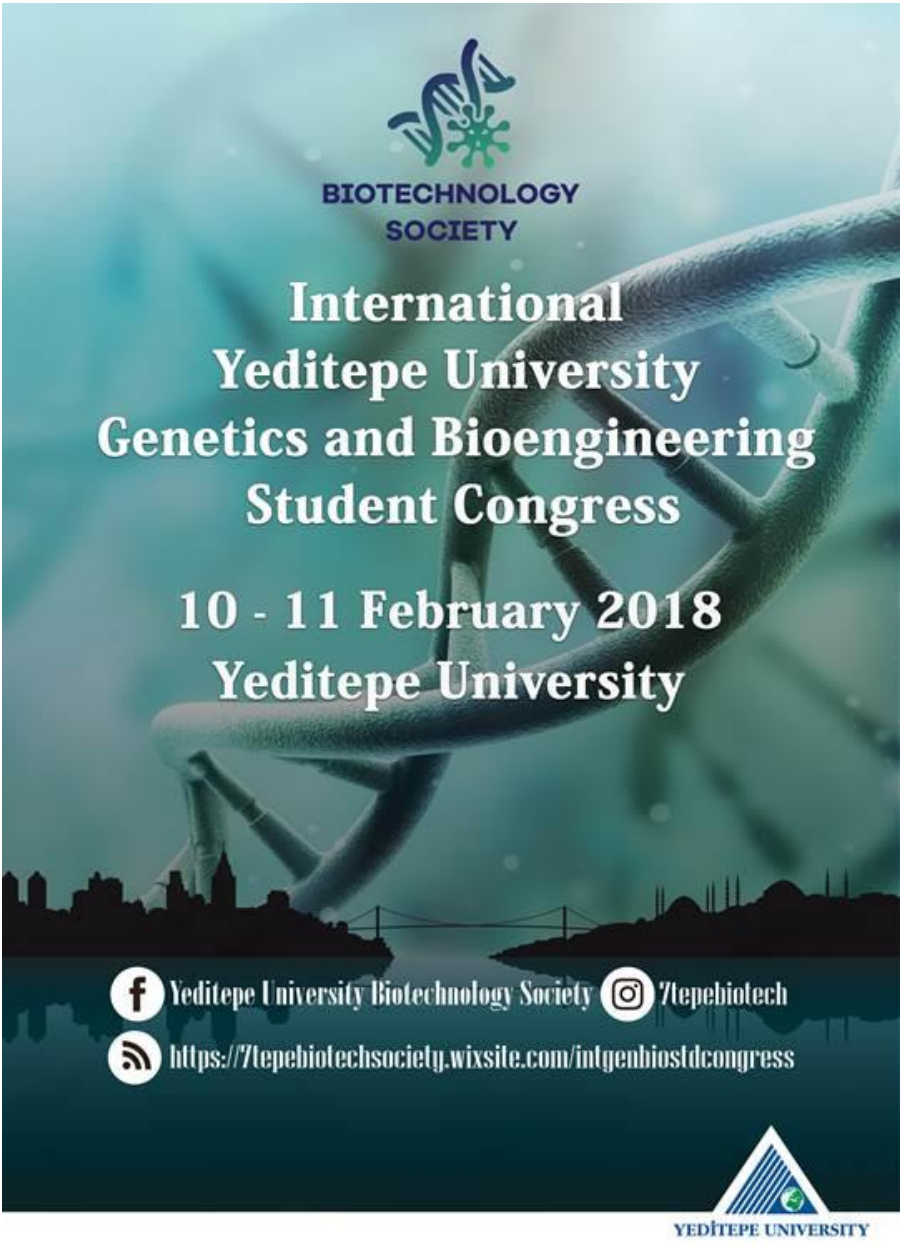
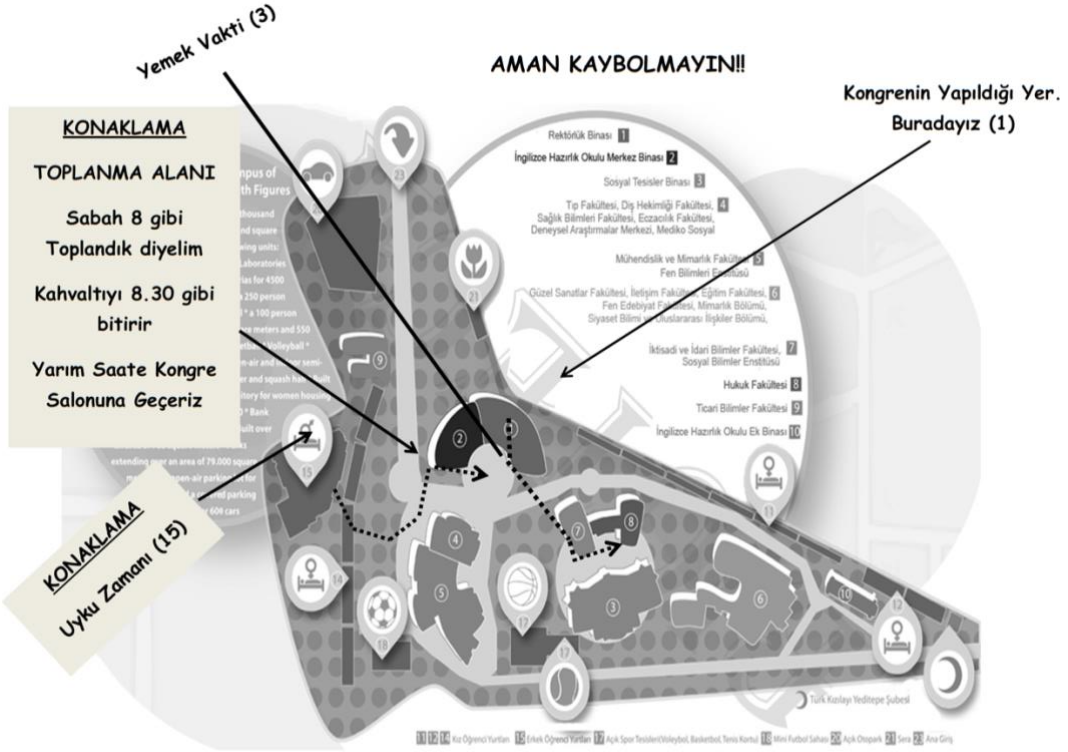


ABSTRACT BOOK



"Konaklama" başlıklı açıklamalar sadece
Konaklamalı katılımcılar için geçerlidir.

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10 February / Saturday

8:40 – 9:20 Registration

9:20- 10:00 Opening ceremony

10:00-10:50 **Assoc. Prof. Dr. Pedro Gil Frade Mourouco-** R&D Biofabrication Group at the Centre for Rapid and Sustainable Product Development, Sport Sciences at the Polytechnic Institute of Leiria (IPL)

Four-dimensional bioprinting: stimuli-responsive mechanisms for biomedical applications

10:50-11:10 Coffee Break

11:10-12:00 **Assist. Prof. Dr. Shirin Tarbiat-** Uskudar University

PPARs, Obesity and Cardiovascular Diseases

12:00-12:50 **Assist. Prof. Dr. Yongsoo Park-** Koç University

miRNA exocytosis by large dense core vesicle fusion

13:00-14:00 Lunch Break

14:00-14:50 **Assist. Prof. Dr. Andrew Harvey-** Yeditepe University

14:50-15:40 **Assoc. Prof. Ralph Meuwissen-** Dokuz Eylül University

Lung Cancer

15:40-16:00 Post-doctoral Researcher Presentation

16:00-16:30 Coffee Break / Workshop

16:00-17:00 Poster Session

11 February /Sunday

10:00-10:50 **Prof. Dr. Minoo Rassoulzadegan -** University of Nice Sophia Antipolis

RNA-mediated epigenetic heredity: experimental mouse models of an acquired pathology

10:50- 11:40 **Dr. Cristopher Mayack -** Sabancı University

Ecology, evolution and animal behavior

11:40-12:00 Coffee Break

12:00-12:50 **Assist. Prof. Dr. Andres Octavio Aravena Duarte -** Istanbul University

Bioinformatics + Biotech in high impact strategic industries

13:00-14:00 Lunch Break

14:00-14:50 **Assist. Prof. Dr. Gerhard Wingender –** İzmir International

Biomedicine and Genome Institute (IBG), Dokuz Eylül University

Immunology of Innate T Cell's

14:50-15:40 **Assist. Prof. Dr. Allen Liu** - University of Michigan

Microfluidics for single cell mechanobiology

15:40-16:00 Post-doctoral Researcher Presentation

16:00-16:20 Coffee Break

16:20-17:00 Poster Sessions & Closing ceremony

CONTENT

1. Speaker abstracts

Assoc. Prof. Dr. Pedro Morouco,

"Four-dimensional bioprinting: stimuli-responsive mechanisms for biomedical applications"

Three-dimensional (3D) bioprinting emerged has a highly versatile technology able to produce customized structures. The ability to produce those structures in a layer-by- layer fashion allowed a precise control over geometry, morphology and pore interconnectivity. However, those 3D structures may not be the most suitable approach for the clinical requirements. Indeed, four-dimensional (4D) bioprinting seems to promise a technology with the ability to induce planned changes at the structures, bridging the gap between the laboratorial constructs and the native human tissues. In summary, 4D bioprinting main goal is to develop biological 3D structures, which are suitable to change their properties (e.g. stiffness, shape, volume) when triggered by a pre-defined stimulus (e.g. electricity, ionic force, light, magnetic field, pH and temperature). If on one hand it is important to develop and design new materials and processes, making those materials biocompatible is also crucial. The audience will be dared to think further on the applications of this technology. How will the stimulus be provided? By who? And on which conditions, are some of the topics which will be addressed.

Assoc. Prof. Dr. Allen Liu,

"Microfluidics for single cell mechanobiology"

The proper responses of cells to mechanical stimuli are important in numerous physiological processes. With the development of microsystem engineering tools, controlled and repeatable application of active mechanical input to single cells is becoming more available. Several microfluidic platforms have been developed for mechanotransduction research over the last decade that many focus applying a single mechanical perturbation and often to a population of cells. Here we develop a multilayer polydimethoxysilane (PDMS)-based microfluidic device with the goal of applying controlled aspiration and compression to single cells. Two independent pneumatically controlled channels above the flow channel serve to facilitate cell loading and compression when they are actuated. As a model system of cell and to demonstrate the salient features of our device, we generated water-oil- water double emulsion droplets and demonstrated trapping, aspiration, and compression of double emulsion droplets.

More recently, we have combined this with microcontact printing to confine the size of single cells and investigate the effect of static vs. cyclic compressive stress to single cells. Our unique and versatile microfluidic compression device will provide tremendous opportunities for future single cell mechanotransduction studies.

Assoc. Prof. Dr. Gerhard Wingender,

"The role and therapeutic potential of invariant Natural Killer T (iNKT) cells in health and disease"

The immune system is commonly divided in innate and adaptive immune system. The innate immune system (a) is composed of elements that are expressed in all individuals in basically an identical form; (b) responds immediately within minutes or hours; and (c) recognizes brought patterns of molecules that are e.g. expressed by various pathogens. In contrast, the adaptive immune system, consisting of B and T cells, (a) is unique in every individual; (b) is highly specific for unique structures; and (c) has the ability to remember (memory); however, (d) it is slow to respond and requiring days for full activation. The majority of T cells, also called conventional T cells, recognize protein fragments (peptides) that are presented to them by MHC molecules.

Besides these conventional T cells, a distinct, but smaller population of T cells called invariant Natural Killer T (iNKT) cells have been describe. iNKT cells bridge the two branches of the immune system, as they share features with innate NK cells and T cells. Several unique characteristics distinguish iNKT cells from conventional T cells: (1) Their T cell receptor (TCR) does not recognize protein fragments on MHC molecules, but rather glycolipids on the non-polymorphic CD1d molecule. (2) They do not require a lengthy differentiation phase after activation, but rather develop already as fully functional effector cells.

In line with their effector/memory phenotype, iNKT cells rapidly produce copious amounts of cytokines following stimulation, and often present the first response to infections. Thereby, iNKT cells can have a pronounced effect on the immune system, impacting a dazzling variety of different immune reactions, ranging from responses to pathogens and tumors, to autoimmune responses.

Here, I will introduce the role iNKT cells can play in various diseases and will give an overview over approaches to target them for immunotherapy.

Assist. Prof. Dr. Shirin Tarbiat,

"PPARs, Obesity and Cardiovascular Diseases"

Peroxisome proliferator-activated receptor (PPAR) belongs to nuclear receptor super family of transcription factors, and consists of 3 isoforms (i.e., PPARα, PPARβ [also known as δ], and PPARγ). PPARα is predominantly expressed in tissues with a high oxidative capacity such as the heart and liver, PPARγ is highly expressed in adipose tissue, and the expression of PPARβ/δ is more ubiquitous. The PPARs can be activated by an array of natural endogenous ligands. Synthetic ligands have been designed for the PPAR isoforms with the purpose of therapeutic application. On ligand-binding, PPARs transactivate gene expression by heterodimerization with another member of the nuclear receptor super family, the retinoic X receptor, and this complex bind to a direct repeat sequence designated as PPAR-responsive element.

PPARα reduces hepatic fat accumulation by inducing mitochondrial, peroxisomal, and microsomal fatty acid oxidation. In addition, PPARα reduce inflammatory reactions in the arterial wall via suppression of several proinflammatory genes like MCP-1, TNFα, vascular cell adhesion molecule-I (VCAM I), intercellular adhesion molecule-I (ICAM I), and interferon-γ (IFNγ).

PPARγ is considered the master regulator of adipogenesis, and has been extensively studied in the context of obesity. At least two different isoforms of PPARγ are known: PPARγ1, which is the form expressed in nonadipose tissues, and PPARγ2, which is adipose-tissue specific. Unsaturated fatty acids and several eicosanoids serve as endogenous agonists of PPARγ, while antidiabetic drugs, the thiazolidinediones, act as synthetic agonists. Target genes of PPARγ are involved in adipocyte differentiation, lipid storage, and glucose metabolism. PPARγ activation strongly reduces inflammatory gene expression.

Compared to PPARα and PPARγ, much less is known about PPARβ/δ and its natural ligands. Hence its role has been poorly explored. PPARβ/δ has been directly linked to the development of obesity. Due to the anti-inflammatory properties of PPARβ/δ in macrophages, it is plausible that atherosclerosis is affected by PPARβ/δ-activation. Whether, the biological effects of PPARs are because of inhibiting inflammation, remains to be determined.

Assoc. Prof. Dr. Yongsoo Park,

"MicroRNA exocytosis by vesicle fusion as a novel neuromodulator"

By combining interdisciplinary techniques that include cell biological, biophysical, and biochemical tools, we aim to investigate the molecular mechanisms of microRNA (miRNA) exocytosis. Although non-coding RNA (ncRNA) that include miRNA regulates gene expression inside the cell where they are transcribed, extracellular RNA has been recently discovered outside the neurons. Using next-generation RNA sequencing, vesicle purification techniques, and synthetic neurotransmission, we observed that LDCVs contain a variety of miRNAs including miR-375. miRNA exocytosis is mediated by the SNARE complex and accelerated by synaptotagmin-1, a Ca 2+ sensor. Our results are opening the new field and concept that miRNA can be a novel neuromodulator, which is stored inside the vesicle and released together with classical neurotransmitters by vesicle fusion, thereby contributing to cell-to- cell communication.

Prof. Dr. Minoo Rassoulzadegan,

"RNA-mediated epigenetic heredity: experimental mouse models of an acquired pathology"

We reported over the recent years several instances of non-Mendelian heredity in the mouse (paramutations). Transcriptional upregulation of major control loci resulted either in fur color variation (Kit gene), heart hypertrophy (Cdk9 gene), or in increased body size and cognitive ability (Sox9). Experiments involving microinjection of purified RNAs in fertilized eggs had led us to the conclusion that sperm RNA was the transgenerational vector of these epigenetic states. We further observed a requirement for cytosine methylation by the Dnmt2 methyltransferase at defined sites in the inducer and target RNAs [1-4]. Further examples of sperm RNA-mediated inheritance were recently reported by others, namely a distinct instance of the Kit paramutation [5] and heritable neuropathological conditions [6, 7]. Transgenerational determination by sperm RNA provides theoretical grounds for several unexplained but well documented instances of non-Mendelian paternal heredity and suggests experimental approaches. We will report mouse models of paternal RNA-mediated determination pertinent to two pathologies, hereditary transmission of the diet-induced metabolic syndrome (obesity, type 2 diabetes) [8, 10] and the paternal control of the length of telomeres and of the telomere diseases [9].

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Dr. Christopher Mayack,

"Ecology, evolution and animal behavior"

Robert Trivers once said, “everybody has a social life”, but even though social behavior is quite pervasive throughout the animal kingdom and humans demonstrate highly social behavior, a dedicated field to the study of it wasn’t really recognized until Edward O. Wilson coined the term ‘Sociobiology’. This talk will focus on two approaches used to study the evolution of social behavior.

The first will focus on discussing the underlying proximate mechanisms (genes, hormones and neurobiology) that gives rise to social behavior. The second will address how this first approach is integrated with studying why social behavior has evolved, which turns to understanding the function of the behavior and aims to find an adaptive explanation. I will discuss the theoretical underpinnings used to explain how it is that being social behavior may or may not lead to an increase in fitness. I will also discuss a range of taxa, from bacteria to humans, to draw common themes as it has evolved independently, multiple times, throughout evolutionary history.

Assoc. Prof. Dr. Andres Aravena,

"Bioinformatics + Biotech in high impact strategic industries"

Biotechnology has changed a lot in the last 10 years, and it will probably keep changing. The same is true in general for all science and technology. Experiments that used to be expensive and slow, are today cheap and fast. Producing and analyzing huge volumes of data is easy and inexpensive. Everybody can build new instruments, or cheaper versions of the standard instruments at home, and even do synthetic biology in any lab. How are you going to succeed in this brave new world?

In this talk we will speak about some of the challenges that you as a biotechnologist will face in the following years, and what we can learn from previous experiences (if possible). We will show the case of Chile, where biotechnology is used for the rational exploitation of natural resources (mainly copper, but also wood, fishes, fruits and wine), which are the main source of national income. Biotechnology has been essential for the efficient use of resources, transforming the industries and have a huge positive effect on the whole economy.

A key part of this successful biotechnological experience is due to bioinformatics and computational biology. Using mathematical and informatic tools allows us to design the best experiments, simulate the possible outcomes and extract meaningful knowledge from the results.

Assoc. Prof. Dr. Andrew Harvey,

"Plant Cell Wall Biotechnology: Perspectives and Future Directions"

Plants, both as a whole and at the cellular level, are defined by the size, shape, and thickness of their cell walls. These walls are primarily made up of cellulose and non-cellulosic polysaccharides which represent the largest source of renewable carbohydrates in the world. The ever-rising global need for energy makes the fermentable sugars present in these carbohydrates a desirable goal for creating renewable liquid transport fuels. In addition, the polysaccharides of the plant cell wall are essential components of the diet as dietary fiber, particularly those of certain cereal grains, and their roles in reducing the incidence of diseases such as type II diabetes, cardiovascular disease, colorectal cancer, and inflammatory bowel diseases. Other areas of study on plant cell walls include their use in biofibers, paper and pulp industry biomaterials, sustainable construction, bioplastics, sustainable agriculture, bioactive molecules, biocontrol, pharmaceutical industry, and nutraceuticals. An overview of current plant cell wall research will be given and possible future directions explored.

Assoc. Prof. Ralph Meuwissen,

"Biology and Molecular Therapy of Lung Cancer"

Although in the last 30 years much scientific progress has been made in understanding some of the genetics, molecular and cellular biology of lung cancer, this did not result in lowering the mortality rate for lung cancer which is still the highest for any cancer around the world (and certainly for Turkey). In our lab, we focus mainly on the research of Small Cell Lung Cancer, the most lethal form of human lung cancer.

In the last decade, vast scientific progress has been made in genetic characterization of SCLC, which led to development of genetically engineered mouse models (GEMMs) that closely mimic human SCLC However, current SCLC models such as cultured clonal tumor cell lines and GEMMs poorly represent the complex genetic heterogeneity of human SCLC. We therefore also include human primary SCLC samples in patient derived xenotransplant (PDX) models for thorough genetic analyses and as basis for testing immunotherapeutic approaches against SCLC.

The Meuwissen lab research consists of 3 main thematic:

- Characterize the tumor plasticity in SCLC during tumor onset progression and (chemo)therapy response based on SCLCs from GEMMs and/or human PDXs Full cellular heterology of tumor lesions will be examined and subpopulations will be characterized through genetic analyses, specific growth and marker characteristics leading to the unravelling of molecular mechanism governing epithelial mesenchymal transition and drug resistance.

- Human SCLC PDXs are maintained on humanized mice background. These mice with fully activated human adaptive human response will serve as platform for immunotherapeutic research against SCLC.

- Applying latest techniques of liquid biopsy dependent analyses of circulating tumor DNA and RNA for diagnostic and therapeutic purposes.

In conclusion, our studies should provide us with a better understanding of the phenotypic complexity of SCLC and its implications for comprehending the underlying molecular and cellular mechanisms that govern SCLC metastatic behavior, drug resistance and evasion of an adaptive immune response.

Moreover, our new SCLC PDX models will be of valuable use for extensive drug screens and should thereby lead to discover new candidate genes that control some of these pivotal molecular pathways.

Our combined results therefore will improve the design of new, more efficient (immuno) targeted- and chemo- therapeutic approaches against SCLC.

2. Post-doctoral researcher presentation abstracts

Dr. Esra Aydemir Çoban - *A twist effect in chordoma*

Objective: Chordoma is a rare tumor of bone, which is slow growing but locally invasive neoplasm with tendency to metastasize with rare events ranging from 3 to 40% and usually occurs at the late stage of the disease. Therefore, it is important to discover new therapeutics targeting genes involved in the metastasis event. Epithelial mesenchymal transition (EMT) might have a robust effect on the metastasis of a tumor bulk. However, up to date no data has shown the possible role of EMT in chordoma metastasis. In this study we aim to investigate the possible role of Twist, a key player of EMT, on chordoma metastasis**.**

Materials and Methods: Twist gene was knocked down in a chordoma cell line, MUG-Chor1 and its role in metastasis was investigated with a wound healing/gap closure assay and invasion assays.

Results: Twist silenced MUChor1 cells were found to be less migratory and less invasive when compared to its negative control.

Conclusion: Twist might have role in metastasis of chordoma and can be targeted against chordoma metastasis

Dr. Pakize Neslihan Taşlı - ***Loading of hEGF onto Exosomes Derived from Bone Marrow Stem Cells and Its Characterization***

The role of stem cells in repair of damaged tissue and generation of whole organ has been widely studied by numerous research groups in the field of regenerative medicine. Although their key role in the process has been well-established in last decade, researchers recently point to the importance of nano-sized cellular vesicles called exosomes that are released by the stem cells. Stem Cell Exosomes (SCEs) contain miRNAs, growth factors, hormones, cellular messages, and other cellular components, which are essential tools for tissue engineering studies. In this study, characterization of human Epithelial Growth Factor (hEGF) loaded onto SCEs derived from bone marrow tissue was evaluated in a dose-dependent-manner. Cell Culture Media (CCM) supplemented with exosome-depleted fetal bovine serum was collected from stem cells. Exosomes were isolated from CCM that was treated either without or with 5 ng/mL, 10 ng/mL and 20ng/mL hEGF using ExoSpin exosome isolation kit according to the instructions of manufacturer. Isolated SCEs without hEGF were characterized based on their shape, size distribution, and cell-surface antigens. Scanning Electron Microscopy (SEM) imaging was performed to show their round-like shape, zeta sizer was used to measure their diameters, and Flow Cytometry was used to characterize the exosomal surface antigens including CD9, CD63 and HSP70. Lastly, to evaluate hEGF-uptake by the SCEs, hEGF Enzyme-Linked Immunosorbent Assay (ELISA) was performed.

Obtained results show that vesicles isolated from bone marrow stem cells have exosomal characteristics in terms of shape, size, and antigen-content. Also, hEGF can be loaded onto the SCEs successfully in a dose-dependent-manner. As a conclusion, hEGF is an important growth factor in forming tissue-like structures and use of hEGF-loaded-exosomes can be very useful in the field of tissue engineering and regenerative medicine.

3. Poster Abstracts

Onur Çelik - *Micropropagation of Grapefruit (Citrus paradisi Macfad) Seeds*

Aim of the study: Because of their chemical composition which is used some traditional treatment as antibacterial, antifungal, anti-inflammatory, antimicrobial, antioxidant, antiviral, astringent, and preservative, grapefruit (Citrus paradisi Macfad) is one of the most important medicinal plants. It has also been used for cancer prevention, cellular regeneration, lowering cholesterol, cleansing, detoxification, heart health maintenance, Lupus nephritis, rheumatoid arthritis and weight loss. Although tissue culture of citrus species is well studied, several publications report a strong genotype dependence. Moreover, citrus tissue culture is mostly confined to more common species like C. reticulata, C. aurantifolia, C. jambhiri, C. aurantium etc. There have been few reports on micropropagation of C. paradisi. Current work aimed to develop an efficient micropropagation protocol for grapefruit.

Results: Use of seeds as the explants was found to be an effective method for in vitro clonal multiplication of C. paradisi. We studied the germination response of seeds of this species cultured on MS medium supplemented with 0.1uM gibberellic acid and 20gL-1 sucrose. Germination was evaluated four weeks after the C. paradisi seeds were transferred to germination medium. Seeds that produced at least one morphologically normal seedling were considered germinated. Seedlings derived from germinated seeds had well-formed shoots and roots and were easily acclimated to greenhouse conditions.

Keywords: Citrus spp. seeds, in vitro, gibberellic acid, MS medium.

Öykü Boraka - *NaB Treatment Downregulates Energy Metabolism in Prostate Cancer Cells*

Prostate cancer is the second most lethal cancer type among men after lung cancer with an incidence rate of 37 per 100.000. One of the known features of proliferating cancer cells is the decrease in oxidative phosphorylation (OXPHOS) with an increase in glycolytic pathways. This altered energy metabolism is found in many types of cancer cells which are in their proliferative state and is called as the Warburg effect. Proliferating prostate cancer cells have also been found to display Warburg effect [1]. One possible mechanism for inhibition of oxidative phosphorylation can be through acetylation of oxidative phosphorylation proteins which can be reversed by the action of NAD+-dependent deacetylase SIRT3 [2]. SIRT3 is also a binding partner of sodium borate (NaB) and this interaction activates deacetylation activity of SIRT3 through an unknown mechanism [3]. The aim of this study was to reprogram energy metabolism of prostate cancer cells by deacetylating, thus, activating OXPHOS proteins by NaB treatment. The differences in proteomic profile of whole cells were investigated to detect metabolic changes by analyzing mass spectrometry-based data with MaxQuant, Perseus, and Blast2GO software. While there is no change in metabolism-related protein levels of PNT-1A with NaB treatment, the proteomic change in PC-3 and DU-145 cell lines seems to have downregulatory effects on energy metabolism in general.

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Bihter Özdemir - *Proteomic Analyses Of Celery Exosomes*

Extracellular vesicles (EVs) have been identified as higher potential vesicles for intracellular communication. They have a higher potential for transfer proteins, lipids or nucleic acids. Physiological role of EVs have not been identified clearly. Recent studies show that EVs contain RNA, protein and lipids in their structure. EVs have 3 subgroups which are apoptotic bodies, ectosomes and exosomes. Exosomes are 50-100 nm-diameter particles and their RNA's and proteins are specific to originated cell and they have critical role for cell-cell communication and promote cellular activities on the living organisms. Exosomes could be a different approach for biomarker design and cellular targeting based on their RNA and protein specification. Plant cells also have exosomes but even so the studies on the plant exosomes have been limited. Although there is animal-based exosomes-focused database, there are no database for plant exosomes. Know the protein contents of the exosomes have been great importance for using them as targets. Celery plant was chosen because of their health benefits. In this study, celery plant exosomes were characterized by mass spectrometry based proteomic analysis.

Mehmet Ali Karaca - *Effect Of Sodium Borate (NaB) Treatment On Prostate Cell*

Cellular energy metabolism in cancerous cell plays an essential role for their growth, survival, proliferation and long-term maintenance. Recently studies on energy metabolism in cancerous cells known as a Warburg effect state indicate cellular protein acetylation level as one of the post transcriptional mechanism has regained in energy metabolic pathway. Sirtuins known as NAD^+ dependent deacetylatilase or ADP ribosyltransferase regulate cell survival and change cellular energy state in cancerous cell. Additionally, boron as a chemo preventative agent has been used for inhibition of androgen independent prostate cancer cell lines DU-145 and PC-3 dose dependent manner and also interacts with NAD^+ molecule. Aim of this study is to investigate interaction between boron and NAD^+molecule directly effect on mitochondrial metabolism of both health prostate epithelial PNT1A and prostate cancer cell lines DU-145 and PC-3. Effect of NaB treatment is investigated via western blotting experiment to show acetylation statues of the cellular protein, amount of oxphos complexes, cell viability assay and NAD^+/NADH ratio.

Duygu Orak

Chitosan is a natural polymer that has anti-cancer, anti-oxidant properties. However, it may have solubility and viscosity problems in specific applications. In order to overcome this problem, chitosan may be modified. In this study, caffeic acid modified chitosan (CFA-Ch) and methylated chitosan, N,N,N-trimethyl chitosan chloride (TMC) The aim of this study is the proteomic analysis of the anti-cancer effects of chitosan and its derivatives on breast cancer cells in order to understand their mechanism. In preliminary studies, among the treatment samples, TMC 60 min. And TMC 80 min. reduced cell proliferation of MCF-7 cells. After cell culture observations, alterations in OXPHOS complexes were investigated by using western blotting. As a result, there is a significant decrease in Complex III-cytochrome c oxidoreductase in 10 µg/ml of 10 mM CFA-CH treatment and an increase in Complex II-succinate dehydrogenase in 10 µg/ml of TMC 60 treatment were detected.