protein interactions where, GFP protein is separated into two fragments which are expressed independently from two different vectors. Green fluorescence is observed only upon reassembly of these fragments which is dependent on the interaction of their fusion partners. In this study, the suitability of this system for detecting TIR domain interactions is tested. Human TIR domain adaptor proteins are cloned as GFP fusions and their interactions in E.coli Rossetta 2 cells are investigated. The positive results of the study will enable the use of GFP system to test TIR domain interactions between human and bacterial TIR domain proteins. Acknowledgements: This work is supported by TÜBİTAK (116Z299).

Keywords: GFP fragments reassembly, Protein interaction, TIR domain

PT 024

Investigating the Use of Zymomonas Mobilis Levansucrase for Levan Production

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Levan is an important industrial polymer with its amphiphilic, fat-like, hydrocolloidal, antioxidant and biofilm formation properties and finds use in both medicine and food industries. Most striking uses of levan in foods includes, as prebiotic additives, as fat replacers and for increasing the shelf life of bread. Levans can be produced by microbial levansucrases. Levansucrase produces short chain fructooligosaccharides or levan depending on both the microbial origin of enzyme and reaction conditions. Zymomonas mobilis produces an extracellular levansucrase in the presence of sucrose. The aim of this study is to investigate the use of crude enzyme for levan production in order to eliminate the demanding purification steps and thus to present a sustainable method. Following these, Z.mobilis levansucrase was produced by static culture fermentations and the cell free supernatants were used for both sucrose hydrolysis and levan production experiments. The effect of incubation time and temperature for optimum levan production were investigated and found as 24 h and 25 °C.

Keywords: Zymomonas mobilis, Levansucrase, Levan, Reaction conditions,

PT 025

Identification Of Long Non-Coding RNAs That Regulate Apoptosis In Human

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Apoptosis is programmed cell death triggered by various stimuli as ligation of cell surface receptors, treatment with cytotoxic drugs or irradiation. In contrast to miRNA, lncRNA involvement in apoptosis has not been clarified yet. In this study, HeLa cells were treated with cisplatin, doxorubicin, Fas mAb and TNF-alpha, to identify differentially expressed lncRNAs in apoptosis. Total RNAs of control and treated group were subjected to deep sequencing which resulted in differential expression of 1644, 506, 584 and 807 lncRNAs in cisplatin, doxorubicin, anti-Fas and TNF-alpha, respectively. GTF2A1-AS was selected as one of the upregulated lncRNA candidates. After silencing with custom-designed GapmeR, apoptotic phenotype was confirmed by flow cytometry and caspase-9, -8 and -3 expression by western blot. GapmeR silencing led to 46% apoptosis, while the rate was 17% by negative control GapmeR. Cleaved caspase expressions were also identified as indicators of apoptosis. These results suggest that GTF2A1 may have potential in regulation of apoptosis through an antisense lncRNA.

Keywords: Long non-coding RNA, Apoptosis

PT 026

Structural Analysis of Polymerization Dynamics of PYRIN and CARD Domains of ASC Protein

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ASC protein is a 22 kDa protein containing conserved PYD and CARD domains. Homotypic interactions between PYD-PYD and CARD-CARD domains occur via certain surfaces of contact (Type I, Type II and Type III). ASC has the ability to form a supramolecular globular complex called the ASC speck. When expressed in truncated form as PYD and CARD separately, these domains form fiber-like polymeric structures. Our aim is to elucidate the importance of specific locations on PYD-PYD and CARD-CARD homotypic interaction surfaces during the polymerization process. Using site-directed mutagenesis method, certain mutations were created and their effects were visualized. Homotypic interactions were also analysed using Förster Resonance Energy Transfer (FRET) technique and certain mutations were identified that block FRET signal. Besides, our Atomic Force Microscopy (AFM) based analysis on homotypic interactions provide quantitative result about how physical strength of the homotypic CARD interactions change. Our study provide better explanations about oligomerization dynamics of ASC.

Keywords: ASC, Inflammasome, Protein-protein interactions, FRET

PT 027

Expression of Panton-Valentine Leukocidin (PVL) Gene in Foodborne Staphylococcus Aureus Strains

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Panton-Valetine Leukocidin is one of the life treathening exoprotein toxins in S. aureus lead to severe clinical infections including furunculosis and necrotising pneumonia. In this study, PVL gene carrying foodborne S. aureus strains M1-AAG42B, PY30C-b and YF1B-b and positive control S. aureus HT480 strain were examined on the basis of lukSF-PV gene expression in 6, 12, 24 and 48 h periods in CCY modified medium. gyrB gene was used as a housekeeping gene and expressions were determined in LightCycler 480II Real-Time PCR system. Real-Time PCR results showed that an increase in the expression of PVL gene in S. aureus M1-AAGG42B, PY30C-b and HT480 strains was detected at 24 h compared to other incubation times. The expressions start to decline at 48 h in these strains. According to the expression results, PVL toxin is produced at highest amount at 24 h and it can lead to infection.

Keywords: Staphylococcus aureus, PVL, Gene expression

PT 028

Physicochemical Properties Determine Poly-reactivity and Self-interaction of Monoclonal Antibodies

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Use of therapeutic monoclonal antibodies has been increasing dramatically. Therapeutic antibodies are mostly discovered by in vivo techniques which don't allow optimization for essential characteristics. However, smaller antibody fragments can be engineered and optimized easier with many in vitro technologies which speed up therapeutic antibody discovery and development. Most commonly used in vitro technique is phage display where antibody fragment libraries are displayed on the surface of bacteriophages to screen for antigen binding. Because of its many successful examples, phage display gains more attention. However, phage display derived antibodies might show undesired attributes such as self-interaction and poly-reactivity which should be further improved. In this project, we aim to investigate whether complementary determining regions of antibodies play a role in those attributes by comparing antibodies derived with phage display or other techniques. We find that physicochemical characteristics might determine undesired properties in phage display derived antibodies.

Keywords: Antibody, Phage Display, Complementary Determining Region, Physicochemical Properties

PT 029

An Inflammation Targeted and Controlled Release System as a specific Transglutaminase Inhibitor

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Atherosclerosis comprises 31% of deaths worldwide. In pro-atherosclerotic phase migration of monocyte to intima region is stimulated by inflammatory cytokines such as ICAM-1 and suggested to be carried out by tissue type transglutaminases (TG2). We aimed to develop an inflammation targeted and controlled drug release system. We characterized one of previously selected specific aptamers against ICAM in cell culture by flow cytometry. Aptamer conjugated mesoporous silica nanoparticles loaded with T101, a TG2 active site inhibitor, (Apt-T101-MSNP) was first synthesized and HUVECs were cultured with 0.5, 1 and 2 nM Apt-T101-MSNP or 10μM and 1 nM T101 for 24h. TG2 activity was detected by FITC-cadaverine staining with florescence microscopy. Our results demonstrated that targeted and controlled drug release system resulted in higher inhibition of TG2 activity compared to application of TG2 as single agent. This drug delivery system might be a promising approach in treatment and prevention of atherosclerosis.

Keywords: Aptamers, ICAM-1, Atherosclerosis

PT 030

A Toxicogenomic Approach for Evaluation of the Nongenotoxic Effects of Caper (Capparis ovata)

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Capparis ovata's potential anti-neuroinflammatory application for the treatment of multiple sclerosis were suggested in our recent investigated.This study aimed to evaluate the possible toxicological impact of water extract of Capparisovata on mice liver.The extract was administered intragastrically determined dose and the expression levels of transcripts were analyzed.A whole-genome transcriptomic-based screen of liver tissue from mice treated with demonstrated534genes were upregulated and 452 genes were downregulated as compared to control tissue.GeneOntology examinationrevealed that the significant modificationsin GOclasses for immune system process, peptidase inhibitor activity that were among upregulated genesand neurogenesis that was in downregulated genes.Pathway enrichment analysis of bothupregulated and downregulated genesuncovered significant changes in the control of immune system processes.The resultssuggest that COWEexposure at thementioned dose elicited no toxicity at the molecular level and considered to be safe as an alternative therapeutics in MS treatment.

Keywords: Toxicogenomics, Capparis ovata, Evaluation, Multiple sclerosis

PT 031

Identification of Key Genes Implicated in Resistance/Sensitivity to Cancer Thermotherapy Using Bioinformatics Approaches.

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Application of heat above 43 C and up to 47 C, the so called "thermal ablation" range, leads to tumor cell destruction either by apoptosis or necrosis. However, tumor cells have developed mechanisms of defense that render them thermoresistant. Of importance, the in situ application of heat for the treatment of localized solid tumors can also prime specific anti-tumor immunity. The aim of our study was to identify key genes implicated in thermoresistance and immunogenic cell death (ICD) by employing bioinformatics approaches. To this end, both literature-derived and microarray gene expression profile data were processed, followed by functional enrichment analysis. Two important functional gene modules were detected in hyperthermia resistance and ICD, one including members of the heat shock protein (HSP) family of molecular chaperones and the other including immune-related molecules, respectively.

Keywords: Thermotherapy, Cancer, Bioinformatics analyses

PT 032

Effect of TGF-β Cytokine on NONO/p54nrb Gene Expressıon in Hepatocellular Carsinoma Model

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NONO/p54nrb, belongs to DBHS protein family. This family has three members in mammals: NONO/p54 nrb, SFPQ, also known as PSF, PSPC1. NONO /p54 nrb encodes an RNA-binding protein which plays various roles in the nucleus namely, pre-mRNA splicing process, transcription termination, nuclear retardation, transcriptional regulation as a activator or suppressor, inflammation, DNA repair process and cancer.The transforming growth factor-beta (TGF-β) which is a tumor suppressor factor belongs to a superfamily of cytokines that act on protein kinase receptors at the plasma membrane. It induces biological signals. Dysregulation of its pathway causes pathologies, including cancer. In this study, we aim to determine TGF-β mediated NONO/p54nrb gene regulation in hepatocellular carcinoma model, Hep3B. Cells were treated by 20ng/mL of TGF-β cytokine at different time intervals , 0h, 1h, 3h, 6h, 24,and 48h. After total RNA extraction, qRTPCR was performed.We observed that TGF-β cytokine upregulates NONO/p54nrb gene expression same effect was also detected in protein level.

Keywords: NONO/p54nrb, TGF-β, hepatocellular carcinoma, expression

PT 033

PLGA Nanoparticles as Tool for Enhanced Delivery of Teicoplanin

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Antibiotics are quite successful in inhibiting bacteria. Besides, the effects of other microorganisms, loss of antibiotic dose while going to the target and side effects cause disadvantages in using antibiotics. PLGA is biocompatible copolymer for nanoparticular delivery system. However, there is not any available study in the literature about delivering teicoplanin antibiotic based on PLGA nanoparticles. The aim was to prepare, synthesize and characterize of teicoplanin loaded PLGA to decrease side effects. Teicoplanin was encapsulated in PLGA nanoparticles by double emulsion solvent evaporation method. Teicoplanin encapsulation efficiency was detected 99% by using HPLC at 218 nm. BET, SEM, AFM, FTIR, DLS analyzes were performed to determine surface morphology and size of nanoparticles. Given that synthesized particles were smooth spherical shaped, nano-sized and narrow sized distributed. Sustained slow release of teicoplanin from nanoparticles propose that nanoparticular system can be antibiotic delivery candidate against gram positive bacteria infections

Keywords: PLGA, Teicoplanin, Characterization, Delivery system

PT 034

Investigation of Cytotoxic and Anti-Metastatic Effects of Carboplatin on Etoposide-Resistant A549 Cell Line

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In non-small cell lung cancer, firstly acquired resistance to drugs administered as chemotherapeutic agents also show highly negative results in patients. Adjuvant therapies for treatment of acquired resistance is very important in increasing quality of life and longevity of patients. In spite of positive results for treatments, cancer cells can develop resistance against etoposide chemotherapeutic over time. Carboplatin is a platin-derived drug also used for non-small cell lung cancer (NSCLC) treatment. Its use in adjuvant therapy often demonstrates success. In this study, we developed etoposide resistance on A549 NSCLC cell line. We examined the cytotoxic effects of various doses of carboplatin on parental A549 cell line and etoposide-resistant A549/90E cell line. At IC50 values for carboplatin, we determined changes in caspase-3 and MMP-2 enzyme activities in both cell lines at the determined doses of carboplatin.

Keywords: Etoposide, Carboplatin, MMP-2, Caspase-3

PT 035

Characterization of GPR139 and Investigating Its Possible Role in Brain Development

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In this ongoing study, GPR139 will be characterized and the possible role of GPR139 in brain development will be investigated. In order to test our hypothesis, we are in the process of creating a Gpr139 knock-out mouse strain and examine various variables such as morphological changes of the brain and changes in transcriptome compared to wild type mice. Knock-out mice will then be subjected to behavioral tests to assess possible effects of Gpr139 on behavior. Various experiments hae also been conducted for further characterization of the receptor. Bioinformatic analysis by data-mining public databases and projects such as Gene Expression Omnibus and Encyclopedia of DNA Elements Project have been conducted to examine the expression pattern, differential methylation levels of CpG's and histones as well as examination of other regulatory elements such as promoter and CTCF binding motifs.

Keywords: GPR139, CRISPR/Cas9 Bioinformatics, Knockout mice

PT 036

Centriolar Satellites are Dynamic Cellular Structures that Regulate Centrosome/Cilium Proteins

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Centriolar satellites are membraneless granules that localize around the centrosome in mammalians and their function and molecular mechanism of action is poorly understood. In this study, we propose that the distinct spatial organization of the satellites around the centrosome is crucial in order to efficiently regulate the structure and the function of the centrosome/cilium complex. To test our hypothesis, we employed a chemically inducible heterodimerization assay to mislocalize satellites and showed that this approach targeted the key satellite protein PCM1 either to the periphery or to the centrosome. Analysis of these cells revealed regulatory functions for satellites in centrosome homeostatis and centrosome functions including cilium formation and cell cycle progression. Together, our results show for the first time that the particular localization of the satellites around the centrosome is essential for the regulation of the centrosome/cilium complex through maintaining centrosome homeostasis.

Keywords: centriolar satellites, PCM1, Centrosome, Primary cilium

PT 037

The Centrosome and Cilium Complex Protein CCDC66 Functions in Ciliogenesis and Ciliary Trafficking, and is Regulated by Centriolar Satellites

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Centriolar satellites are an array of membrane-less granules localizing around the mammalian centrosome/cilium complex. They regulate the function of this complex and are implicated in ciliopathies. Underlying mechanism of this regulation is not known. We propose that satellites act through regulating the dynamics of centrosome/cilium proteins. To address this model, we study the regulation of retinal degeneration gene product CCDC66. Previously, we identified CCDC66 in our BioID proximity mapping analysis for a known satellite protein, CEP72. We showed that CCDC66 localizes to the centrosome, centriolar satellites and primary cilium, associates with microtubules, is required for ciliogenesis and ciliary recruitment of another centriolar satellite protein, BBS4. Here, we studied dynamics of CCDC66 and identified components responsible for its centrosomal association by performing FRAP in cells where microtubules, centriolar satellites or dynein/dynactin complex are perturbed. These analyses identified critical roles for all these components in regulating dynamics of CCDC66

Keywords: Centriolar satellites, FRAP, Centrosome

PT 038

Analysis of Mitotic Functions of Mastl Kinase

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Mitosis is the last phase of the cell cycle in which the parental eukaryotic cell divides into two daughter cells. Mitosis progresses rapidly and in irreversible steps. Transition through successive mitotic events are regulated by mitotic kinases. Studying biological functions of such enzymes may require fine spatiotemporal analyses, as they have distinct roles in different stages of mitosis. Gene knockout and silencing approaches to study a particular kinase can not provide the needed instant loss of function to resolve the function in a short time period. Acute chemical inhibition of the subject enzyme would be the most suitable approach. However, it is not easy to find specific inhibitors for a given kinase, as the ATP binding pockets are very similar. A methodology called "chemical genetics" involves redesign of kinase molecular structure to accomodate bulky ATP anologues as inhibitors. In this study we aim to develop such analogue sensitive versions of a mitotic kinase - MASTL.

Keywords: Mastl, Chemical genetics, Mitosis, Cell cycle

PT 039

Multiplex Nanoparticle-Assisted PCR (NanoPCR) for Detection of Clinically Important Bacterial and Fungal Pathogens

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Nano-PCR is a technique that uses the physicochemical properties of nanomaterials in order to enhance specificity and sensitivity of PCR. Several studies showed the potential application of nanoparticles (NPs) for detection of bacterial, parasitic, and viral infections. However, to our knowledge, NPs have not been used to detect fungal and bacterial pathogens in a single PCR. Here, we aimed to develop and optimize a novel multiplex nano-PCR assay for detection of health-threatening fungal and bacterial strains. For this bpurpose, conserved regions in the genomes of pathogens were amplified using the species-spesific primers by multiplex PCR. After confirmation of PCR products by agarose gel electrophoresis, multiplex nano-PCR was performed in the presence of gold NPs, quantum dots, and metal NPs. The effect of each nanoparticle on PCR was evaluated by comparing the PCR cycle number, limit of detection, and amplification efficiency. In conclusion, we developed an effective tool serving as spesific, sensitive and faster alternative to conventional pathogen detection methods

Keywords: Pathogen Detection, Nanoparticle, Nano-PCR, Multiplex nano-PCR

PT 040

New Age Vaccination Using ASC Speck Delivery System

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Pathogen-associated molecular patterns(PAMPs) and danger-associated molecular patterns(DAMPs) are sensed by nucleotide binding oligomerization domain-like receptor(NLR) family of proteins in cytosol for regulation of innate immunity responses. Certain NLRs like NLRP3 induce formation of inflammasome complexes. Caspase-1 is activated within inflammasome multiprotein complex via interaction with apoptosis-associated speck-like protein(ASC). The purpose of project is purification of ASC specks with antigen epitopes and development of vaccines using these specks as carrier or/and adjuvant. Nowadays, influenza is a common threat in the world so, importance of vaccination about influenza is emphasized. Hemagglutinin is one of the most relevant antigens on influenza. Therefore, we will use ASC specks conjugated with avian-flu-virus antigenic coat glycoprotein "hemagglutinin-H5" as a prototype influenza vaccine. After injection of vaccine on mice, stimulation of immunity will be checked by several studies to demonstrate antigen delivery ability and adjuvant effects of ASC specks.

Keywords: Inflammasome, ASC, Influenza, Vaccine

PT 041

Role of Connexin 32 on Tumorigenicity of MCF7 and Hs578T Breast Cancer Cells

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Gap junction channels allow selective exchange of molecules between adjacent cells. Primary components of gap junctions are connexins (Cx), which along with their channel forming functions, also play role in cell cycle progression, migration, and metastasis in connexin and cancer dependent manner. Through overexpressing Cx32, its functions in breast cancer cells were investigated. Cx32 overexpression increased cellular proliferation in Hs578T cells by 6% and MCF7 cells by 5.6%. Cell cycle analysis demonstrated 11.2% increase in S phase in Hs578T cells while not showing any effect on MCF7 cells. On the other hand, Cx32 overexpression reduced the migration capacity in Hs578T and MCF7 cells by 15.3% and 22.9% respectively. Hs578T cells showed reduction of mesenchymal and increase of epithelial marker expressions, while the opposite was observed for MCF7 cells. In conclusion, presence of Cx32 might increase the proliferation and metastasis potential of MCF7 cells, while reducing aggressiveness in Hs578T cells. Acknowledgement: This work was supported by TUBITAK grant 114Z874.

Keywords: Connexin 32, Breast Cancer, Gap Junctions

PT 042

MAPK and AKT Pathway Intersection in Neuroblastoma Cells

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Neuroblastoma is the most common type of pediatric extracranial solid tumor and 98% of patients are under 10 years of age. One of the most important contributing factors for neuroblastoma development is the aberrant activation of mitogenic MAPK and AKT survival pathways. Abnormal activities of these pathways also indicates poor prognosis as a result of drug resistance in cancer treatment. It is revealed that there is a cross-talk between these two signaling cascades and they act together by one triggering the other performing an anti-apoptotic effect. However, it is still unknown what is there at the heart of this interaction. Since there are studies giving insights about certain cell cycle regulators which may be involved in the intersection of these pathways such as Speedy/RINGO, in our ongoing study, function of Speedy/RINGO in between MAPK and AKT pathways is being examined.

Keywords: Neuroblastoma, MAPK, AKT, Speedy/RINGO

PT 043

Gene Expression Analysis of bZIP Gene in Some Sunflower (Helianthus annuus L.) Varieties in Response to Cold Stress

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Cultivated sunflower (Helianthus annuus L.), is the one of the main crops used for edible vegetable oil, in many countries of the world, including Turkey. In this study, changes in the expression of the bZIP gene, one of the transcription factor genes, with 4 °C cold treatment applied to roots and leaves of the Saray, Tarsan 1018, Tr-3080 sunflower cultivars for 10 days, were investigated by quantitative real-time PCR. Content of malondialdehyde and total protein were determined. In roots, an increase in bZIP gene expression level was determined. In leaf tissues of Saray and Tarsan 1018 sunflower cultivars, that bZIP gene expression profiles decreased in the first days compared to the control, and increased in later days. The leaves samples of Tarsan 1018 has the highest bZIP gene expression profile on the 10th day and statistically significant at the $p<0.05$ level. Malondyaldehyde concentration and total protein levels showed notable variability.

Keywords: Helianthus annuus L, Transcription factors, Cold stress, Quantitative real time PCR

PT 044

Rapid de- and Regeneration of The Zebrafish Olfactory System

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The peripheral olfactory epithelium (OE) has an exceptionally high regenerative capacity. We use an experimental injury model in zebrafish to study the cellular responses underlying OE regeneration. Nasal irrigation with the detergent Triton X-100 results in the loss of up to 80% of the olfactory sensory neuron population within 24 h and near complete recovery within 7 d. We use BrdU incorporation assays and expression analysis of cell type-specific markers to describe the dynamics of the regeneration response and to identify relevant progenitor populations contributing to OE regeneration. We identified a basally located cell population, which expresses the stem cell markers sox2, krt5, and tp63, which shows increased neurogenic activity upon injury and is distinct from cells that contribute to maintenance neurogenesis. Using transcriptome analysis over the time course of de- and regeneration, we have identified candidate molecular pathways that may be critical for the selective activation of repair neurogenesis. Supported by TUBİTAK 113T038.

Keywords: Olfactory Epithelium, Adult Neurogenesis, Regeneration, Stem Cell

PT 045

Extracellular Production of a Fungal Xylanase in Recombinant P. Pastoris

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In this project xylanaseB gene, UNENxynB2, from the local isolate A. niger MRC200803 was used as gene source. It was expressed by the inducible AOX1 promoter in P. pastoris GS115 by utilizing the pPIC9 and pHIL-S1 vectors carrying HIS4 region. The codon optimized synthetic xynB (SxynB) gene fused to alpha factor and PHO1 signals which provides enzyme secretion. After transformation of the xynB subcloned secretion plasmids, 200 His+ clones were obtained, 71 clones were PCR analyzed. Recombinant xylanaseB activity was analyzed from crude extracts of 25 clones obtained from the fed-batch fermentation using shake flask, by inducing %0.5 methanol. Pichia Mut+ and Muts clones expressing the fungal xynB, were visualized by using %0.2 azo-dye crosslinked wheat arabinoxylan which allowed selecting SxynB expressed recombinants. Presence of a protein band about 20 kDa was observed in soluble crude extracts. For the high level of the heterolog enzyme expression and secretion, culture conditions will be optimized. Supported by TUBITAK ARDEB 1003 program, the UN-EN Project, #1150052.

Keywords: Xylanase, Protein expression

PT 046

Lps-Induction in Bend.3 Cells

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Endothelial cells are essential components of the blood brain barrier that regulate the exchange of solutes between the vasculature and the brain parenchyma. BBB integrity is disrupted following CNS injury and has been associated with the Sur1-Trpm4 channels. Once these channels are opened, Na+ flows into the cells causing edema and ultimately, cell death. To mimic CNS injuries in vitro, LPS was used as an endotoxin to initiate proinflammatory mediators to increase endothelial permeability. To demonstrate the role of Sur1-Trpm4 channels following LPS induction, we determined LPS cytotoxicity in bEnd.3 cells by Caspase-3 expression and cell viability assays. Furthermore, our results reveal that 24 hour exposure to LPS was sufficient for NfKB nuclear translocation, along with a statistically significant increase in Tnfa and Trpm4 expression. Taken together, LPS induction in bEnd.3 cells can be used to investigate endothelial cell dysfunction due to inflammation in stroke and trauma models.

Keywords: LPS, LPS induced inflammation, Brain microvascular endothelial cells

PT 047

Investigating Molecular Mechanisms Underlying Resistance to Notch Inhibitors in Breast Cancer

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Notch signaling is a crucially functioning, conserved ligand-receptor pathway which is playing role in regulation of cell proliferation, survival, and apoptosis. This pathway is commonly dysregulated in breast cancers and responsible for poor prognostic outcome. Notch receptor inactivation via DAPT and RO-4929097 (Gamma secretease inhibitors) have shown successful results in treating breast cancer patients in clinical trials. Resistance of cancer cells against chemotherapy and targeted therapy is clinically a vast problem and the mechanism behind this is not well understood. In this study, we aim to investigate molecular mechanisms responsible for resistance against Notch inhibitors. To this end, we generated MDA-MB-231 and MCF-7 breast cancer cell line clones that are resistance to DAPT and RO-4929097. We analyzed the phenotypic and molecular changes in resistant clones compared to parental cells. Identifying candidate genes functioning in Notch resistance can have both molecular and clinical beneficial outcomes to make anti-Notch therapies more successful.

Keywords: Notch signalling pathway, Breast cancer, Chemoresistance, Gamma secretease inhibitors

PT 048

Analyzing the Expression Profile of WRKY Gene under Cold Stress in Sunflower (Helianthus annuus L.)

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Cold stress can cause serious membrane damage, which can adversely affect product yield and lead to major crop losses. Membrane damage leads to a signal for cold tolerance related genes and transcription factors to mediate stress tolerance. This investigation shows the expression levels of WRKY transcription factor gene from sunflower under cold stress (+4oC) conditions. Three different sunflower varieties were exposed to cold stress for 0, 2, 4, 6, 8 and 10 days. Expression profile of WRKY gene, soluble protein contents and the extent of lipid peroxidation were determined in leaves and roots. In this study, it was determined that the level of expression of the WRKY gene has changed considerably. At the roots of the Tr 3080 sunflower variety, an increase of about 14 fold was observed on the eighth day when compared to the control. The level of WRKY gene expression was generally reduced in the foliage between the three sunflower species.

Keywords: Sunflower, WRKY, Gene expression, Abiotic stress

PT 049

Frequency Dependent Mechanical Intervention of Adipogenesis with Low Intensity Vibrations

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Cells are able to sense and respond to mechanical signals, and these signals have physiologically significant roles in cellular events from proliferation to differentiation. Mechanicals signals, even in extremely small magnitude are anabolic to bone tissue when applied in higher frequencies (>30Hz), directing osteoblasts to commit osteogenesis. Recent studies revealed that effect of low intensity vibrations (LIV) extends to commitment of bone marrow stem cells by reducing adipogenesis and increasing osteoblastogenesis. However, up to date studies involving LIV adopted arbitrary frequency applications and therefore no evident relationship between the regimen of the applied signals and the cellular response was shown for inhibition of adipogenesis. Here, we aimed to establish a relationship between applied frequency (from 30 to 120 Hz) in daily vibration and the response of 3T3-L1 bone marrow preadipocyte cells in adipogenic commitment in terms of cell viability, triglyceride content and gene expression.

Keywords: Adipogenesis, Mechanical signals

PT 050

In Situ Biofabrication of Scaffold and Label Free Cellular Structures with Weightlessness

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Magnetic levitation is one of the most recent Earth-based techniques to mimic weightlessness environment. However, there is an unmet need for validation of the method for long term cell culturing and for availability of the method to facilitate biofabrication of in situ scaffold-free three dimensional (3D) cellular structures. In this study, magnetic levitation technique was optimized for long term levitated cell culture and controllable in situ 3D cellular assembly models were developed via magnetic levitation. The strategy established here presents a fast, easy, cost effective and biocompatible way to simulate weightlessness condition and to test biological effects of this condition on 3D cellular models formed in the same device. This system, allowing real-time imaging at the same time, may offer great opportunities for a wide range of gravitational biology researches. Acknowledgements This study was supported by The Scientific and Technological Research Council of Turkey (215S862).

Keywords: 3D cellular assembly, Magnetic levitation

PT 051

Investigation of the Role of Wnt/ß-Catenin Signaling in Brain Regeneration in the Adult Zebrafish Model

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Wnt/β-catenin signaling has major roles in tissue renewal both during homeostasis and in response to injury. Unlike mammals, having lifelong neurogenesis, the zebrafish brain is a valuable model to elucidate the mechanisms of neuroregeneration. Our aim is to understand the functional role of Wnt/β-catenin signaling in brain regeneration in response to traumatic injury using zebrafish. For this purpose, we performed traumatic lesion assay, qPCR and immunohistochemistry. Zebrafish Wnt/β-catenin reporter line Tg(6xTCF:dEGFP) were used to measure the pathway activity via reporter expression at different time points after injury. We found that Wnt signaling is upregulated at very early stages of regeneration, i.e. at 20 hours post lesion, while it is differentially downregulated in the two hemispheres of the brain at 3 days post lesion. Thus our data suggest Wnt/β-catenin pathway is activated specifically in early damage response of the brain.

Keywords: Zebrafish, Wnt/β-catenin, Brain regeneration

PT 052

Investigation of the Role of a Novel Death Domain Protein in Regulation of Wnt/ß-Catenin Signaling by Using the Zebrafish Model

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Wnt/β-catenin signaling is involved in cell fate determination, cell migration, cell polarity, neural patterning and organogenesis during embryonic development. Therefore, misregulation of the signaling pathway causes cancer, congenital defects and degenerative diseases. Although the mechanism of the Wnt/β-catenin pathway is well established, novel modulators that can modify the pathway need to be defined for therapeutic interventions. Our next generation RNA-sequencing (RNA-seq) analysis data shows that a novel death domain gene belonging to the tumor necrosis factor receptor superfamily acts as a promising Wnt feedback regulator. Here, we aim to reveal the molecular mechanism of the potential regulatory role of this gene in Wnt pathway by using the zebrafish model. Besides we have generated a knockout of the gene by TALEN to unravel the link between the apoptotic and pathway regulatory roles of the gene. We believe that characterization of this specific regulator of Wnt/β-catenin signaling pathway will contribute to discovery of novel drugs targeting the pathway.

Keywords: Wnt, β-catenin, Zebrafish, Death domain protein

PT 053

Analysis of Genes In CML Etiology and Drug Resistance

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Chronic myeloid leukemia(CML)is a hematopoietic malignancy resulting in the fusion of BCR and ABL genes.Even if imatinib is an effective treatment,by passing time drug resistance may occur in patients.The aim of the study is to analyse the mechanisms of resistance in patients.This study has been performed on CML patients with imatinib sensitive(n=10)and resistant to imatinib(n=10).BCR-ABL mutations has been investigated.Moreover,we analyzed the expression levels of genes responsible for apoptosis(BCL-2,P53)and other genes(Scd1,PTEN).None of the patients were found to carry mutations.In a group of patients resistant to imatinib,a decrease in Scd1 and an increase in BCL-2 gene expression levels was observed.In this case,the Scd-1 gene was thought to act as a tumor suppressor.The increase expression levels of PTEN and P53 genes,indicated that they were trying to slow down the cell cycle in patients who develop resistance.It has been suggested that the Scd-1 and BCL-2 genes may be mechanisms responsible for resistance,apart from mutations.

Keywords: Chronic Myeloid Leukemia, Imatinib resistance, BCR-ABL mutations, Gene expression analysis

PT 054

Characterization of the Cellular Localization and Expression of AEBP1/ACLP Transcripts with an Unknown Function in Myoblasts

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AEBP1/ACLP is a gene with ambiguous function with several attributed roles in development and postnatal life. Among these, regulation of adipogenic differentiation, cell adhesion, pattern development and fibrosis are the well-understood. Two mRNA transcripts are attributed to this gene with protein products of obscure functions. A short isoform acts as a transcriptional repressor and a long isoform harbors a leader sequence that directs the peptide to the extracellular compartment. Since in silico analysis of these transcripts was depicting contradicting localizations, we cloned and expressed both transcripts in myoblasts to elucidate cellular localization of proteins. Furthermore, we performed RNAseq analysis to investigate the abundance of these transcripts in cells from different skeletal muscle compartments that only verified the presence of the long isoform. Both isoforms were overexpressed in mesenchymal cells (myoblasts, preadipocytes and fibroblasts) and RNAseq analysis provided functional insights for AEBP1 in extracellular remodeling during fibrotic degeneration.

Keywords: Tissue remodeling, Extracellular matrix, Fibrosis, Skeletal Muscle,

PT 055

Molecular Specificity of TAM Family Receptors Towards Different Ligands

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The transmembrane receptor tyrosine kinase TAM (Tyro3, Axl, Mer) family regulates an intriguing mix of cellular processes. TAM members are activated when their extracellular domains are bound to one of their two paralogous ligands, Gas6 and Pros1. Although Gas6 and Pros are significantly similar, Gas6 can bind to all TAM receptors with different affinities, while Pros can interact only with Tyro3 and Mer. Expanding on this, we aim to characterize TAM family's ligand selectivity through a structure-based approach. For this, we modeled the complex structures of all TAM-ligand interactions that was followed by the refinement of each complex with HADDOCK. Detailed analyses revealed the basis of TAM receptor selectivity towards its ligands: While Gas6 prefers electrostatic interactions, Pros' binding is majorly guided through van der Waals contacts. Further, we will investigate complementarity of interface residues on receptor and ligand sites. Then we will integrate coevolution data into our analyses, which should lead us to the deduction of TAM-ligand interaction fingerprints.

Keywords: Specificity, Binding Affinity, TAM Receptors

PT 056

Effects of Combination of Quercetin and Selenium on Ishikawa Cell Line

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In this study, the effects of quercetin and selenium against oxidative stress caused by hydrogen peroxide in Ishikawa cell line were examined. Five experimental groups were used: group I, no quercetin and selenium; group II, 300 µM H2O2; group III, 30 nM selenium; group IV, 100 µM quercetin; and group V, 100 µM quercetin and 30 nM selenium treatment. Ishikawa cells were collected to examine total protein and malondialdehyde levels, and for gene expression studies. Cell viability was measured at different concentration range of quercetin (50-100 µM) and sodium selenite (10-50 nM) in the MTT assay. Gene expression levels of apoptotic mediators (p53, caspase 8, cytochrome c, Bad) were analysed using real time-polymerase chain reaction. Acridine orange/ethidium bromide staining was applied to detect apoptosis. In conclusion, the combination of selenium and quercetin has synergistic effects against oxidative stress caused by hydrogen peroxide in Ishikawa cells for the first time.

Keywords: Ishikawa cell line, Malondialdehyde, Quercetin, Selenium

PT 057

Investigating the Role of SEMA6D in Breast Cancer Cell Lines

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SEMA6D belongs to semaphorin family which is key regulator of neurogenesis, heart development and also tumorigenesis. SEMA6D was functionally validated as an oncogene in human osteosarcoma. Also, Sema6D and its receptor plexin-A1 were identified to be expressed at high levels in gastric cancer. In breast cancer, high level of SEMA6D was found to be correlated with better survival and enhanced mesenchymal markers. However, functional importance of SEMA6D in breast cancer is not known. So, we focused on revealing effect of SEMA6D on proliferation, migration and invasion of breast cancer cells. We showed that SEMA6D overexpression decreased proliferation yet promoted migration in non-invasive breast cancer cells MCF-7. However, proliferation was not significantly affected while migration was slightly decreased in invasive breast cancer cell MDAMB231 in response to SEMA6D overexpression. Also, invasion was reduced in MDAMB231 upon SEMA6D overexpression. In conclusion, SEMA6D can be involved in breast tumorigenesis through regulation of proliferation and migration of tumor cells.

Keywords: SEMA6D, Breast cancer,

PT 058

Phenotyping of Leukocytes Infiltrating into the CNS in the Experimental Allergic Encephalomyelitis as Marker for Disease Progression

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Aim of the study: EAE is an MS disease model that is widely used to study autoimmune inflammation within the CNS. It is known that specific immune cells play in the induction and consequent determination of CNS inflammation. However, the extraction and treatment of the CNS, having a very different composition and fairly few immune cells involved in the inflammatory response, is more intricate and complicated. Materials and Methods: C57BL/6 mice, 6-8 weeks of age, obtained from KOBAY Laboratory of Animal Production Inc. were used. EAE was induced using MOG35-55 injections as describes elsewhere in detail. Conclusion: Results have shown that FACS analysis of leucocytes fractions within the CNS infiltrate at the peak of the disease can be used to determine inflammation state by clearly counterstaining with CD45+-CD3--Ly6G--CD11b+-Ly6Chigh to highlight antigen-presenting cell populations as monocytes and macrophages.

Keywords: Experimental Allergic Encephalomyelitis (EAE), Leukocyte infiltration, Multiple sclerosis, Flow cytometry

PT 059

Identification of Immunological Genes Important for Cytotoxicity

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Cytotoxicity by CD8 lymphocytes and natural killer (NK) cells is a critical attribute of the mammalian immune system. We have set out to identify the genes that regulate this process. Recently 7 genes were identified as being important for cytotoxic T lymphocytes. We are testing whether these genes have a conserved cytotoxicity function in the human NK92 cell line. We confirmed the expression of these genes in the NK92 cell line by RNAseq and qRT-PCR and found that five are expressed at robust levels. We targeted these genes using CRISPR/Cas9 genome editing, generating INDEL mutations by NHEJ. We used third-generation lentivirus to deliver the CRISPR into NK92 cells. To single cell clone NK cells, we generated feeder cells with a Thymidine Kinase suicide gene. The presence of mutations in these infected cell pools will be determined by the T7 endonuclease assay, qRT-PCR and western blotting. The effect of these genetic mutations on cytotoxicity towards the K562 CML cell line is analyzed by a degranulation assay (CD107a staining) and live cell imaging.

Keywords: Human NK92 cell line, Cytotoxicity, CRISPR, Degranulation

PT 060

The Dynamic Behavior and Pro-Tumorigenic Effect of Connexin 32 in Breast Cancer Cells

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In tumor tissues, cancer cells display dynamic changes in phenotype during progression. Connexins (Cx), which are the main gap junction proteins play a role in these changes by providing direct cell to cell communication. Although both pro-tumorigenic and tumor suppressor roles of Cx32 was reported in different cancer types, the effect of Cx32 on breast cancer is not exactly known. We investigated temporal role of Cx32 in both 3D and 2D in breast cancer cell lines. We demonstrated that Cx32 led to an increase in proliferation and migration from 3D environment to the plate in MDA MB 231 cells. Further, gap junction plaque formation was observed between migrated cells, signifying distinct phenotype from both breast cancer cells and normal breast epithelial cells cultured in 2D environment. Further, when cells were cultured in 2D for longer period, Cx32 localization and expression were altered based on cell type in a time dependent manner. Acknowledgment: This work was supported by TUBITAK 114Z874 grant

Keywords: connexin 32, Breast cancer, Proliferation

PT 061

Determination of Effects of Btb-Zf Transcription Factors in Cancer

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BTB-ZF proteins are evolutionarily conserved transcription factors that repress target gene expression. In the human genome, 49 genes are responsible for encoding these proteins, which are involved in a range of physiological functions such as immune system development, fertility, skeletal and neurological development. Mutations in the members of this protein family are associated with different types of cancers, especially lymphomas. In this study, we aimed to clone the BTB domains of selected proteins of the family. We have started to express these proteins in E.coli and started to purify the proteins by affinity and size exclusion chromatography. The purified proteins will be used to determine rules of homo and heterodimerization as well as interactions with co-repressors such as Ncor/Bcor/SMRT by using Biacore surface plasmon resonance (SPR). Finally, we aimed to generate mutations in the genes encoding these proteins by CRISPR/Cas9 genome editing to identify their significance in cancer development.

Keywords: Cancer, Transcription Factor, CRISPR/Cas9 genome editing, BTB-ZF proteins

PT 062

Development of novel compounds as Chemotherapeutic Drugs Targeting the MDM2-p53 Interaction

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The tumor suppressor protein p53 is the main mediator of growth arrest, senescence, and apoptosis in response to cellular damage. The interaction between p53 and MDM2 regulates cell cycle arrest and apoptosis. We aim to examine the p53-dependent apoptosis inducing activity of novel compounds. In this project, preclinical experiments were conducted by using novel compounds generated by in silico design and organic synthesis, which were designed for blocking the interaction of p53 and MDM2. The activity of these compounds was tested by western blot and reporter expression analysis in HCT116 colon cancer cell lines. The dissociation of MDM2 from p53 were examined using a fluorescent two hybrid assay with live cell imaging. Moreover, we generated HCT116 p53-/- Mdm2-/-, HCT116 p53-/- Mdm4-/- and HCT116 P53-/- Mdm2/Mdm4 double knockout cell lines by CRISPR/Cas9 genome editing. These new cell lines will be used in high content and high throughput assays to show the specificity of the drugs. Acknowledgements: This project is supported by TUBITAK 215S011

Keywords: CRISPR/Cas9, p53, MDM2, MDM4

PT 063

IKK-Related Kinase Involvement in Hepatocellular Tumorigenesis

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Hepatocellular carcinoma (HCC) is the second leading cause of cancer-related death due to poor prognosis and lack of therapeutic options. The current and the only drug approved for HCC patients, sorafenib, cannot extend the overall survival more than 4 months. Among mechanisms underlying tumor initiation and development, chronic inflammation plays central role. IKKε is a non-canonical IKK-related kinase and its role in inflammation is well known as a modulator of interferon and NF-κb signalling. Recently IKKε has been linked to various cancer types acting as an oncogene and a regulator of PI3K/AKT pathway. Our group wanted to explore roles of this kinase in HCC through loss of function model using shRNA lentiviral transfection. Molecular analysis in protein and mRNA levels revealed a partial EMT phenotype upon IKKε depletion. Additionally, IKKε depletion increased proliferation in vitro and lead to larger tumor formation in xenograft models in vivo. Our observations suggest a tumor suppressor role of IKKε in HCC.

Keywords: IKK-related kinases, Hepatocellular carcinoma

PT 064

Determination of mRNA Expression Levels of Cell Cycle Gene Retinoblastoma (Rb) in Sunflower (Helianthus annuus L.) under Salinity Stress

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Environmental effects may alter molecular signaling networks, which coordinate cell cycle. In this study, mRNA expression levels of Retinoblastoma (Rb) gene, which is responsible for basic mechanisms of cell cycle, were studied by Real Time PCR in four different sunflower varieties (Helianthus annuus L.) that were applied 100 and 150 mM NaCl stress. Total protein levels were determined by Bradford analysis. Along with the time increase, some ups and downs in the total protein amount have been observed. MDA analysis, widely used as a marker of oxidative injury, was also conducted. MDA levels contrary to protein levels, showed decrease under the same conditions. Some differences were observed in mRNA expression levels of Retinoblastoma (Rb) gene in accordance with the variety of plant, amount of salinity stress and time. The results of the current study will shed insight to the future studies on cell cycle genes in plants under abiotic stress.

Keywords: Helianthus annuus L., Cell cycle, Retinoblastoma (Rb), Salt stress

PT 065

Mutated ccdc124 Gene; a Suggested Inducer of Hodgkin Lymphoma Reed–Sternberg Cells Phenotype

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Coiled coil domain containing protein-124 (Ccdc-124) is a centrosomal protein that translocates to the midbody region during cytokinesis. Previously we showed that a CRISPR/Cas9 induced mutation of the ccdc124 gene in HEK293T cells resulted in failure of cytokinesis and formation of large multinucleated cells. Our mutated cells show an attempt to divide into multiple cells that rapidly refuse and form large cells; a phenotype mainly characteristic of Hodgkin Lymphoma Reed–Sternberg cells. Here we present our work on two Hodgkin Lymphoma cell lines (L428 and HDLM2) where DNA sequencing of the ccdc124 gene revealed the presence of multiple SNPs and mutations. We also show that over expression of mutant Ccdc124 in wild type HEK293T cells or Hela FUCCI cells also resulted in a multinucleated cell phenotype. In conclusion, our results point to an association between mutations in the Ccdc124 protein, cytokinesis failure and lymphoma development.

Keywords: Coiled-coil domain-containing protein-124, Hodgkin Lymphoma, Cytokinesis, Multinucleated cells

PT 066

Identification of Novel Small Molecule Ligands Targeting Interleukin-1 Receptor by SPR-based Screening

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Surface plasmon resonance (SPR) is a cutting-edge label-free biophysical method for the screening of small chemicals, protein-protein interactions, and drug discovery. We used SPR for small molecule chemical screening against a membrane protein, interleukin 1 receptor (IL-1R). In the innate and adaptive immune system, IL-1R plays an important regulatory role; its misregulation results in uncontrolled inflammation. The cytokine interleukin 1 beta (IL-1b) binds to IL-1R and this complex recruits IL-1R accessory protein (IL-1RAcP). Rheumatoid Arthritis patients lack IL-1R antagonist protein (IL-1Ra), a competitive inhibitor resulting in inflammation. In this project, we assembled the IL-1/ILRa/IL-1RAcP complexes on SPR chips and screen a small molecule library to identify drug candidates which inhibit IL-1 ternary complex formation and inflammation. We identified nanomolar affinity interactors of the IL-1R. The inhibitory activity of these molecules is being further tested in vivo and in vitro experiments.

Keywords: Cytokine, Interleukin-1 recepto, Surface plasmon resonance Inflammation,

PT 067

Identifying Regulation of Cant1 During Endoplasmic Reticulum Stress-Induced Cell Death

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Calcium-activated nucleotidase 1 (CANT1) is a member of apyrase family of enzymes which are responsible for hydrolysis of extracellular nucleoside tri-phosphates. CANT1 is an endoplasmic reticulum(ER)-resident protein, therefore other suggested roles for CANT1 are related to ER mechanisms. In this study, we aimed to identify the regulation of CANT1 expression during ER stress-activated cell death in breast cancer cell lines MCF7, SK-BR-3 and MDA-MB-468. We induced ER stress-related cell death and investigated how the protein expression, mRNA level and subcellular localization of CANT1 change. CANT1 protein expression was altered during ER stress while we did not observe any change in CANT1 mRNA level. Additionally, subcellular localization of CANT1 protein upon ER stress was detected by laser scanning confocal microscope and we obtained increasing colocalization of CANT1 protein with ER but not with mitochondria. Here, we reported how CANT1 expression levels and its subcellular localization change in breast cancer cells upon drug-mediated ER stress-induced cell death.

Keywords: CANT1, ER stress, Cell death, Breast cancer

PT 068

Investigation of NLRP7's Interaction Partners in Endometrial Cancer Cells

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NLRP7 is a cytosolic protein involved in the activation of proinflammatory caspases by participating in inflammasome oligomerization. . Little is known about NLRP7's function and it is proposed to have an oncogenic role since its expression levels increase in testicular seminoma and endometrial cancer tissues. Our tumor xenograft experiment results indicate that stably NLRP7 overexpressing cells enhances tumor growth in mice compared with that of the control cells. Next, liquid chromatography mass spectrometry applied with Hec1a cells after pulling down of NLRP7 and its interactor proteins using anti NLRP7 antibody. To detect most robust interactions, results were normalized using intensity based absolute quantification(iBAQ) and the list of candidates was narrowed down. Then, Ingenuity Pathway Analysis tool was used to identify the protein classes of NLRP7 interactors. Currently, Co-IP experiments are ongoing in our laboratory to validate binding partners. Our findings might provide the understanding the potential role of the NLRP7 in endometrial cancer.

Keywords: NLRP7, Endometrial cancer, Mass spectrometry,

PT 069

Computational Investigation of Novel Sphingosine Kinasel Inhibitors

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Sphingosine kinase 1 (SPHK1) is a lipid kinase that catalyzes the conversion of sphingosine to sphingosine-1-phosphate (S1P) which plays a vital role in biological processes including lymphocyte trafficking, cell growth, apoptosis, mitogenesis, and angiogenesis. Increased S1P levels in the cell as a result of SPHK1 overexpression is known to promote uncontrolled cell growth and differentiation together with increased metastases rates. In this study, 7 novel curcumin and anthraquinone derivatives as potential SphK1 inhibitors together with 50 non-sphingosine inhibitors of SphK1 with known IC50 values, including PF-543, which is known to be the most potent inhibitor up to date, were modelled and docked. Two of the novel ligand molecules were determined to bind the correct binding pocket of the enzyme. One of the ligands together with eleven of the known inhibitors showed a high correlation between experimental IC50 values and computed cluster energies and were determined to form at least one H bond with the Asp170 residue of the enzyme. Molecular dynamic studies are ongoing.

Keywords: Sphingosine Kinase 1 Inhibitors, Curcumin, Anthraquinone, Molecular docking,

PT 070

Label Free Density Profiling of Bone Marrow Stem Cells During Adipogenesis with Magnetic Levitation

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Adipocyte hypertrophy is an important parameter in describing abnormalities in adipogenesis leading to obesity. Although detection of an adipocyte through microscopy is straightforward, their separation is tedious. Mature adipocytes cannot survive passage through nozzles and therefore cellular enrichments are limited to pre-adipocytes using cytometry. Moreover, separation of cells usually requires labeling of cells or usage of fluids with different densities. Magnetic levitation is a novel label free method with the principle of movement of cells in a magnetic gradient based on their density. Here, we used a magnetic levitation device for density-based single cell detection of differentiated adipogenic cells in heterogeneous populations. Results showed that levitation platform is sensitive to changes in lipid content of mesenchymal stem cells committing to adipogenesis. The technology established here may potentially be modified to sort adipogenic cells that are detected during the procedure. Acknowledgements This study was supported by TUBITAK (215S862).

Keywords: adipogenic cells, Density profiling, Magnetic levitation

PT 071

The Long Journey of Finding the Open Reading Frame (ORF) of the Allatostatin-C Receptor of Thaumetopoea Pityocampa (T.pit)

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Allatostatins (ASTs) are insect neuropeptides having very important roles in managing most of the physiological behaviors of the insects. Their relevant receptors are G-protein Coupled Receptors (GPCRs). Identification of these receptors are very crucial for the development of the next-generation pesticides. The allatostatin receptor of the T.pit moth was identified in this study. In the first approach, through designing degenerate primers a part of the transmembrane region was identified. Then, to find the 5' and 3' ends of the sequence RACE technique was used which resulted into the amplification of the 5' end but not the 3' end. Alternatively, the extracted gDNA from the head tissue was sent for the Whole Genome Sequencing (WGS). The 150bp read paired-end HiSeq illumine 1.9 platform sequencing technology was used and de novo assembly performed. The sequence of the desired receptor was identified as a non-interrupted gene and it was confirmed by sanger sequencing.

Keywords: Insects, Neuropeptides, GPCR, WGS

PT 072

Assessment of mRNA Expression Levels of E2F Transcription Factor Gene in Sunflower (Helianthus annuus L.) under Cr (VI) Stress

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Sunflower (Helianthus annuus L.) is an important agricultural plant. Cr(VI) is the most phytotoxic form of the chromium. In this study, mRNA expression levels of E2F gene, which is transcription factor in cell cyle regulation, were determined in four sunflower varieties subjected to Cr (VI) stress at different concentrations (80, 160, 320, 640 ve 1280 mM) by Real Time PCR. Bradford total protein and MDA analysis were also performed. Some differences were observed in accordance with the types of plant and Cr (VI) stress concentration in mRNA expression levels of E2F gene. A reduction in MDA levels was observed resulting from the application of 80 ppm Cr (VI) stress in all varieties. The levels of protein tended to decrease by increased Cr concentration. It was thought that this study would give a light to the future studies about the cell cycle under Cr (VI) stress condition.

Keywords: Sunflower, E2F transcription factor, Real Time PCR, Cr (VI) stress

PT 073

Prediction of the Window of Implantation in a Minimally Invasive Method Via miRNA Biomarkes.

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IVF success rates obtained from ART clinics, indicate the need for new technologies, which will help improve the percentages of childbirth obtained via reproductive technologies. One reason for unsuccessful IVF is implantation failure of the embryo to the endometrium. The reason behind it is due to, most prominently, the window of implantation (WOI), a 3-4 day window in which the endometrium is receptive to the embryo, being misidentified. Currently there is no technology that can predict the WOI of a patient in the same cycle of sample collection. We identified specific microRNAs, using bioinformatic approaches, that are differentially expressed in the endometrium of females throughout their menstrual cycle with respect to the WOI. The candidate miRNAs that are highly expressed in serum were identified as well and their expression profiles in endometrium throughout the menstrual cycle have been determined. Our aim is to validate these miRNAs in serum samples, of patients and determine those that can be used as possible predictors of WOI in the same cycle.

Keywords: Window of Implantation, microRNA, Endometrium Receptivity, Serum

PT 074

Quantification of Serum Autologous Anti Tumor Antibodies as Small Cell Lung Cancer (SCLC) Biomarkers for Early Diagnosis

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Quick progression of Small Cell Lung Cancer (SCLC) is an obstacle on early diagnosis, treatment options and clinical studies. With the intention of addressing these problems 50 SCLC patient sera are pooled together, in parallel of 50 healthy sera pool, to be evaluated with Protein Array (PA) (of 25000 proteins). 180 autologous antibodies with highest serapositivity selected, and re-evaluated in individual SCLC patients' sera, which led to narrowing of the list to 13 biomarkers on the basis of Receiver Operating Characteristic (ROC) curve performances. Combination ROC curves are generated, and a panel of 4 proteins with best sensitivity & specificity levels (60% sensitivity, 100% specificity) is selected. This is significantly different and better than the only commercially available biomarker kit EarlyCDT Lung (41% sensitivity, 90% specificty) and our previous ELISA results. The difference in performance between ELISA and PA indicates method limitations such as lower limit of detection. Therefore, we are currently working on validating these results in different platforms.

Keywords: Early Diagnosis, Small Cell Lung Cancer (SCLC), Autologous Anti Tumor Antibodies, Protein Array, Elisa, Quartz Crystal Microbalance, Proximity Ligation Assay

PT 075

Functional Investigation of the Anti-neuroinflammatory Activity of the Novel Ciproxifan-Derivative ST-1505 in SH-SY5Y Cells as Multitarget Agent for Multiple Sclerosis and Cognitive Impairment

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ST-1505 is a novel ciproxifan derivative with potent histamine H3 receptor antagonist potency. The present study examines its potential anti-neuroinflammatory activity along with FTY720 in SH-SY5Y neuroblastoma cells. For this purpose, first, the cytotoxic effects of both FTY720 and ST-1505 were studied in SH-SY5Y cells to determine the none toxic doses. Then the changes in the mRNA expression level of the selected genes from the different inflammatory pathways (CSF1R, IL1B, IL6, IL10, IL13, IL18, TNF, LTA, IL2, IL2R A) were examined at non-toxic doses of both FTY720 and ST- 1505.Application of ST-1505 decreased CSF1, IL1B, IL6, IL10, IL13, IL18, TNF, LTA, IL2, IL2RA CCL3, CXCL10, CXCL11, CXCR3 CD28, CD40, CD44 and NFKB mRNA expression levels in SH-SY5Y cells by 3.5, 2.1, 1.1, 7.1, 4.3, 2.1, 6.0, 3.7, 5.6, 2.9, 5.8, 3.4, 3.6, 3.4, 2.1, 1.3-fold respectively; while IL-2 and IL-2RA showed an increase of 5.7, 2.4-fold respectively. The results support that ST-1505 inhibits T cell activation and proliferation and leukocyte migration. Therefore, it can be postulated that ST-1505 can be used as a multitargeting drug in the therapeutic treatment of cognitive-related disorders along with inflammatory responses in MS.

Acknowledgments: This work was supported by the Pamukkale University [PAU-BAP-2017FEBE050].

Keywords: ST-1505, FTY720, Fingolimod, Neuroinflammation, Multi-target, Multiple Sclerosis, Cognitive Impairment

PT 076

The Strigolactone and Karrikin Signaling Pathways in Prunus Species; an in Silico Analysis of the D14 A/B Hydrolase Protein Family, Dwarf14 (D14) and Karrikin intensive2 (KAI2) Genes

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As a recently identified phtyohormones, the Strigolactones (SLs) regulate plant architecture by modulating shoot and root branching. Recently, the several studies have been revealed transcriptome and genome data through next generation sequencing in Prunus spp., but SLs signalling pathways are still unknown. D14 belongs to α/β hydrolase superfamily and functions as SLs receptor. While, KAI2 determined as a paralogue of the D14. Since the chemical structure of karrikins and SLs are similar, those pathways should be investigated in detail. In our works, we obtained D14 and KARRIKIN INSENSITIVE2 (KAI2) sequences from available Prunus spp. databases and conducted a phylogenetic tree. Then, the gene structures and protein characteristics such as the signalling and functional sequences in promoter regions, sub-cellular localization, conserved regions, ligand receptor simulations and ligand binding site were determined with various bioinformatic tools.

Keywords: Strigolactone, Karrikin, DWARF14, KARRIKIN INSENSITIVE 2

PT 077

In-Vivo Determination of Colonic Mucin Degradation in Breastfed Infants with Altered Gut Microbiome

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Human colonic mucin glycoproteins (contain mostly O-glycans) protect the gut epithelium by keeping gut microbes from direct contact with the gut epithelium. Some gut bacteria such as Bacteroides and Akkermansia target these glycans to utilize them as a carbon source. In this study, we analyzed fecal samples obtained from 20 infants, 10 from infants colonized by Bifidobacterium infantis EVC001, which does not consume mucin glycans, and 10 from infants colonized by higher levels of mucolytic taxa (controls), including Bacteorides. Advanced mass spectrometry was used to compare microbiome profiles to assess how different gut microbiomes affected colonic mucin degradation. Mucin-like glycan species from control infants composed 37.2% (+/- 4.3% SD) of the total glycan structure pool, whereas mucin-derived glycans made up only 1.5% (+/- 0.9% SD) of the total in B. infantis EVC001 samples. These results suggest that colonization of infants by B. infantis may diminish colonic glycan degradation and help maintain the barrier function of mucus in the gastrointestinal tract.

Keywords: Mucin-like glycans, Bifidobacterium infantis, Glycome

PT 078

Comparison of Toxic and Antitoxic Effects of Cisplatin and cAMP, at C1A1 Gene Expression Level of Wistar Albino Type Rat Liver

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Throughout the course of cancer treatment with cisplatin or even suicide cases, no study has been conducted in vivo or in vitro on how gene expression changes are brought after the exposure to cAMP. cAMP is a chemotherapy chemical with antioxidant properties. İn this study as a model organism, liver tissues from Wistar-type albino rat, known as the laboratory rats was used. The toxicology related to one of the cytochrome p450 genes; the C1A1 gene expression in cells and tissues was examined, and TBP housekeeping genes was preferred for normalization. The results showed that; gene expression was reduced in tissues subjected independently to cisplatin and cAMP, however the tissues subjected to cAMP showed further reduction in gene expression. In contrast, tissues subjected to both cisplatin and cAMP showed an increase in gene expression. This study aims to provide an alternative perspective for comparative toxicology cases and will also serve as a guide for elucidation of cases connected with forensic toxicology.

Keywords: Cisplatin, cAMP, C1A1 gene, Forensic toxicology

PT 079

Investigation of NLP Recognition and Immune Response in Brassica Napus by Bulk-Segregant Analysis

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Brassica species are important crops used in bioenergy production as well as being an important food source consumed widely around the world. The first level of the plant immune response is PAMP-triggered immunity (PTI). PAMPs (Pathogen associated molecular pattern) are conserved molecules of microorganisms that elicits host`s defence response. NLPs (Necrosis & Ethylene-inducing like peptide 1-like proteins) are found in a wide range of pathogenic fungi infecting Brassica species, so improved understanding of their recognition could enable more disease resistant crops to be developed. To identify genes controlling NLP response, Bulk Segregant Analysis(BSA) will be used. Responsive and non-responsive lines had been crossed and DNA samples will be bulked with regards to responsiveness to NLP PAMP molecules after following sequencing reaction the outcome will be analysed by comparing to parental genotypes. Results will enable identification of gene markers that could be used to develop more durable disease resistance in Brassicas.

Keywords: Brassica napus, PAMP Triggered Immunity, Bulk Segregant Analysis, NLP-Recognition

PT 080

HOTAIR as a Prognostic Predictor for Multiple Human Malignant Diseases: a Meta-Analysis

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Several studies suggest that upregulated expression of the long non-coding RNA HOX transcript antisense intergenic RNA (HOTAIR) is a poor prognostic indicator in several cancers. However, there is an apparent inconsistency in the results of these studies. We conducted a meta-analysis to further investigate the prognostic value of HOTAIR expression in various types of cancers. To this end, a systematic literature review was conducted to select scientific studies relevant to the association between HOTAIR expression and cancer patients' overall survival (OS). 45 eligible studies including a total of 4300 patients were enrolled in the current meta-analysis. Pooled Hazard ratios (HRs) with their corresponding 95% confidence intervals (CIs) for patients' OS were calculated to assess the relationship between HOTAIR and the clinical outcome of cancer patients. High HOTAIR expression was found to predict poor OS. Therefore, HOTAIR could serve as a reliable prognostic biomarker in cancers.

Keywords: HOTAIR, Prognosis, Meta-analysis,

PT 081

Investigating Sequence Specificity in Mammalian De novo DNA Methyltransferases through Structural Insight

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De novo DNA methylation plays a significant role in mammalian embryonic development. It is carried out by two types of methyltransferases: DNMT3As and DNMT3Bs. DNMT3s impose DNA methylation more abundantly on CpG sites compared to non-CpG sites, i.e. CpA, CpT and CpC. Having this background as a basis, we aim at investigating the factors tuning the selectivity of DNMTs towards preferential methylation sites by using molecular modeling techniques. To understand preference towards CpG sites, we modeled bacterial methyltransferase and DNMT3A complexes. The models were optimized by simulated annealing through HADDOCK. We found structurally conserved recognition mechanism in complexes through comprehensive interaction network analysis. Furthermore, time-dependent behavior of DNMT3A complex was examined with molecular dynamics. This elucidated that DNMT3As' specificity towards CpG sites is strengthened by an arginine residue. We will further characterize the binding of DNMT3B to CpG site and DNMT3A/B to each non-CpG site.

Keywords: Specificity, De novo methyltransferases, Haddock, Molecular Dynamics

PT 082

Extracellular Production of a Fungal Xylanase in Recombinant P. Pastoris

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In this project xylanaseB gene, UNENxynB2, from the local isolate A. niger MRC200803 was used as gene source. It was expressed by the inducible AOX1 promoter in P. pastoris GS115 by utilizing the pPIC9 and pHIL-S1 vectors carrying HIS4 region. The codon optimized synthetic xynB (SxynB) gene fused to alpha factor and PHO1 signals which provides enzyme secretion. After transformation of the xynB subcloned secretion plasmids, 200 His+ clones were obtained, 71 clones were PCR analyzed. Recombinant xylanaseB activity was analyzed from crude extracts of the clones obtained from the fed-batch fermentation using shake flask, by inducing %0.5 methanol. Pichia Mut+ and Muts clones expressing the fungal xynB, were visualized by using %0.2 azo-dye crosslinked wheat arabinoxylan which allowed selecting SxynB expressed recombinants. Presence of a protein band about 20 kDa was observed in soluble crude extracts. For the high level of the heterolog enzyme expression and secretion, culture conditions will be optimized.

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Keywords: Xylanase, Protein expression,

PT 083

Cerium Oxide Nanoparticles Altered DNA Transition in Chlamydomonas Reinhardtii

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Cerium oxide (CeO2) nanoparticles are mostly used in industrial products. It is also a common nanoparticle in diesel engines due to getting better fuel combustion. CeO2 nanoparticles are common used nanomaterials and their potential effect on the environment has still not completely understood. In the present study, we investigated that effect of CeO2 nanoparticles on cell growth rate of Chlamydomonas reinhardtii, lipid peroxidation rate and macromolecular structure such as protein, lipid, and DNA using by FTIR analysis. Particle size and purity of CeO2 nanoparticles were determined by Scanning Electron Microscopy (SEM). FTIR analysis results indicated that β-sheet protein structure increased during the first 24 h, exposure to CeO2 nanoparticles. However, α-helix protein structure decreased at 72 h. Total lipid content was increased within 24 h after exposure to nanoparticles, while total lipid content decreased at 72 h. In the present study, we showed that DNA conformation structure was changed. CeO2 nanoparticles induced a transition from B-to Z-DNA.

Keywords: DNA, Cerium oxide nanoparticle, FTIR, Chlamydomonas reinhardtii

PT 084

Comparison of the Moleculer Mechanism of Melanocyte Regeneration and Melanoma Using the Zebrafish

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Molecular mechanisms of regeneration and cancer have always been a challenging question. At late stages,regenerating cells lose proliferation and are restricted to differentiation phase contrary to cancer cells. Furthermore, late stage regenerating cells lose migratory features whereas cancer cells maintain mesenchymal characteristics. Therefore, we hypothesized that molecular mechanism shared by cancer and regeneration is similar at early stages. However, cellular mechanisms must become dissimilar at late stage.We established melanocyte regeneration and melanoma models of zebrafish. We determined early and late stages of melanocyte regeneration. We checked expression of early and late melanocyte regeneration markers in hyper-pigmented and hypo-pigmented melanoma. Hypo-pigmented melanoma displays reduced expression of late melanocyte regeneration markers, which indicates that hypo-pigmented melanoma loses differentiated state and become more like a stem cell. This study would provide ground for the future studies that seek answer to similarities of these distinct processes.

Keywords: Melanocyte, Regeneration, Melanoma, Early/Late Regeneration

PT 085

AXL as a Potential Target in Liver Cancer

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The receptor tyrosine kinase AXL is overexpressed in various cancers and its overexpression is usually correlated with poor clinical outcomes.We identified AXL as a potential target of p73 protein and it is overexpressed in mesenchymal-like HCC cells. Previously, AXL was shown to be involved in invasion and metastasis in HCC. However, the exact mechanism in HCC has not been elucidated. Our study aimed further explore role of AXL in HCC. We found acute silencing of AXL expression by RNA interference abrogates invasion, migration and sorafenib resistance of some HCC cell lines.However, AXL knockdown by CRISPR–Cas9 strategy showed no significant change in metastasis, migration, proliferation and sorafenib resistance. Our knockdown studies disproved earlier reports involving AXL as a critical molecule for cancer malignancy. This phenotype in cancer cells could be due to their adaptation to AXL-free conditions during establishment of clones. Alternatively, AXL may play unexplored roles in cancer cells which will require further investigations.

Keywords: AXL, HCC

PT 086

Application of Genome Editing Techniques in Livestock

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Genetic modification technologies for targeted genomic regulation are relatively new molecular tools in the field of biology. For many years, genetic modifications in animals were based on transgenic technologies in the form of direct transfer of DNA sequences to embryos. However, in recent years, new programmable DNA nuclease techniques have emerged, such as ZFN, TALEN and CRISPR/Cas9. All these DNA nucleases, relying on protein-DNA binding, form DNA double-strand breaks (DBS) in a predetermined chromosomal region and mediate targeted genetic changes by increasing the DNA mutation rate. The results of the current studies show that any nuclease can be used in many applications such as in livestock genetics and breeding, improving growth performance, milk composition and animal welfare, producing non-allergenic animal products, and providing animals with resistance against infections and diseases. The aim of this study is to provide information on the principles of these three technologies and DNA nuclease applications in the regulation of farm animals' genomes.

Keywords: livestocks ZFN, TALEN, CRISPR/Cas9

PT 087

Determination of β-lactamase Genes in Antibiotic Resistant Acinetobacter Baumannii Clinical Isolates

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Antibiotic resistance is the ability of bacteria or other microorganisms to resist the antibiotic effect. Various mechanisms have been developed that may lead to antibiotic resistance in bacteria. The most common mechanism is the enzymatic inactivation of antibiotics. Resistance rates are increasing among pathogens causing serious hospital-acquired infections, including Acinetobacter spp. The aim of the study is to identify genes that play a role in resistance mechanisms in antibiotic resistant A.baumannii strains by molecular methods. 46 antibiotics resistant A.baumannii were provided. Antibiotic resistance determinants were determined by PCR method. blaOXA-51 is used for the identification of A. baumannii and blaOXA-51 was detected in all strains included in this study. According to PCR result, strains carried, blaOXA-23 (42/46), blaOXA-24 (1/46), blaOXA-48 (1/46) and blaOXA-GES (4/46). VEB, GIM, PER-2 and VIM genes were not found in isolates. The results show that class D beta lactamases are common in A. baumannii isolates.

Keywords: Resistance, Beta-lactamase

PT 088

IR Spectroscopic Approaches for the Study of Live Cells

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Infrared spectroscopy is a 'rejuvenated' technique widely used for many years. Recently, it has become popular for study of biological specimens (tissues, cells). Particularly, Fourier transform infrared spectroscopy combined with an attenuated total reflection (ATR-FTIR) unit provides rapid and label-free measurements without requirement of complex sample preparations. It has been successively used for sensitive probing of cells on the molecular level. IR spectra of cells provide valuable information about structural, compositional, dynamical and biophysical properties of biomolecules comprising mainly of lipids, proteins, nucleic acids and carbohydrates. Herein, live cell types (cancer, stem etc.) were measured with ATR-FTIR spectroscopy with application of unsupervised multivariate statistics. This work showed applicability of IR spectroscopy for tracking of modifications in composition, concentration and structure of cellular components, which might improve understanding of cellular mechanisms and deciphering of biomarkers crucial for targeted therapy against diseases.

Keywords: Live cells, Infrared spectroscopy, Cancer cells, Unsupervised multivariate statistical analysis

PT 089

Engineering and Functional Validation of Clonal Cell Lines with Stable Cas9 Expression for Genome-Wide CRISPR Screen in Malignant Pleural Mesothelioma

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Malignant pleural mesothelioma (MPM) is a rare cancer with an increasing incidence and low survival rates. Because existing treatment options are insufficient novel therapeutic modalities need to be discovered. In the present study, we employ genome-wide negative selection CRISPR-Cas9 screening to identify cancer cell essential genes and druggable targets in MPM. To this end, we engineered clonal sublines with permanent Cas9 nuclease expression in a panel of cell lines. For this aim, target cells were initially transduced with pLentiCas9-EGFP lentiviral vector and the highest eGFP expressing cells were FACS-sorted and further processed to generate single cell clones with consistent, uniform and high-level Cas9 expression. In addition, Cas9 protein expression and genome editing efficiencies were validated accordingly. Meanwhile we also amplified the Brunello gRNA library and are currently undertaking the necessary steps to initiate the in vitro screen. We highly anticipate that findings of this study will form the basis of our target discovery efforts in MPM.

Keywords: CRISPR-Cas9, Genome-wide screen, Malignant pleural mesothelioma

PT 090

The Role of Malt1 Paracaspase in Hepatocellular Carcinoma

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Hepatocellular carcinoma (HCC), the most common type of liver cancer is a multistage disease characterized by limited treatment options. It is well documented that NF-κB signaling is activated during hepatocarcinogenesis by different factors. Malt1 is a paracaspase that cleaves and removes negative regulators, thereby governs the activation, of NF-kB pathway. Based on TCGA HCC cohort data, elevated expression of Malt1 correlates with poor survival. Nonetheless, the role of Malt1 in HCC is elusive. In this study, we interrogated the effects of Malt1 inhibition in several HCC cell lines. shRNA-mediated gene silencing or pharmacological inhibition with MI-2 reduced cell growth in vitro. Furthermore, we employed a competition assay using CRISPR-Cas9 system to test for Malt1 dependency in HCC cells. Conclusively, our preliminary results suggest that Malt1 plays an important role in HCC growth. We are currently studying the molecular mechanisms underlying the growth regulating effects of Malt1. By all means, inhibition of Malt1 in HCC is a promising avenue to be explored further. Cas9 system to test for Malt1 dependency in HCC cells. Conclusively, our preliminary results suggest that Malt1 plays an important role in HCC growth. We are currently studying the molecular mechanisms underlying the growth regulating effects of Malt1. By all means, inhibition of Malt1 in HCC is a promising avenue to be explored further.

Keywords: Hepatocellular carcinoma, Nf-κB, MALT1, CRISPR

PT 091

Development of Gelatin Aptamer for Utilization in Biosensors

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Food authentication is gaining importance every day due to; increasing food fraud events and the production of food, which is subject to more processing with industrialization. This priority is a challenge for food analysis techniques and biotechnological studies. In this context, it is of utmost importance to discover and utilize functionally validated molecular biomarkers. Gelatin is an important and striking example of this area as it is present both as an expected content of some food and as an agent of fraudulent activities in other food. In this presented study, aptamers as affinity molecules were used to detect gelatin in samples. Aptamers are nucleic acid-based antibody alternatives with faster and cheaper development and utilization potential. They were selected from a pool of single-stranded random oligonucleotide library via SELEX method as a combinatorial approach. The selected and characterized gelatin-specific aptamers have the potential as the affinity molecule required to develop the lateral-flow-based gelatin biosensor.

Keywords: Gelatin, Aptamer, Biosensor, SELEX

PT 092

Functional Analysis of Glioma Associated SNP rs55705857 Located at 8q24.21

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SNPs are critical to our understanding of genetic susceptibility to cancer. rs55705857 is a SNP at 8q 24.21 that confers the highest risk on IDH-mutant glioma. Our group for the first time has shown that rs55705857 acts as a distal MYC enhancer and rs55705857-G allele increases this activity by omic analysis of patient tumors, as well as in vitro studies. To gain a more mechanistic understanding of how this risk allele acts, we CRISPR-edited iPSCs to create isogenic stem cell lines that differ only at rs55705857. Next, we differentiated iPSCs to OPCs (Oligodendrocyte Progenitor Cells), as these cells are believed to be the cell of origin of gliomas. OPCs are transduced by lentiviral Tet-On vector to create cells that stably express mutant IDH1 in a inducible manner. Studies (i.e. 4C-Seq, methyl-seq) are underway to characterize the epigenomic state of this locus and its dynamics in response to IDH1-R132H expression.

Keywords: Oligodendrocyte Progenitor Cells, SNPs, IDH1-R132H, 4C-Seq

PT 093

Topical Delivery of Heparin with Polymeric Microparticles

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Transdermal delivery systems designed to release drugs or bioactive agents through the skin. They are important in two ways. First, it minimizes the harmful systemic effects of the drug on patients by delivering the most of the drug locally. Also, it allows for better management of serious skin injury/illnesses such as burns, wounds, infections and cancer. In this study, heparin which is drug used for many clinical treatments will be encapsulated with various polymeric microparticles to achieve treatment of wounds and burns through skin. The loading of heparin to microparticles and entrapment efficiency of the heparin drug into the microparticles, the controlled release of drug from these microspheres will be examined. The purpose of the study is rapid and effective healing in the region that has deformed by wounds or burns because of the controlled release of drug into the target region.

Keywords: Heparin, Transdermal delivery, Micro particles,

PT 094

The Effects of Anti-Cancer Agents on 2D and 3D Cell Cultures in Breast Cancer Cell Lines

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Two-dimensional cell culture models used in vitro cancer research provide convenience and low cost, whereas it causes limited cell-cell interactions and changes in cell morphology, polarity, and cell division. Therefore, two-dimensional cell culture models can not exactly mimic in vivo tumor microenvironment. Three-dimensional cell cultures have morphological and physiological characteristics that are more similar to tumor structure compared to 2D cell cultures. Responses of 3D cell culture models to anticancer drugs will differ from those of 2D cell models. In this study, the effects of certain anticancer drugs on MCF-7, and MDA-MB-231 breast cancer cell lines were examined and compared in 2D and 3D cell culture models.

Keywords: 3D Cell Culture, Breast Cancer

PT 095

Investigation of Dimerization of Gα Protein by Förster Resonance Energy Transfer Method

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Ras family proteins are structurally analogous with the Gα proteins, therefore, they called as small G-protein. Recent studies show that Ras proteins are dimerized and this dimerization leads to many important signaling pathways in the cell. Similarly, dimerization is also observed in Dynamin protein which includes the GTP binding domain (G-domain) and it has an important role in GTPase activity. The hypothesis of this study is that Gα proteins can form dimers similar with Ras and Dynamin family protein. Within this scope, dimerization of the Gαi1 protein that is a member of the Gα protein family will be investigated with Förster Resonance energy transfer (FRET) which is an advanced fluorescent microscopy technique in live N2a cells. In addition, the effects of wild-type dopamine 2 receptors which signal through Gαi1 proteins by inhibiting adenylyl cyclase and wild-type Gαi1 protein on this dimerization will be studied. This work is supported by TUBITAK 117Z868.

Keywords: Gα protein, Dimerization, FRET

PT 096

Investigation of the Cellular Mechanisms of TGF-β-Induced Senescence-Resistance in Hepatocellular Carcinoma

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Hepatocellular carcinoma (HCC), the fifth most common cancer in the world, has high mortality rates due to lack of effective therapies. Senescence, a state of irreversible cell cycle arrest, is considered to be a barrier against tumor development. We previously reported that short-term exposure of well-differentiated HCC cells to Transforming Growth Factor-Beta (TGF-β) induced an immediate senescence response, proving to be a potential therapeutic window. However, the effects of long-term exposure to TGF-β is unknown. Here, we show that prolonged TGF-β treatment invoked a senescence resistance phenotype in Huh7 cells, characterized by hybrid epithelial/mesenchymal features. While the ontogeny of resistant cells and the molecular cues governing the onset of resistance (intrinsic or acquired) remain to be elucidated, our preliminary data impose that TGF-β-induced Smad signaling remains intact and further argue that other cell-autonomous mechanisms play a role. Comparative transcriptome analyses are currently being undertaken to identify key regulators of this phenomenon.

Keywords: Hepatocellular carcinoma, TGF-β, Senescence, Resistance,

PT 097

Modeling and Deorphanization of Orphan GPR141

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G protein-coupled receptors (GPCRs) are the largest transmembrane signaling molecules and regulate variety of physiological processes including metabolism, hematopoiesis, immune function and homeostasis. Although the roles of the many GPCRs have been identified in mammals, functions, expressions or ligands of them are not completely elicited and most of them remain orphans. To identify one of the orphan GPCRs, we analyzed the pattern of GPR141 mRNA expression across tissues from adult mouse. The receptor is highly expressed in endocrine tissues, however central nervous system is not showed any GPR141 expression. Our findings also showed that both the human, mouse and rat GPR141 sequences are highly conserved within transmembrane regions, but any orthologous genes are not exist in fish. Overall, this study will provide deorphanization of GPR141 by eliciting functions, internal ligands and expression patterns and may assist in the identification of therapeutic targets.

Keywords: G protein coupled receptors, Deorphanization, GPR141

PT 098

Systematic Comparison of Constitutive Promoters in Chinese Hamster Ovary Cells

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Following the developments in molecular biotechnology over the past two decades, the production of recombinant biological drugs has increased significantly. Chinese Hamster Ovary (CHO) cells are essentially the most preferred mammalian cell expression system for industrial manufacturing of biotherapeutics because of easy introduction of foreign DNA, adaptation to grow in suspension and most importantly human-like post translational modifications. In the present study, using recombinant DNA technology, we engineered a novel all-in-one dual-promoter reporter system to systematically compare the strength of natural viral, mammalian and endogenous promoters for high level of protein expression in various lines of CHO cells. We studied a large panel of candidate promoters and showed that CMV achieved the highest reporter activity. Conclusively, the dual-promoter reporter system minimized the variations typically observed in luciferase based tests and proved to be a useful system to identify strong regulatory elements ensuring high levels of expression in CHO cells.

Keywords: Biotherapeutics, CHO, Recombinant DNA technology, Promoter strength

PT 099

Identification of Small Molecules Stabilizing the Cryptochrome in the Mammalian Circadian Clock

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Circadian clock mechanism helps to maintain a daily rhythm of sleep/wake cycle, metabolism, and many other physiological processes. At the molecular level, circadian clock mechanism consists of a transcriptional-translational autoregulatory feedback loop. Cryptochrome proteins CRY1 and CRY2 are core clock proteins along with PER1/2, BMAL1 and CLOCK. The stability of CRY proteins can affect the period and amplitude of the circadian rhythm. The aim of this study is to identify small molecules that enhance CRY stability considering they can be effective for type 2 diabetes treatment. Initially, small molecules were selected by computational docking of small molecules to FBXL3-CRY1 interaction pocket. Experimental methods were used to characterize small molecules that either stabilize or destabilize CRY proteins in vitro. Two promising small molecules TW63 and TW68 increased half-life of CRY1/2 proteins, increased endogenous CRY1/2 levels and lengthened the period of the circadian rhythm in Bmal1-dLuc reporter U2OS cells.

Keywords: Circadian clock, Cryptochrome, Small molecule, Type 2 diabetes

PT 100

Triptolide Inhibits Proliferation, Migration and Epithelial–Mesenchymal Transition by Modulation Snail, Slug and Twist Expression in CD133+/CD44+ Colon Cancer Stem Cell

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Cancer stem cells (CSCs) are thought to be responsible for tumor initiation, relapse and metastasis. The association of epithelial-mesenchymal transition (EMT) and CSCs is considerable attention. Triptolide (TPL), a natural compound isolated from Tripterygium wilfordii, which has been shown to have cytotoxic effects and is recently reported to be associated with inhibition of migration, invasion and metastasis. The effect of TPL on cancer stem cells is not yet fully understood. The aim of the current study was to investigate whether TPL is effective against colon CSCs, and to elucidate the possible mechanisms for those effects by cell cytotoxicity, apoptosis, cell cycle, spheroid formation and migration assays. According to the results, TPL treatment induced cell death, apoptosis and cell cycle arrest and inhibited spefoid formation and migration. In addition, TPL significantly decreased snail, slug, and twist expression. The results indicated that TPL could be a useful therapeutic agent for colon CSCs.

Keywords: Cancer stem cell, Epithelial-mesenchymal transition, Triptolide, Spheroid formation

PT 101

The Axolotl Model for Limb and Spinal Cord Regeneration

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Axolotl (Ambystoma mexicanum) is a critically endangered salamander species and a model organism for regeneration and aging research due to its exceptional regeneration capacity. Despite life-long lasting neoteny in nature and in captive-bred colonies, metamorphosis can be experimentally induced by administration of Thyroid hormones (THs). Induction of metamorphosis leading to drastic decrease in capacity and fidelity of regeneration and molecular basis of this alteration is still unknown. In this study we compared the limb and spinal cord regeneration capacity of neotenic and metamorphosed Axolotls by following the transcriptomics and proteomics approaches in combination with gene expression modulation tools. Our results indicate the differential regulation of gene expression for cell adhesion and signaling molecules at early steps of regeneration for neotenic and metamorphosed animals. Our current effort to establish transgenic and knockout Axolotls would provide novel insights into molecular players of regeneration.

Keywords: Axolotl, Regeneration, Omics, Metamorphosis

PT 102

Verification of Novel Wnt/B-Catenin Pathway Targets

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Wnt/B-catenin pathway is found to be one of the most important intracellular pathways leading to cancer(1). Previous studies in our laboratory identified BRI3 and MGAT1 genes as novel targets of Wnt/B-catenin pathway(2). Functional characterization of both genes proved that Huh7 cells (hepatocellular cancer cell line) stably expressing either BRI3 or MGAT1 have greater proliferative and invasive capabilities compared to wildtype Huh7 cells, and when subcutaneously injected into NUDE/SCID mice resulted in tumor formation. Tumors were subjected to RNA-Sequencing for further investigation. We observed differential expression of certain genes involved in several cellular pathways. Among these genes, we continued with YAP1, CSNK2B, and AFP in BRI3 expressing cells; and EDNRB, ADAM17, and HSPA8 in MGAT1 expressing cells. We validated differential expression levels by using Western Blot and Q-PCR techniques. We further aim to shed light into the crosstalk between different signaling pathways involved in cancer progression.

Keywords: Hepatocellular cancer, Wnt/B-catenin pathway, BRI3, MGAT1

PT 103

Citric Acid Stress Results with Cell Cycle Abnormalities and Activates GPD1 Expression in MAPK Hog1p/p38 Dependent Manner.

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Citric acid is the natural intermediary metabolites and widely used in pharmaceutical and food industry. We have investigated the effects of citric acid stress on the cell cycle and on the transcriptional regulation GPD1 gene in S. cerevisiae. Our results indicated that citric acid activates Hog1p, which is ortholog of human p38 kinase, involves in regulation of various cellular processes in response to multiple stress conditions. In the presence of excess citric acid, yeast cell cycle arrested at G2 and/or mitosis stage and formed abnormal budding patterns. In addition citric acid activates the transcription of GPD1 gene at least 3-fold in a Hog1p dependent manner. GPD1 is the key enzyme that required for the maintenance of cytoplasmic redox balance. Results of this study indicate that citric acid stress affects cell cycle progression and redox balance in eukaryotic cells in a MAPK Hog1p/p38 dependent manner.

Keywords: Citric Acid, Hog1/p38 Kinase, Cell cycle arrest, GPD1

PT 104

HIV-1 Tat Induces SLPI Expression in African Green Monkey Cells

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Although Old World Monkey Cells (OWMs) are resistant to Human Immunodeficiency Virus-1 (HIV), high titer of virus can lead an infection. However, following infection, viral load drops. We hypothesized that OWMs exhibit such post-infection resistance by changing expression of specific genes via viral proteins. Since Tat is the first protein to be synthesized during post-infection, we induced stable Tat expression by applying transfection in CV-1 and Vero cell lines. Mass spectrometry data revealed that Secretory Leukocyte Protease Inhibitor (SLPI) was overexpressed in OWMs in the presence of HIV-Tat. Moreover, SLPI overexpression studies demonstrated that SLPI downregulated LTR promoter of HIV in the presence of Tat gene. Currently, we are working on the generation of an SLPI null CV-1 cell lines using Crispr-Cas9 approach to confirm the effect of SLPI on LTR promoter. Targeting SLPI may provide therapeutic opportunities to reduce pathogenicity in HIV-positive individuals.

Keywords: African green monkey, Human Immunodeficiency Virus, SLPI, Tat

PT 105

Assessment of Prenatal Screening Performance for Aneuploidies in 13, 18, 21 and Sex Chromosomes Using Massive Parallel Sequencing Technique

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The goal of our study is to retrospectively evaluate the performance of massively parallel sequencing of cell-free deoxyribonucleic acid (DNA),with a special focus on samples where the fetal DNA fraction is calculated to be relatively low. Study was designed as a multicenter observational study of samples collected from expecting mothers, who have made the decision to pursue non-invasive testing for prenatal genetic testing using the NIPT test after detailed introduction of the analysis, its limitations and performance. Massively parallel duplexed-read sequencing of cell-free DNA was performed in maternal blood samples using Illumina® systems. Data analysis was completed using sequence reads from all chromosomes. Our retrospective study demonstrates that non-invasive prenatal analysis of cell-free deoxyribonucleic acid from maternal blood plasma is an accurate advanced screening test with extremely high sensitivity and specificity for trisomy 21, trisomy 18, and trisomy 13, but with less sensitivity for common aneuploidies observed in the sex chromosomes.

Keywords: Massively parallel sequencing, Prenatal genetic screening Fetal DNA fraction, Sensitivity

PT 106

Comparison of Molecular Properties of Breast Milk and Formula using Fourier Transform InfraRed Spectroscopy

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The aim of our study is to quantitatively compare molecular properties of breast milk and commercial infant formula samples using Fourier Transform Infrared (FTIR) Spectroscopy. Breast milk samples were obtained from Celal Bayar University, and infant formulas were purchased locally. Spectrums were obtained for each breast milk sample and their binary mixtures with different formulas prepared in proportions of 10, 20, 30, 40, 50, 60, 70, 80 and 90%. Multivariate Analysis of the obtained spectra was performed to quantitatively analyse the differences. A successful breast milk and formula discrimination and classification were achieved using Principal Component Analysis (PCA). The results of the study indicated that human breast milk and infant formula samples can be quantitatively monitored by the FTIR technique relatively fast and with high accuracy. In conclusion, this technique could be used as a new alternative method for analysis of breast milk and formula contents.

Keywords: FTIR, Breast milk, Infant formula, Principal Component Analysis (PCA)

PT 107

Analysis of ROBO2 Dependent Gene Signature in Huh7 Hepatocellular Carcinoma Cells

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ROBO2 is a member of SLIT-ROBO family and its role in axon guidance is well-described as a receptor for SLIT ligands. SLIT-ROBO interactions are also implicated in other physiological context in mice, like lung and kidney development. Here, we identified genes associated with human ROBO2 by stably knocking down ROBO2 in Huh7 hepatocellular carcinoma cell line and comparing gene expression patterns in knock-down and control cells by microarray analysis using Cytoscape software and ClueGO pathway analysis tools. Our results show that human ROBO2 has functional interaction with genes in the regulation of systemic arterial blood pressure, and complement and coagulation cascades. Low stringency biological process analysis revealed the ROBO2's known physiological functions like cardiac septum development and kidney development. Furthermore, in validation experiments, we showed that ROBO2 downregulation results in increased expression of CD133, a well-known cancer stem cell marker. Overall these results pinpoint the role of ROBO2 in physiological context.

Keywords: ROBO2, shRNA, Hepatocellular carcinoma, Microarray

PT 108

Mechanistic Dissection of Centriolar Duplication Proximity Maps Identifies a Novel Regulator of Centrosome/Cilium Complex

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Centrosome is composed of two centrioles and a pericentriolar material (PCM). While centrioles act as basal bodies to form the cilium, a nexus for important signaling pathways, PCM nucleates the radial microtubule array. Defects in centrosome/cilium complex are associated with numerious diseases. Previously, we generated proximity interaction maps for centriole duplication proteins to identify candidate regulators of centriole duplication. Given its high proximity to known duplication proteins, we chose to characterize CEP103 for its localization, interactions and functions. CEP103 localizes to the proximal end of the pericentriolar material and interacts with the microcephaly protein CEP63. Moreover, it binds to microtubules and localizes to the interphase microtubule network, spindle microtubules and spindle midzone in mitotic cells. Cells depleted for CEP103 results in defects in cilium formation, length and microtubule localization. Together, our findings identify a novel centrosome protein with important functions in cilium and microtubule-related processes.

Keywords: Centrosome/Cilium, Microtubule, CEP103, CEP63, Centriole Duplication

PT 109

The Expression Analysis of Genes in Unfolded Protein Response System in PRKAG2 in vitro Mutated Cells

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Accumulation of mutant proteins causes ER stress, then the cell activates UPR consisting of three pathways controlled by IRE1, PERK and ATF6 proteins. We evaluated in vitro E506K, E506Q and R531G mutations in PRKAG2 gene, which are causing PRKAG2 cardiomyopathy, in terms of ER stress. Wild-type and mutant-types which made with site-directed mutagenesis on PRKAG2 gene was transfected to HEK293 cells. BiP, CHOP, GADD34, ATF4, EDEM1, PDIA4, TRAF2, ASK1, XBP1 and HERP genes analysed in Tunicamycin treatment and transfected cells by q-PCR. Also IRE1α, PERK, ERO1A and BiP proteins were examined by western blot. GADD34, XBP1, HERP, TRAF2 and EDEM1 transcripts were decreased in some mutant cells. In protein analysis of mutant cells, IRE1 and PERK levels were increased 1.3-fold (were decreased in other 2 mutants) while ERO1A and BiP levels were decreased in E506K mutants. Mutant cells did not show significant ER stress but there were differences in the transcriptional and protein levels of selected UPR genes. This study was supported by IU BAP(TYL-2017-27803) and TUBITAK (115S137).

Keywords: ER Stress, Unfolded Protein Response, AMPK, PRKAG2 Cardiomyopathy

PT 110

Molecular Identification of DNA Sequence Variants Using Fourier Transform Infrared Spectroscopy

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Attenuated Total Reflection Fourier Transform Infrared (ATR-FTIR) spectroscopy was utilized to analyze a panel of simple oligonucleotides designed to represent selected sequence variants. Combining this analysis with multivariate analysis (MVA), we were set to determine whether the variation can be detected using the molecular signatures embedded in the ATR-FTIR spectrum. Oligonucleotides that were 21 bases long were used in our studies to enable identification of molecular signatures associated with the sequence variations. Careful selection of DNA fragments to be analyzed, along with modifications associated with oligonucleotide preparation will enable the technique to be utilized as a screening method for circulating cell-free DNA analysis for prenatal tests. ATR-FTIR spectroscopy combined with MVA was able to accurately show differences in the sequences, suggesting that this can be used as a rapid, effective and inexpensive alternative to current technologies interrogating different forms of DNA sequence.

Keywords: Mutation Polymorphisms, FTIR, NIPT,

PT 111

Myogenic Differentiation and Fusion Defects in Myoblasts Lacking LAP1B

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Loss-of-function of the ubiquitously expressed nuclear membrane protein LAP1B (lamina-associated polypeptide 1, isoform B) causes muscular dystrophy. However the mechanisms responsible for muscle specificity caused by LAP1B deficiency and its role in muscle is not known. We established an in vitro model using LAP1B-mutant fibroblasts isolated from patient and differentiated in muscle cells by using MyoD gene transfer. Although transduction efficiencies were similar, differentiation and fusion indexes were significantly lower in mutant cells compared to control. While control myoblasts started to express myosin-heavy chain isoforms 2 days after induction, expression was observed after 5 days in mutant myoblasts. We also created LAP1B-mutant C2C12 mouse myoblast cell lines using CRISPR/Cas9 and observed a delayed myogenic differentiation in mutant cells. In conclusion, we hypothesize that LAP1B could have a transcriptional regulatory function in muscle cells by interacting with proteins involved in myogenic signaling. This study is funded by TUBITAK (Project No 116S307).

Keywords: LAP1B, Myogenic differentiation, CRISPR/Cas9

PT 112

Investigation of Irf4 Regulated Epigenetic Factors in Melenoma Cells

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Interferon regulatory factor 4 (IRF4) transcription factor has key roles in development and function of various cells such as immune cells, and melanocytes. Studies have shown high IRF4 expression in hematopoietic and melanoma cancers. Recent studies from our lab and elsewhere have shown that melanocytes and melanoma cells are sensitive to IRF4 expression. Yet, there are no studies about IRF4 transcriptionally regulated genes in melanoma. Here, we aim to identify genome-wide target genes of IRF4 in melanoma cells. We carried out high-throughput sequencing of immunoprecipitated chromatin in melanoma cells (ChIP-seq). Following transcriptome analysis, we defined small set of IRF4 target genes for further investigation. Among this set, we found several genes with vital roles in transcriptional regulation of melanoma tumorigenesis. Furthermore, we validated those targets, their effects on epigenome and downstream pathways in melanoma cells. Our results suggest a potential role for IRF4 as regulator of the epigenome in melanoma.

Keywords: IRF4, Melanoma, Gene regulation

PT 113

Disease Modeling in Zebrafish: Limb-Girdle Muscular Dystrophy 2R

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The objective of this study is to model LGMD2R (MIM 615325) in zebrafish. We created a frameshift mutation (c.1273delAG) in desma gene by TALEN. Whole-mount in-situ hybridization results showed mutant desma transcript is expressed in embryos (48, 72 and 96 hpf), however the expression levels of mutant desma was decreased about 66% in embryos and 55% in skeletal muscle of adult zebrafish (p=0.0003). Desmin expression in mutant adult zebrafish skeletal muscle was also showed by WB and IF. To understand the neuromuscular defect caused by mutation, motility assay was performed on 48 hpf embryos. The results showed that mutant embryos were significantly slower than WT controls (p=0.0004). In adult mutants, ultrastructural analysis (TEM) and calcium influx experiments showed degenerative muscle and delayed decay of calcium transient. We suggest this is a proper model for LGMD2R. However, it still needs additional data which confirms that skeletal muscle phenotype is similar with the patient's. This project is funded by TUBITAK (Project no: 214S174).

Keywords: Zebrafish, Desmin, Disease modeling, LGMD

PT 114

Characterization of Circulating Exosomes and Analysis of Exosomal microRNAs

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Exosomes are 30-120nm sized nanovesicles which are the carriers of molecules such as microRNAs(miRNAs), lipids, proteins and they can be found in many biofluids. In this study, we aimed to techniqually optimize isolation and characterization of exosomes by TEM technique and analyze exosomal miRNAs. For this purpose, exosomes were isolated from 0,5 or 1,5ml blood serum and plasma with miRCURY Exosome Serum/Plasma Kit. For TEM analysis, formvar coated carbon grids were used, exosomes were fixed with Osmium tetroxide(OsO4) and stained with uranyl acetate(UA) or %2 phosphotungstic acid(PA). MiRNAs were isolated from exosomes by using miRCURY RNA Isolation Kit. We demonstrated that exosomes can be visualised under TEM in both staining conditions but PA gave better results compared to UA. Also, the concentrations of RNA isolated from exosomes of 1,5ml serum/plasma and 0,5ml serum/plasma starting material varied in between 5-12 ng/µl and 1-8 ng/µl respectively. This work was supported by Hacettepe University Scientific Research Coordination Unit. Project Number: THD-2017-16316

Keywords: Exosome, microRNA, Transmission electron microscopy

PT 115

The Effect of CDP-Choline on Mitophagy and Mitochondrial Dynamics in Monocytic Cell Line

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Damaged and dysfunctional mitochondria can cause cellular degeneration, which then leads to neurodegenerative, metabolic and cardiovascular diseases. CDP-Choline is the source of choline and cytidine and is an important key factor in the Kennedy Pathway for production of phosphatidylcholine (PC). PC is one of the most abundant phospholipids of mitochondrial membranes. During mitophagy, the level of phosphatidylcholine is decreasing on mitochondria. In this study, we investigated the effect of CDP-Ch on mitophagy in U937. Mitophagy was induced at different points by CCCP in the presence and absence of CDP-Ch. Mitochondrial dynamics and mitophagy were investigated upon pretreatment of CDP-Ch by western blotting and flow cytometry. We observed changes in mitochondrial superoxide, membrane potential, and content. Different indicator proteins of both mitophagy and mitochondrial dynamics DRP1, MTF2, TOMM20, COXIV, PINK1 were also analyzed.

Keywords: Mitophagy, Lipids

PT 116

DNA Methylation Analysis Pipeline

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DNA methylation is the most studied epigenetic modification and associated with a number of key processes including genomic imprinting, repression of transposable elements, aging etc.. DNA methylation studies are increasingly being considered for discovering biomarkers for patients at risk of developing disease. The number of tools developed for whole genome bisulfite sequencing has been increasing steadily as the researches in this area increase. The purpose of this study is to provide a methylation analysis pipeline starting with data processing and ultimately getting differentially methylated regions at CpG sites. The pipeline is based on Linux and R platforms and it comprises 3 main steps: first of which is quality control of raw data and editing (FastQC for data quality check, Cutadapt, TrimGalore and Trimmomatic for editing), second of which is alignment (bismark, bsmap, bsSeeker2), the last step is differential methylation analysis (methylkit, methyArray). This pipeline can be used as a guide for researchers to select appropriate tools for methylation analysis.

Keywords: Epigenetics, DNA methylation, Data processing, Methylation analysis pipeline

PT 117

Mineralocorticoid Receptor and Aldosterone Signaling in Breast Cancer

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Only recently, mineralocorticoid receptor (MR) together with its natural ligand, aldosterone, has gained attention in cancer biology. Our study focuses on MR and aldosterone signaling in breast cancer. Initially, we showed differential MR mRNA and protein expression among breast cancer cell lines and normal-tumor breast tissue. Next, transcriptome alterations of MR-overexpressing and MR knock-down (siRNA) models were studied employing RNA-Seq. Aldosterone-treated MR-overexpressing MCF7 cells showed significant changes in transcriptome, which was reversed by the MR antagonist, spironolactone. MR-knocked-down T47D cells also modulated transcriptome to a lesser degree than in the overexpression model. Additionally, we showed significant effects of MR overexpression on cell viability and proliferation in the presence of aldosterone and spironolactone by MTT assay in MCF7 cells. We are currently in the process of developing a zebrafish xenograft model for in vivo validation of our in vitro cell viability and proliferation findings. This study was funded by TUBITAK (114S226).

Keywords: Mineralocorticoid receptor, Aldosterone, Breast cancer, RNA-Seq, zebrafish xenograft

PT 118

High-Resolution Melt Analysis of FOXP3 TSDR Methylation in Peripheral Blood of Psoriasis Patients

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Psoriasis is a common, immune-mediated inflammatory disease which is characterized by red coloured plaques with silvery-white dry scales on the skin. Regulatory T (Treg) cells, which are responsible for suppressing the activity of effector T cells, are characterized by high levels of FOXP3 expression. Methylation level of Treg cells is thought to have an impact on the pathogenesis of autoimmune diseases and psoriasis. In this study, we aimed to determine the levels of FOXP3-TSDR methylation with HRM-PCR and the levels FOXP3 mRNA expression with real-time PCR in the peripheral blood samples of psoriasis patients. In the patient (n=38) and control (n=20) groups, FOXP3-TSDR was fully methylated. There was no significant difference between the melting temperature values and FOXP3 mRNA levels of two groups. In conclusion, it is suggested to analyse the FOXP3-TSDR methylation level of patients with psoriasis using more precise methods and larger sample sizes in further studies.

Keywords: Psoriasis, Regulatory T cell, FOXP3 TSDR, Methylation

PT 119

In-Vitro Phenotypic Rescue of Citrullinemia Disease Specific Liver Organoids

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Stem-cell-derived organoids offer increasingly sophisticated models for studying human development and disease, as well as powerful emerging tools for personalized medicine. Here, we first developed a novel method to produce human Induced Pluripotent Cells (iPSC)-derived liver organoids for modeling Citrullinemia type I, an inherited urea cycle disorder of the liver that results from deficiency of the enzyme argininosuccinate synthase (ASS1). Upon differentiation of the organoids from FACS-enriched endodermal progenitor cells, we obtained functional hepatic organoids from healthy donors and citrullinemia patients and showed disease phenotype in vitro as decrease in ammonia elimination capacity. We then overexpressed the wild-type ASS1 gene in the patient derived organoids and observed the significant phenotypic rescue in vitro. Therefore, this study provides us a powerful technology which can be used in personalized drug screening and cell-based therapies as well. This study was supported by TUBITAK projects with no: 115S465 and 213S182.

Keywords: Liver organoids, iPSC

PT 120

Transcriptomics Analysis Reveal Cancer Stem Cell Alters Trio-Pathways; Androgen, Inflammasome, and RAB GTPase in Prostate Cancer

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Aim: We investiagted differential gene expression (DGE) analysis between prostate cancer cell-line enriched with Cancer Stem Cell (DU145+CSC) and prostate normal epithelial cell-line (RWPE) and their possible roles in Androgen, Inflammasome, RABGTPase pathways to find underlying reasons for oncogenesis and their relationship. Methods: "edgeR" and "limma" R packages were used for normalization and linear-model fitting. "clusterProfiler" package used to enrich DGE. Results: In DU145+CSC, inflammasome-related NLRP2, PYCARD, CASP1, IL18,IL1ß, and 19 Rab-family genes were significantly down-regulated, however, IL6 and 10 Rab-family genes were significantly up-regulated. Although Androgen Receptor (AR) expression was insignificant, 658 genes of the Androgen pathway and 471 genes were significantly down-regulated and up-regulated, respectively. Surprisingly, MMP14 was found significantly down-regulated (adj.p <0.0001). Conclusion: Enrichment of CSCs in prostate cancer cell lines may play imperative roles in altering the Androgen, Inflammasome, and Rab-GTPase pathways.

Keywords: Cancer Stem Cells, Prostate Cancer, Androgen, Inflammasome, RAB GTPase, Bioinformatics Pipeline

PT 121

Dissection of NK Cell-Tumor Cell Interactions Using Genetically Modified NK-92 Cells

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NK cell-mediated cytolysis relies on a complex balance between several activating and inhibitory receptors that either promote or dampen killing upon receptor-ligand interactions. Here, we aim to upregulate a single NK cell receptor at a time and their comparison may reveal understanding the basics of this interaction. NK-92 cells were genetically engineered by using lentiviral vector backbones encoding for 20 different NK cell surface receptors. New cell lines, each overexpressing a specific receptor, were subjected to phenotyping and assessment of effector functions. Degranulation against K562 cell line showed significantly higher cytotoxicity especially in CRACC, DNAM-1, NKG2D transduced NK-92 cells compared to wildtype and backbone controls. Lentiviral genetic modifications did not disrupt or hamper cytotoxicity of NK-92 cells but rather induced enhaced cytolysis against specific tumor ligands. Unravelling this mechanism has potential use in developing NK cell-based immunotherapy approaches.

Keywords: Molecular Immunology, NK cells, Cancer immunotherapy

PT 122

Molecular Characterization of a Novel lncRNA

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Apoptosis induction can kill cancer cells without harming the individual. For this purpose, novel methods are developed to fight the cancer cells and one of them is based on long noncoding RNAs (lncRNAs). LncRNAs are differentially expressed in cancer cells and they regulate and interact with essential pathways. In this study, candidate lncRNA was determined based on RNA-Seq data. Then apoptosis was induced in HeLa cells with cisplatin and qRT-PCR was performed with isolated RNAs from cells to validate the data. Then GapmeR specific to candidate lncRNA was designed and transfected into HeLa cells to induce apoptosis. Then total RNA and protein were isolated from the cells. qRT-PCR was performed to validate RNA-Seq data. Western blot was performed to characterize candidate lncRNA by controlling its effects on different apoptosis pathways. Results show the resemblance between GapmeR-induced and cisplatin-induced apoptosis. Candidate lncRNA is directly regulating the apoptosis in HeLa cells and in this study, some of the pathways that are regulated with this lncRNA were shown.

Keywords: long non-coding RNA, Apoptosis, HeLa, Cancer

PT 123

Regulation of hTERT Promoter in Brain Cancer Cell Lines

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To avoid cellular senescence, cells need to either reactivate catalytic subunit of telomerase or lengthen their telomeres by alternative lengthening of telomeres (ALT). Recent studies show that DNA methyltransferases and their expression levels impact both telomerase- and ALT mediated lengthening of telomeres, and can have different outcomes in different tissue types. Using zebrafish as a model, we observed differences in methylated regions between young and old brains and we hypothesized that these regions were associated with telomere shortening. By silencing DNMT1 in brain cancer cell lines, we investigated the changes in gene expression of related genes, telomerase activity and Sp1 binding to the hTERT promoter. To further investigate hTERT regulation, we introduced mutations to the Sp1 binding sites in promoter region and measured the promoter activity with luciferase assay.

This work has been supported by a TUBITAK 1001 grant (no: 114S548) and Hacettepe University BAP grant (THD-2017-15492).

PT 124

Identification of Novel Targets for The Role of PKC Isozymes on The Regulation of Autophagy

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Protein Kinase C isozymes are Serine/Threonine kinases that are important in regulation of cellular mechanisms and intracellular signal transduction pathways including autophagy. In this study, we aimed to find novel proteins targeted by PKC isozymes during autophagy mechanism. Lentiviral shRNA library was used for silencing of the genes in signalling pathways. MEF GFP LC3 transgenic cells were treated with PKC activators. Upon activation of the kinases, cellular autophagic machinery was examined with GFP-LC3 puncta count, LC3 shift assay and P62 accumulation. In basal condition of monoclonal cells, the autophagosome formation was increased by ceramide, PMA and ionomycin. The positive clones were selected, and their genomic DNA was isolated for target gene sequencing. Consequently, the role of PKC isozymes in the regulation of autophagy was determined by identifying targets upon treatment. (This work was supported by The Scientific and Technological Research Council of Turkey (TUBITAK). Project No:114Z836)

Keywords: Autophagy, PKC, ceramide, PMA, ionomycin

PT 125

ERα regulates Adipogenic Differentiation of Mesenchymal Stem Cells Through Modulating Epigenetic Modifications

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ST-1505 is a novel ciproxifan derivative with potent histamine H3 receptor antagonist potency. The present study examines its potential anti-neuroinflammatory activity along with FTY720 in SH-SY5Y neuroblastoma cells. For this purpose, first, the cytotoxic effects of both FTY720 and ST-1505 were studied in SH-SY5Y cells to determine the none toxic doses. Then the changes in the mRNA expression level of the selected genes from the different inflammatory pathways (CSF1R, IL1B, IL6, IL10, IL13, IL18, TNF, LTA, IL2, IL2R A) were examined at non-toxic doses of both FTY720 and ST- 1505.Application of ST-1505 decreased CSF1, IL1B, IL6, IL10, IL13, IL18, TNF, LTA, IL2, IL2RA CCL3, CXCL10, CXCL11, CXCR3 CD28, CD40, CD44 and NFKB mRNA expression levels in SH-SY5Y cells by 3.5, 2.1, 1.1, 7.1, 4.3, 2.1, 6.0, 3.7, 5.6, 2.9, 5.8, 3.4, 3.6, 3.4, 2.1, 1.3-fold respectively; while IL-2 and IL-2RA showed an increase of 5.7, 2.4-fold respectively. The results support that ST-1505 inhibits T cell activation and proliferation and leukocyte migration. Therefore, it can be postulated that ST-1505 can be used as a multitargeting drug in the therapeutic treatment of cognitive-related disorders along with inflammatory responses in MS.

Acknowledgments: This work was supported by the Pamukkale University [PAU-BAP-2017FEBE050].

Keywords: ST-1505, FTY720, Fingolimod, Neuroinflammation, Multi-target, Multiple Sclerosis, Cognitive Impairment

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