MOLEKÜLER KANSER ARAŞTIRMA DERNEĞİ
MOKAD

2nd INTERNATIONAL

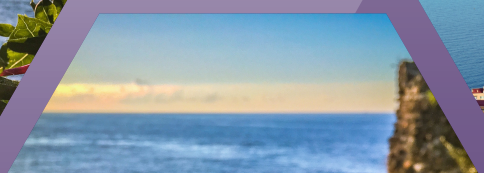
MULTIDISCIPLINARY CANCER RESEARCH CONGRESS

21-24 JULY 2022

ABSTRACT BOOK







EACR European Association for Cancer Research

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Dear Basic Cancer Researchers,

You are cordially invited to participate in the 2nd International Multidisciplinary Cancer Research Congress to be held in Giresun, TURKEY, a lovely seaside city in the middle of The Blacksea Region from 21 to 24 july 2022.

This is a congress organised by MOKAD (Molecular Cancer Research Association of Turkey). MOKAD congresses are a particular platform for young researchers being gathered and share their works with each other. The congress particularly aims to provide the participants with lots of time to exchange their ideas during a long social event (a trip to highland) and through many short talks.

The congress will also be unique in one important thing. Molecular biologists will understand their future close collaboration (as a profession) with the medical oncologists. One of the panels is dedicated to this aim. A well-known medical oncologist using molecular biology tools for tailoring his treatments for patients will give a lecture in addition to the other lecturers who will talk in the same direction.

2nd International Multidisciplinary Cancer Research Congress welcomes the short talks of wide range of topics, including precision oncology, cancer stem cells, exosomes in cancer, liquid biopsy as future of oncology, epithelial-mesenchymal transition, novel anticancer small molecules, cell death (apoptosis/necrosis and autophagy) in cancer, epigenetics and cancer, cancer immunotherapy, nanoparticles against cancer, DNA damage, anticancer drug resistance, cancer microenvironment, and others.

Young researchers will have ample opportunity to present their own research results during open slots for short talks and poster sessions. Young applicants who make excellent presentation during short talks and poster sessions will be awarded! There will also be regular MOKAD awards.
In the congress, a small-scale workshop will also be held on the topic of better evaluation of cytotoxicity and cell death methods. All participants are welcomed to this no fee-event. Also, the congress fee is kept minimum to allow young researchers to be able to attend.

Giresun is a Blacksea city with amazingly green surroundings. It is known to be the capital of nut and cherry, and famous for highlands and ecotourism.

Hope to see you at the congress

All the best,
Chair, Engin Ulukaya
Istinye University
Head of Molecular Cancer Research Center

Co-chair, Ayşegül Çebi
Giresun University
Dean of Health Sciences Faculty

21-24 JULY 2022

2nd INTERNATIONAL

MULTIDISCIPLINARY CANCER RESEARCH CONGRESS

SCIENTIFIC PROGRAM

GİRESUN, TÜRKİYE





SCIENTIFIC PROGRAM

THURSDAY (HALL-I)

13:45-14:15	**OPENING CEREMONY + MUSICAL PERFORMANCE**
14:15-15:00	**AÇILIŞ KONFERANSI** **CHAIR:** Gamze TANRIÖVER Mutlu DEMİRAY, TÜRKİYE **Tümör Agnostik Çağda Kanser Tedavisi ve Klinik Kanser Biyologlarının Rolü**
15:00-15:30	**COFFEE BREAK**
15:30-17:30	**PANEL 1: Sinergism Between Oncology and Molecular Biology/Bioinformatics** **CHAIRS:** Mutlu DEMİRAY, Şehime Gülsüm TEMEL
15:30-16:00	Abdullah KAHRAMAN, SWITZERLAND (ONLINE) **Comprehensive Genomic Profiling and Its Interpretation at Molecular Tumor Boards**
16:00-16:30	Atıl BİŞGİN, TÜRKİYE **Kanser Tanı ve Tedavisinde Gelecek Vizyonu: Klinik Uygulamalarıyla Geniş Genomik Profilleme Gerçek Dünya Verileri**
16:30-17:00	Aslı KUTLU, TÜRKİYE **Moleküler Biyoloji ve Genetik Bakış Açısı ile Kişiye Özel Kanser Tedavileri**
17:00-17:30	Şehime Gülsüm TEMEL, TÜRKİYE **Multidisiplinary Aporoach to the Personalized Cancer Diagnosis and Treatmeant: Translation of Genomic Data in to the Clinic**

SCIENTIFIC PROGRAM

THURSDAY (HALL-I)

17:30-18:00	**KONFERANS** **CHAIR: Cengiz KARAKAYA** **Muhammet BULUT (Giresun İl Sağlık Müdürlüğü)** **Giresun İli Kanser Verilerinin Analizi**
18:00-19:15	**KEYNOTE LECTURE** **CHAIRS: Mehmet AY** **Bülent ÖZPOLAT, USA** **MicroRNA Therapeutics in Cancer- The New Kid in the Block**
19:15	**COCTAIL PROLONGE + MUSICAL PERFORMANCE**

SCIENTIFIC PROGRAM

FRIDAY (HALL-I)

8:30-10:30	**ÇALIŞTAY** **Engin ULUKAYA & Nazlıhan AZTOPAL, TÜRKİYE** **Hücre Ölüm ve Sitotoksisite Sonuçlarının Doğru Yorumlanması** **(Çalıştaya katılacak kişiler dizüstü bilgisayarlarını yanlarında getirmelidirler.)**
10:30-11:00	**COFFEE BREAK + POSTER SESSION**
11:00-13:00	**PANEL 2: EUROPEAN PANEL** **CHAIRS: Öykü GÖNÜL GEYİK, Didem KARAKAŞ ZEYBEK**
11:00-11:30	**Barış KORKMAZ, FRANCE (ONLINE)** **Cathepsin C Inhibition as a Potential Treatment Strategy In Cancer**
11:30-12:00	**Chiara RAGGI, ITALY (ONLINE)** **Metabolic Aspects of Cholangiocarcinoma Stem-Compartment**
12:00-12:30	**Kıvanç GÖRGÜLÜ, GERMANY (ONLINE)** **Metabolic Dimensions of Metastatic Pancreatic Cancer**
12:30-13:00	**Konstantinos DIMAS, GREECE (ONLINE)** **Development and Characterization of a Novel Lipid-Rich Breast Cancer Patient-Derived Xenograft (PDX)**
13:00-14:00	**LUNCH**

SCIENTIFIC PROGRAM

FRIDAY (HALL-I)

14:00-16:00	**PANEL 3** **CHAIRS: Egemen DERE, Ayşegül ÇEBİ**
14:00-14:25	**Onur Emre ONAT, TÜRKİYE** **Gene Discovery Strategies in Complex Diseases: a Novel Rare Variant Association Approach Using Next Generation Sequencing**
14:25-14:50	**Alexandre TAVARTKILADZE, GEORGIA (ONLINE)** **The New Aspects in Personalized Cancer Treatment**
14:50-15:15	**Özlem ER, TÜRKİYE (ONLINE)** **Solid Tümörlerde Kapsamlı Genomik Profilleme Hangi Hastalara Yapılmalı?**
15:15-15:40	**Ali AKTEKİN, TÜRKİYE** **Cerrah Gözüyle Moleküler Onkolojiye Bakış**
15:40-16:00	**COFFEE BREAK + POSTER SESSION**
16:00-17:15	**PANEL 4** **CHAIRS: Serap ÇELİKLER KASIMOĞULLARI, İbrahim BOĞA**
16:00-16:25	**İbrahim BOĞA, TÜRKİYE** **Kanserde Mutasyon İmzası Tespitine Yönelik Genom Analizleri ve Biyoinformatik Süreçler**
16:25-16:50	**İlker ŞENGÜL, TÜRKİYE** **"Zooming" in Thyroid Nodules with Indeterminate Cytology in Suspense; 1 0-15 mm with AUS/FLUS, TBSTRC**
16:50-17:15	**İrem DOĞAN TURAÇLI, TÜRKİYE** **Molecular and Cellular Changes Induced By Metformin Resistance in TNBC Cells**
18:00-19:00	**LIGHT MEAL (Giresun Pita, University Dining Hall)**

SCIENTIFIC PROGRAM

FRIDAY (HALL-II)

09:00-12:00	**SHORT TALKS** **CHAIRS: Aslı KUTLU, Huri BULUT**
09:00-09:15	**Sema YILMAZ, TÜRKİYE** **Where Are We in Cell Therapy?**
09:15-09:30	**Banu İSKENDER İZGİ, TÜRKİYE** **Prospects For Cell Reprogramming in Cancer Remodelling And Treatment: A Special Emphasis On Bladder Cancer**
09:30-09:45	**Tevhide ÇEVİK, TÜRKİYE** **Meme Kanseri Tedavisinde Nutrigenik ve Nurtigenomik Perspektifte Besinlerin Rolü**
09:45-10:00	**Seda BAYKAL KÖSE, TÜRKİYE** **Zebrafish Modeling İn Cancer Research in The Light Of A Drug-Resistant Chronic Myeloid Leukemia Cell Study Preliminary Results**
10:00-10:15	**Berna AYAR, TÜRKİYE** **Public Cancer Datasets in The Multiomic Era**
10:15-10:30	**Sezen GÜNTEKİN, TÜRKİYE** **The Story Of A Novel Compound Targeting The Hippo Pathway in Hepatocellular Carcinoma**

SCIENTIFIC PROGRAM

FRIDAY (HALL-II)

10:30- 10:45	**COFFEE BREAK + POSTER SESSION**
10:45-11:00	**Ahmet ACAR, TÜRKİYE** **Developing Quantitative Experimental Model Systems To Study Drug Resistance**
11:00-11:15	**Eray Metin GÜLER, TÜRKİYE** **Anticancer Effect Of Phthalocyanine Derivatives On Colorectal Cancer: in Vitro And in Vivo Model**
11:15-11:30	**Berkcan DOĞAN, TÜRKİYE** **Tools and Strategies for miRNAs' Targetome Prediction**
11:30-11:45	**Sara ÖĞRETİCİ ORAL, TÜRKİYE** **Overview of Cancer Drugs Causing Fingerprint Loss "Review"**
11:45-12:00	**Hakan DARICI, TÜRKİYE** **SpheroMake: A New Rapid Spheroid Production Material**
12:00-17:40	**ORAL PRESENTATIONS** **CHAIRS: Ayşegül ÇEBİ, Abdullah YALÇIN, Nazlıhan AZTOPAL**
12:00-12:10	**Zelal ADIGÜZEL, TÜRKİYE** **Investigation Of The Role Of Extracellular Vesicles In Prostate Cancer To Taxane Resistance**

SCIENTIFIC PROGRAM

FRIDAY (HALL-II)

12:10-12:20	Mehmet SARIMAHMUT, TÜRKİYE ***Cichorium intybus L.*** **(Beyaz hindiba) Ekstresi ile Bazı Antikanser İlaç Etkileşimlerinin Belirlenmesi**
12:20-12:30	Onur ÇİZMECİOĞLU, TÜRKİYE **Title of the Abstract: ZAP70 Activation Compensates for Loss of Class IA PI3K Isoforms Through Activation of the JAK–STAT3 Pathway**
12:30-12:40	Nevin BELDER, TÜRKİYE **Integrated Analysis Of Copy Number Variation and Genome-Wide Expression Profiling in Colorectal Cancer**
12:40-12:50	Ömer Faruk KIRLANGIÇ, TÜRKİYE **Anticancer Effects Of Sodium Butyrate Combıned With Cisplatin In Human Neuroblastoma Sh-Sy5y Cells**
12:50-13:00	Elif ERTÜRK, TÜRKİYE **Cu (II) Quercetin Complex Inhibits Migration and Induces ROS-Mediated Apoptosis in Human Lung Cancer Cells**
13:00-14:00	**LUNCH**
14:00-14:10	Çağrı GÜMÜŞKAPTAN, TÜRKİYE **L1Ta Retrotransposons As Endogenous Mutagens In Papillary Thyroid Carcinoma**
14:10-14:20	Seçil DEMİRKOL CANLI, TÜRKİYE **Evaluation Of AKR1B1 Expression In The CRC Tumor Microenvironment**
14:20- 14:30	Ali IMRAN DASTAN, TÜRKİYE **Investigation Of The Relationship between Oxidative Stress and Inflammation Biomarkers With Surgical Treatment in Patients With Prostate Cancer**

SCIENTIFIC PROGRAM

FRIDAY (HALL-II)

14:30-14:40	Ömer Aydın, TÜRKİYE Nanoparçacıklar ile Akıllı Gen Terapi Sistemlerin Geliştirilmesi
14:40-14:50	Beyza Nur ÖZKAN, TÜRKİYE Therapeutıc Effects of Kumquat (Fortunella Japonica Swingle)
14:50-15:00	Beliz TAŞKONAK, TÜRKİYE Investigation of Enhanced Uptake of Hypericin With Chitosan Nanoparticles in Lung Cancer
15:00-15:10	Münevver AKDENİZ, TÜRKİYE Detection of Acute Leukemia From Blood Plasma With Surface-Enhanced Raman Spectroscopy And Machine Learning
15:10-15:20	Kübra BOZALİ, TÜRKİYE Goldenberry (Physalis Peruviana L.) Extract Exacerbates Apoptotic and Autophagic Effects in Epidermoid Carcinoma
15:20-15:30	İlkay ÇINAR, TÜRKİYE Cancer Profile of Giresun City Based on Giresun Training and Research Hospital Datas
15:30-15:40	Gülşah TORKAY, TÜRKİYE Anticancer, Antibacterial, and Antiangiogenic Effects of Green Synthesized Hemocompatible Silver Nanoparticles
15:40-15:50	Şeyma Gül DURGUT, TÜRKİYE The Role of Exosomal Inhibitors in Epigenetic Regulation
15:50-16:00	Ömer Enes ONUR, TÜRKİYE Investigation of the KMT2C Mutation-Induced Multidrug Resistance Mechanism in CRISPR Stable Lung Cancer Cells
16:00:16:10	COFFEE BREAK + POSTER SESSION

SCIENTIFIC PROGRAM

FRIDAY (HALL-II)

16:10-16:20	**Mehmet SARIMAHMUT, TÜRKİYE** ***Echium vulgare* Bitkisinden Elde Edilen Ekstrelerin Büyüme Baskılayıcı Etkilerinin Değerlendirilmesi**
16:20-16:30	**Sendegül YILDIRIM İLDEM, TÜRKİYE** **Indoksimod, Meme Kanseri Hücrelerinin Canlılığını Etkileyerek Tümör Büyümesini Sınırlar**
16:30-16:40	**Zekeriya DÜZGÜN, TÜRKİYE** **FOXM1 inhibitörü FDI-6'nın, Metastatik Meme Adenokarsinom Hücre Hattında VEGFR Protein Etkileşimi ve Ekspresyonu Üzerinde Etkilerinin In-Vitro ve In-Siliko Belirlenmesi**
16:40-16:50	**Aybike SARIOĞLU BOZKURT, TÜRKİYE** **Inhibition Of 6-Phosphoructo-2-Kinase And Ornithine Decarboxylase Oncogenic Properties Of Pancreatic Adenocarcinoma Cells**
16:50-17:00	**Pelin ERSAN, TÜRKİYE** **Kinase Module Of The Mediator Complex Confers Tamoxifen Resistance In ER-Positive Breast Cancer**
17:00-17:10	**Derya YILDIZ, TÜRKİYE** **Sequential Application of an Alternative Drug Repurposing Model Enhances Cytotoxicity in Hepatocellular Carcinoma**
17:10-17:20	**Ece GÜMÜŞOĞLU ACAR, TÜRKİYE** **Validated piRNAs in Ovarian Cancer Stem Cells**
17:20-17:30	**Funda DEMİRTAŞ KORKMAZ, TÜRKİYE** **Lutein'in Tek Başına ve Sisplatinle Birlikte Sitotoksik ve Genotoksik Etkilerinin İncelenmesi**
18:00-19:00	**LIGHT MEAL (Giresun Pita, University Dining Hall)**

SATURDAY

SOCIAL ACTIVITY

A trip to one of the most beautiful highlands in Blacksea region. Local lunch will be served. It will last whole day. Following it (after resting at the hotel for a while), gala dinner will take place at Hotel Ramada's open air terrace overlooking the Blacksea. **Mindfullness will be practiced during the nature walk. Those who wish should bring their mats.**

20:00: Gala Dinner (Ramada Terrace Restaurant)

- **Musical Performance (Çağatay Karadeniz ve Gökhan HAMZAÇEBİ)**

SCIENTIFIC PROGRAM
SUNDAY (HALL-I)

08:30-10:40	**Panel 5** **CHAIRS:** Zelal ADIGÜZEL, Caner GEYİK
08:30-09:00	Gizem Dönmez YALÇIN, TÜRKİYE **Glutamate Metabolism Modulation in Intracranial Tumors and Glioblastoma Cell Line**
09:00-09:25	Didem KARAKAŞ ZEYBEK, TÜRKİYE **Nerves in Pancreatic Cancer: The Unusual Suspects in Cancer Aggressiveness**
09:25-09:50	Öykü GÖNÜL GEYİK, TÜRKİYE **Intratumor Heterogeneity and Drug Resistance in Colorectal Cancer**
09:50-10:15	Caner GEYİK, TÜRKİYE **Multifaceted Roles of Nrf-2 in Cancer**
10:15-10:40	Ercan ÖĞREDEN, TÜRKİYE **Prostat Kanserinde Epidemiyoloji, Etyoloji, Tanı ve Evreleme**
10:40-11:10	**COFFE BREAK + POSTER SESSION**
11:10-11:50	**CLOSING LECTURE** **CHAIR:** Engin ULUKAYA Gamze TANRIÖVER, TÜRKİYE **Rottlerin'in Keskin Kılıcı Tümör Mikroçevresindeki MDSC'leri Harakiriye Zorlar**
11:50-13:00	**CLOSING TALKS & AWARD CEREMONY**

SCIENTIFIC PROGRAM

SUNDAY (HALL-II)

08:30-10:20	**ORAL PRESENTATIONS** **CHAIRS: Yelda KUDU, Öykü GÖNÜL GEYİK**
08:30-8:40	**Gonca TUNA, TÜRKİYE** **Investigation of Triosephosphate Isomerase Targeting in Breast Cancer**
08:40-08:50	**Merve DEMİRBAĞ KARAALİ, TÜRKİYE** **Assessment of Single Nucleotide Variants in hGPRC5A Gene Using in silico Tools**
08:50-09:00	**Oğuzhan AKGUN, TÜRKİYE** **Investigation of the Molecular Mechanism of TET2 Mutation-Induced Metastasis in CRISPR Stable NSCLC Cell Line Models**
09:00-09:10	**Remzi Okan AKAR, TÜRKİYE** **In ovo: dinosaur's offspring as an alternative in vivo mode**
09:10- 09:20	**Yaren YILDIZ, TÜRKİYE** **Soloxolone Methyl Induces Apoptotic Markers in Mammospheres**
09:20- 09:30	**Sibel ÇINAR AŞA, TÜRKİYE** **Anticancer Potential of Novel BenzofuranChalcone Hybrids and Their Water Soluble Sodium Salts on Human Lung and Breast Cancer**
09:30-09:40	**İpek AYDIN, TÜRKİYE** **Synergistic Anticancer Effect of Chalcone Derivatives and Wnt/B-Catenin Pathway Inhibitor Niclosamide Againts Lung Cancer Cells**
09:40-09:50	**Gülay BULUT, TÜRKİYE** **Prunus Armeniaca L. (Acı Kayısı) Çekirdek Ekstresinin Genotoksik ve Sitotoksik Etkilerinin Değerlendirilmesi**
09:50-10:00	**Sıla SIĞIRLI, TÜRKİYE** **Investigation of Effects of Acetylsalicylic Acid On Pancreatic Stellate Cells-Mediated Pancreatic Cancer Aggressiveness**
10:00-10:10	**Melih ÖZTEPE, TÜRKİYE** **Determination of Anti-cancer Activity of 3-Nitrophenyl Chalcone Derivative on Colon Cancer Cells**
10:10-10:20	**Evren ATAK, TÜRKİYE** **Head and Neck Cancer : Functional Gene Enrichment Analysis to Identify the Novel Biomarker Potentials**

SHORT TALK 1

Developing Quantitative Experimental Model Systems to Study Drug Resistance

Ahmet Acar*

***** ODTÜ Biyolojik Bilimler Bölümü, Üniversiteler Mahallesi, Çankaya, Ankara, 06800

It is widely known that secondary resistance inevitably leads to treatment failure through Darwinian evolution. Therefore, quantifying the clonal evolution using experimental model systems can hold a great promise in designing evolutionarily informed therapies, and thus, in predicting drug response. In this talk, I will present our recently developed strategy that contributed to the understanding of collateral drug sensitivity with its direct link to clonal evolution to overcome the drug resistance in non-small cell lung cancer cell line model system[1]. More specifically, high-complexity cellular barcoding allowed us the identification of the resistance that was ultimately driven by the presence and emergence of multiple pre-existing and de novo resistant clones, respectively. Overall, our work highlighted evolutionary trade-offs and provided an opportunity to exploit the tumour's vulnerability. Finally, I will present our ongoing projects in the lab with a particular emphasis on the establishment of Patient-Derived Organoids (PDOs) from metastatic colorectal cancer patients.

References:

1. Acar, A. *et al.* Exploiting evolutionary steering to induce collateral drug sensitivity in cancer. *Nature Communications* **11**, 1923 (2020).

SHORT TALK 2

Prospects for Cell Reprogramming in Cancer Remodelling and Treatment: A Special Emphasis on Bladder Cancer

Banu Iskender Izgi*

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Cell reprogramming technology paves the way for the reversal of somatic cell fate through somatic cell nuclear transfer technology (SCNT), induced pluripotent stem cell (iPSC) technology or direct reprogramming. Current reprogramming technologies offer the potential to render stemness characteristics to any cell of interest. The idea of reprogramming a malignant cell back to a more manageable benign state has been demonstrated to be technically feasible with cell reprogramming technologies, but the underlying mechanisms still represent a huge dilemma. In this study, the current status of cancer cell reprogramming has been discussed in light of recent advances in the literature and our expertise in bladder cancer cell reprogramming using Sendai virus-based iPSC technology.

Since patient-derived tumours only serve as a platform to study mid-to-late stage cancer markers and animal models fail to provide an ideal system due to genetic differences, reprogramming strategies could be utilised in recapitulating cancer progression *in vitro.* We have previously demonstrated although not all bladder cancer cell types were susceptible to reprogramming, reprogrammed cancer cells exhibited differentiation ability that could serve for establishing tailor-made cancer models.

During the reprogramming of cancer cells, the ectopic expression of stemness factors is also known to reorganise the epigenetic state that holds a huge promise for achieving a less tumorigenic cancer cell population. However, the heterogeneous nature of cancer cells and cancer-specific marks in the epigenome represent a major hurdle before the successful reprogramming of all cancer cell types. In our experience, reprogramming kinetics has been defined by the starting cancer cell population. Therefore, elucidating the distinct regulation of genome in various cancer types and how reprogramming changes cancer cell behaviour is essential before effective cancer models to study cancer initiation, cancer cell heterogeneity and therapeutic drug screening could be established.

SHORT TALK 3

Tools and Strategies for miRNAs' Targetome Prediction

Berkcan DOGAN[1,2]

[1] Department of Translational Medicine, Institute of Health Science, Bursa Uludag University, Bursa, Turkey

[2] Department of Medical Genetics, Faculty of Medicine, Bursa Uludag University, Bursa, Turkey

MicroRNAs (miRNAs) are evolutionarily conserved, small non-coding RNAs that are recognized as posttranscriptional regulators of gene expression. These molecules have been shown to play crucial roles in multiple cellular processes and their dysregulations have been reported in various human diseases, including cancer, thus having therapeutic implications. Currently, there is a growing body of literature focusing on the significance of miRNAs and their functions. Novel miRNAs are being identified with high-throughput technologies, but their functions remain uncharted. Therefore, comprehensive miRNA target predictions are helpful to explain miRNA functions. A miRNA's targetome refers to the set of RNA molecules it targets. Multiple computational algorithms have been designed to predict the targetome of particular miRNAs. According to the study's aim, there are many types of miRNA tools and databases, including target validation or prediction, expression, function, sequence and annotation, and roles in pathways and effects on diseases. However, current computational tools for prediction still create large amounts of false outputs and fail to detect a significant number of actual targets. Furthermore, molecular approaches for experimental validation of miRNAs' targetome are costly, laborious and time-consuming, and they may not be accurate in inferring valid interactions. Considering the limitations of current tools, the genuine identification of miRNA–target interactions require more analytical, sophisticated, and user-friendly tools. In the present study, we discuss recent advances and limitations in computational miRNA's targetome prediction and identification. In conclusion, we have provided a comprehensive perspective of web-based databases and *in silico* resources to elucidate the role of miRNAs in the pathogenesis of diseases and to determine their biomarker potential by choosing the appropriate tool according to their needs.

SHORT TALK 4

Public Cancer Datasets in the Multi-omic Era

Berna Ayar[1,2*], Dilek Pirim[3,4]

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[3]Bursa Uludag University, Faculty of Arts & Science, Department of Molecular Biology and Genetics, Bursa, Turkey
[4]Bursa Uludag University, Institute of Health Sciences, Department of Translational Medicine, Bursa, Turkey
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Cancer is one of the most important complex diseases and is a leading cause of death worldwide according to WHO statistics. The invention of technologies such as DNA microarray and next-generation sequencing has led to a wealth of data. Therefore, the storage and management of omic data are extremely important. Various databases have been established for the public storage and reuse of comprehensive multi-omic profiles of cancer patients.

Recent studies suggest multi-omics approaches as promising tools to elucidate the complex mechanisms underlying cancer. Computational multi-omic approaches based on machine learning techniques and artificial intelligence can be used in cancer research for diagnosis, pathway investigation, patient phenotyping, biomarker discovery, and drug reuse. Thus, integrative analysis of high-throughput multi-omic data sets is crucial for personalized and precision medicine as well as translational medicine applications. With integrated analyzes, the genetic, proteomic, metabolic, biochemical and epigenetic processes underlying cancer can be comprehensively investigated.

Increased interest in this era and considerable efforts revealed “big data” which urges researchers to establish several publicly available cancer databases including clinical, genomics and imaging datasets. In this study, we aimed to provide a comprehensive catalog of public cancer databases for cancer researchers including their limitations and advantages.

In this manner, we reviewed the publicly available cancer databases by searching scientific literature and websites.

Each database was examined by authors and classified by data types and applications provided to researchers. Also, the utility of cancer datasets in future cancer research and cancer management strategies, as well as ethical concerns in this era, were discussed. Data provided in this review may shed on light the relevance of the public cancer datasets in the era of multi-omic cancer research and their practical use in different aspects of cancer management.

SHORT TALK 5

Anticancer Effect of Phthalocyanine Derivatives on Colorectal Cancer: *in vitro* and *in vivo* model

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Colorectal cancer (CRC), also known as bowel cancer, colon cancer, or rectal cancer, develops cancer from the colon or rectum. Although 5-Fluorouracil (5-FU) is the primary antineoplastic used in treatment, its low treatment efficiency has led to the search for new agents. Phthalocyanines are aromatic macrocycles that contain four iso-indoline units connected by four nitrogen atoms. Phthalocyanines Derivatives (PD) gradually started to gain importance as anticancer agents. Our study aims to investigate the *in vitro* and *in vivo* anticancer effects of PD and 5-FU combinations on CRC. Cytotoxicity, genotoxicity, apoptosis, i-ROS, glutathione, calcium, and mitochondrial membrane potential were measured in LoVo and CCD18Co cells. Cells were given to nude mice by the xenograft method. After four weeks of single and combination therapy, tumor size was measured by *in vivo* imaging system (IVIS) and caliper. It was examined biochemically and histopathologically in related serum, tissues, and tumors.

Combination treatment *in vitro* dose-dependently increased cytotoxicity, iROS, genotoxicity, apoptosis, and calcium significantly compared to a single treatment ($p<0.001$). DNA damage and apoptosis were induced higher in combined treatment than single treatment and increased statistically significantly ($p<0.001$). It was found that it decreased glutathione and MMP levels statistically ($p<0.01$; $p<0.001$). In all results of *in vitro* studies, PD affected cancer cells more than healthy cells. Combination treatment *in vivo* was found to reduce tumor size and density by a minimum of 66% at 30 days compared to a single treatment.

Our results showed that PD has different anticancer properties *in vivo* and *in vitro*. The combined use of PD and 5-FU may be an option for routine colorectal cancer treatment.

Keywords: Phthalocyanine Derivatives, colorectal cancer, *in vitro* and *in vivo* cancer model

SHORT TALK 6

The Role of Non-Coding RNAs in Necroptosis of Cancer Cells

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Necroptosis is a newly defined type of programmed cell death triggered by signaling pathways. It was named “necroptosis” because it resembles necrosis in cell death morphology and apoptosis because it requires to be induced by a certain signaling pathway. Necroptosis is morphologically characterized by cell rupture, loss of the plasma membrane, and swelling of organelles (especially mitochondria). Moreover, the upstream molecular signaling pathways of necroptosis, like those of apoptosis, are under tight control, and there are studies showing the role of non-coding RNAs in the regulation of this signaling pathway. Non-coding RNAs are functional RNA molecules that are not translated into protein. These molecules can be classified into different categories depending on their size, genomic location, cellular localization, and function. MicroRNAs (miRNAs) are the most studied class of non-coding RNAs, followed by long non-coding RNAs (lncRNAs). Non-coding RNAs have been shown to play an important role in regulating gene expression, cell proliferation, differentiation, and various forms of cell death (apoptosis, necrosis, autophagy, necroptosis etc.). This study aimed to review and discuss current literature on the role of non-coding RNAs in the regulation of necroptosis of cancer cells.

Keywords: cancer, lncRNA, miRNA, necroptosis, non-coding RNA

SHORT TALK 7

Zebrafish Modeling in Cancer Research in The Light of a Drug-Resistant Chronic Myeloid Leukemia Cell Study Preliminary Results

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Zebrafish (Danio rerio) is a valuable non-mammalian vertebrate model widely used to study development and disease, including recently cancer alongside the mouse. Zebrafish has gained attention as a model for cancer research because of its high fecundity, cost-effective maintenance, dynamic visualization of tumor growth in vivo, and the possibility of chemical screening in large numbers of animals at reasonable costs. The availability of transgenic and mutant models, as well as the possibility to transplant cancer cells into zebrafish, provides a wide array of options for studying human cancer. Disease-modeling in zebrafish is versatile and can be approached from many angles, either by creating gene-targeted mutations and stable transgenes or human cell transplantation in several points. Zebrafish has proven to be reliable for modeling and visualizing human cancer cell biology and dynamics, including metastases or tumor tissue neo-angiogenesis, in vivo with xenotransplantation. Toxicity studies of novel drugs can also be studied easily and cheaply in zebrafish embryo. Screening for targeted treatment in zebrafish xenografts also could provide new opportunities for anticancer personalized therapy in the future as recent research has shown that zebrafish studies are reliable in modeling human cancer. Here, cancer modeling in adult and larval stage zebrafish will be discussed theorical and technically with preliminary results of a chronic myeloid leukemia drugresistant cell xenograft project, in the light of all of the above-mentioned topics.

SHORT TALK 8

Cell Therapies in Cancer

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Cell therapy, involves the direct administration of cells into the body for healing purposes, is currently being evaluated, both alone and in combination with other treatments, in a variety of cancer types in clinical trials. The most common type of cell therapy is blood transfusion, and the transfusion of red blood cells, white blood cells, and platelets from a donor. Regenerative medicine is to replace or regenerates human cells, tissues or organs, to restore or establish normal function. Cellular immunotherapy is for using immune or other types of cells for modulation of host immun system or direct elimination of pathogen/tumor.

The common cell therapy is the transplantation of hematopoietic stem cells (HSC) to create bone marrow. For regenerative medicine, the ultimate objective of cell therapy is to establish a long-term graft with the capacity to perform organ functions. A practical example is bone marrow transplantation, in which HSC are the units of therapy, engraft in the bone marrow, and repopulate the entire blood lineage.

Stem cell therapies are classified such as: Embryonic stem cells, Tissue-specific stem cells, Mesenchymal stem cells, Induced pluripotent stem cells.

Adoptive cell therapy, also known as cellular immunotherapy, is a form of treatment that uses the cells of our immune system to eliminate cancer. Some of these approaches involve directly isolating our own immune cells and simply expanding their numbers, whereas others involve genetically engineering our immune cells (via gene therapy) to enhance their cancer-fighting capabilities. Immune cells known as killer T cells are ability to bind to markers known as antigens on the surface of cancer cells. Cellular immunotherapies can be deployed in different ways: Tumor-Infiltrating Lymphocyte (TIL) Therapy, Engineered T Cell Receptor (TCR) Therapy, Chimeric Antigen Receptor (CAR) T Cell Therapy, Natural Killer (NK) Cell Therapy.

SHORT TALK 9

The Story of a Novel Compound Targeting the Hippo Pathway in Hepatocellular Carcinoma

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Hepatocellular carcinoma (HCC) ranks fifth in cancer-related deaths worldwide. There are different treatment options for HCC, but patients' benefit from them is limited. Therefore, the need for both more effective and tolerable treatment options is increasing. Many signaling pathways responsible for HCC are known. One of these, the Hippo pathway, is evolutionarily conserved and is generally defined as a pathway that regulates and controls growth. In most studies on the Hippo pathway, it has been reported that the main task of this pathway is the control of organ development, stem cell function, regeneration and tumor suppression. However, some studies report that this pathway also plays a role in the initiation and progression of the tumor in different types of cancer. Targeting the YAP protein, which is one of the most important components of this pathway, has recently been shown as an important treatment option. Today, drug repurposing through FDA-approved molecules and scanning libraries containing commercial compounds that have not yet received FDA approval with virtual activity scanning approach are frequently preferred methods. The zebrafish model is frequently used by researchers to accelerate drug development steps. Given the high level of conservation between species, the effects observed in zebrafish-based experiments are considered representative of other higher vertebrate species, including humans. In addition, zebrafish larvae provide various technical and economic advantages in high-scale drug screening due to their unique biological properties. Therefore, while providing more valuable information than in vitro studies, it results in less time and cost than working with rodents. Our aim is to find novel target-specific candidate compounds and/or molecules in hepatocellular carcinoma and to obtain information about their mechanisms. Here, studies on the effect of a compound that has never been investigated before on HCC and its toxicity in zebrafish will be mentioned.

SHORT TALK 11

Overview of Cancer Drugs Causing Fingerprint Loss

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Hand-foot syndrome is an acute drug reaction characterized by various degrees of erythema, dysesthesia or paresthesia, and edema in the palmar and plantar regions caused by some drugs used for cancer treatment. These drugs include chemotherapy and targeted drugs. Hand-foot syndrome occurs when the drug leaks from small blood vessels in the hands and feet. The drugs that most commonly cause this reaction include drugs such as capecitabine, doxorubicin, ixabepilon, docetaxel, pazopanib, axitinib, cabozantinib, regorafenib, sorafenib, sunitinib, and vemurafenib. There is a return. In this study, the effects of many cancer drugs, especially capecitabine, that cause fingerprint loss will be reviewed and contributed to the literature.

Material and Method10 years of retrospective articles and books will be examined.

Capecitabine, an oral prodrug of 5-fluorouracil, inhibits DNA synthesis. It received FDA approval for the treatment of metastatic colorectal and breast cancers (Lou et al. 2016). Capecitabine has a serious hand-foot syndrome disadvantage, which limits its clinical use when used as first-line therapy for multiple tumor types (Chen et al. 2016).

In clinical studies, regorafenib has demonstrated a consistent and predictable adverse event profile, with hand-foot skin reaction (HFSR) among the most clinically significant toxicities (McLellan et al. 2015). Sorafenib (SOR) is the most common of the various side effects, with hand-foot syndrome (HFS) (Kamimura et al. 2018). Fingerprint examinations can be facilitated in criminal cases in examinations of hand and foot disease. Interpreted on existing ones. Capecitabine-based research and developments in criminal cases can be accommodated in a multidisciplinary framework.

SHORT TALK 12

SpheroMake: A New Rapid Spheroid Production Material

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Conventional two-dimensional (2D) cell culture methods used for over a century at a low cost but fail to imitate the 3D microenvironment of the organism. Almost all studies including drug developments for various cancers, uses 2D culture methods, where drugs can reach all cells equally, where they lie flattened on the bottom of culture flask with a wide surface for cell-drug interaction. However, tumors in the body forms spheroid structures, where the inner cells survive with low oxygen and nutrients, develop different metabolism, and can avoid chemotherapeutic drugs. Therefore, developing 3D culture methods to mimic tumor spheroids is essential.

Low-attachment multi-well culture plates offer a solution to acquire spheroids in similar sizes however costs are high. Lower cost methods include hanging-drop formations and coating material such as noble agar. In this study we have tested our new coating material, named as SpheroMake (SM), on MDA cells and compared results with Mesenchymal Stem Cells (MSCs). Spheromake were prepared by mixing each vial with 5 ml culture, autoclaving and covering the 6 well culture plates with 800 µl hydrogel, while still warm. Upon crosslinking, plates were used immediately or stored in 4°C fridge. Noble agar (NA) was prepared with the same method, while hanging drops (HD) were prepared with cells on the lid of petri dishes. Initially, MSCs were cultured on SM, NA and HD methods for 3 days. Spheroids were photographed and diameters measured each day. Later, MDA cells were cultured using Spheromake and diameters were again measured.

We found that sizes of MSC spheroids varied greatly in NA and HD groups, due to the attachment of floating spheroids to each other and causing formation of bigger spheroid clumps. Within SM group comparisons of MSCs and MDA cells, MSCs formed spheroids with more uniform size, 90-100 µm size on day 3, while MDA cells had more variations on size. Median spheroid size was 50-80 µm bigger on MDA cells than MSCs.

We think that our material is a cheap alternative to form spheroids more uniform than agar methods, faster and less laborious than HD method and cheaper than low-attachment plate alternatives.

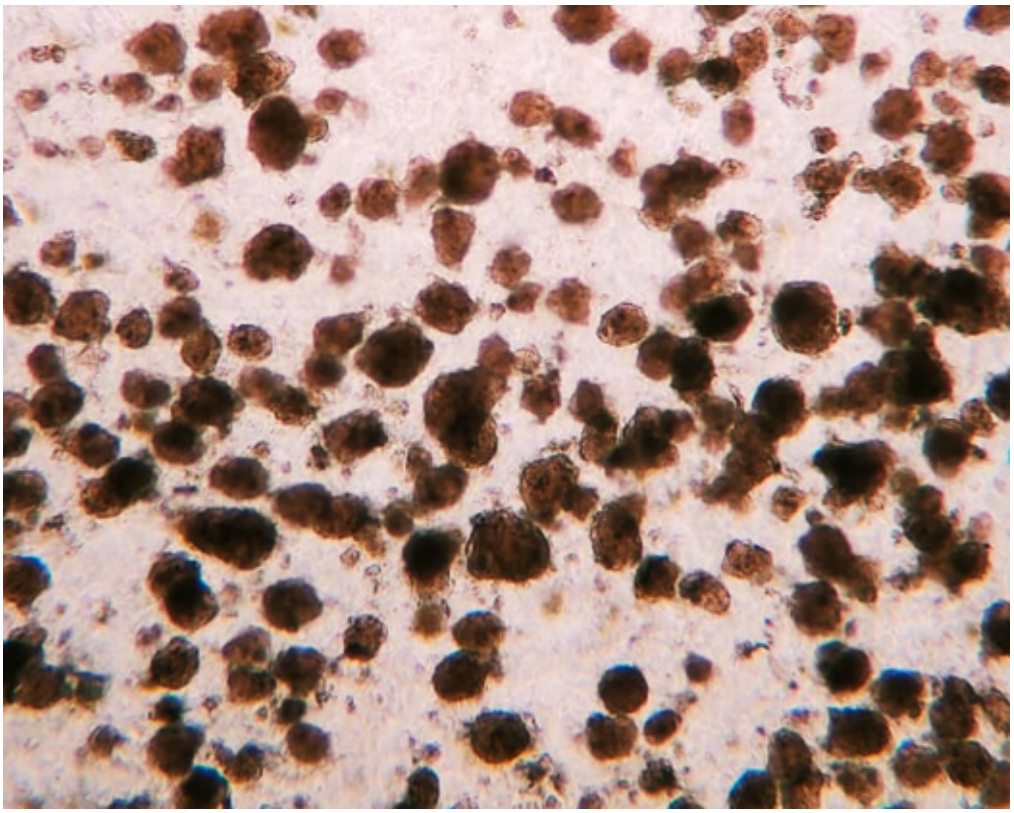

Figure 1: MSC spheroids formed on SpheroMake.

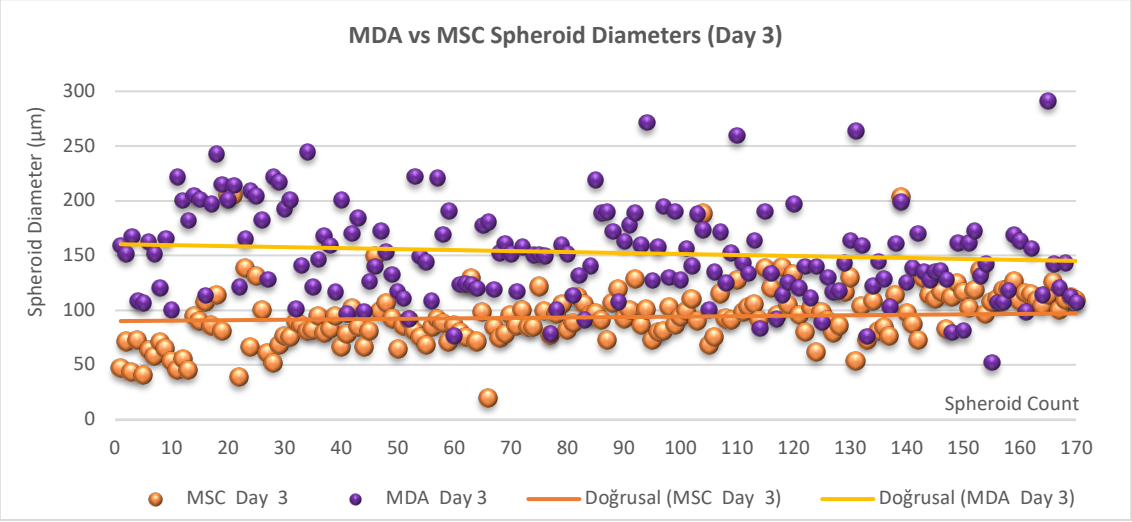

Figure 2: Spheroid diameters on Day 3. Each dot represents a measured sphereoid. MSCs formed spheroids with more uniform size, while median spheroid size were 50-80 µm wider on MDA cells and spheroids were less uniform.

ORAL PRESANTATION 1

Inhibition of 6-phosphoructo-2-Kinase and Ornithine Decarboxylase Oncogenic Properties of Pancreatic Adenocarcinoma Cells

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Introduction &Aim: Pancreatic adenocarcinoma is one of the deadliest cancers, and incidence is on the rise. Novel therapeutic approaches are needed to combat this deadly disease. Activating mutations in the *KRAS* gene confers an aggressive metabolic phenotype in pancreatic adenocarcinoma, which may present therapeutic vulnerabilities. Hyperactive KRAS stimulates glycolysis and polyamine synthesis pathways that are associated with malignant properties, including proliferation and chemoresistance. In this study, we set out to study the effect of dual targeting of 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase-3 (PFKFB3), an activator of glycolysis, and ornithine decarboxylase 1 (ODC1), the rate-limiting enzyme of polyamine synthesis pathway, on the oncogenic properties of pancreatic adenocarcinoma cells.
Material & Methods: PANC-1 and MIA PaCa-2 cell lines were used as pancreatic adenocarcinoma models to test the hypothesis. PFKFB3 and ODC1 mRNA expressions were silenced using specific siRNA molecules. Enzymatic activities of PFKFB3 and ODC1 were inhibited using clinical grade inhibitors, AZ PFKFB3 26 and difluoromethylornithine (DFMO), respectively. Forty-eight hours after silencing or drug treatment, cell viability was assessed by crystal violet assay. Clonogenic assays were also performed to determine the capacity of cells treated with combination of AZ PFKFB3 26 and DFMO to grow as single colonies.
Results: Combined silencing of PFKFB3 and ODC1 potently suppressed the proliferation of the cells, compared with PFKFB3 or ODC1 silencing alone. Combined pharmacological inhibitions of PFKFB3 and ODC1 exhibited a greater cell suppressive effect relative to individual inhibitons. Dual targeting of PFKFB3 and ODC1 markedly decreased the number of colonies, suggesting that PFKFB3 and ODC1 may cooperate to increase the clonogenic and proliferative potential of pancreatic adenocarcinoma cells.
Conclusion: Combined inhibition of glycolysis and polyamine synthesis pathways via PFKFB3 and ODC1 may be a rational therapeutic strategy in the management of pancreatic adenocarcinoma.

ORAL PRESANTATION 2

Investigation of Enhanced Uptake of Hypericin with Chitosan Nanoparticles in Lung Cancer

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Introduction and Aim: Nanoparticles (NPs) are one of the foremost favored materials in drug release systems. Photodynamic treatment (PDT), acts by enacting natural components with light to make radicals and causing passing due to intracellular harmfulness. In this treatment, Hypericin (HY) which was determined from *Hypericum perforatum* (St John's Wort) was utilized as a photosensitizer and anticancer agent. It is now known that cytotoxicity, anti-proliferative and anti-tumor impacts happen after HY-mediated PDT. HY is clustered in an aqueous environment which diminishes its proficiency. Hence, it was favored to be utilized with NP-based carriers. Alternative methods of treatment are increasing, especially in lung cancer. It was aimed to see the effects of loaded NPs on A549 (lung epithelium adenocarcinoma cell line) cells using a natural substance and a therapy method instead of using drugs and conventional methods.

Materials and Methods: HY-loaded chitosan (CH) NPs (HY-CH-NPs) were prepared to increase cellular uptake and for *in vitro* evaluation at 24 and 48 hours. After the application of HY-CH-NPs and HY groups, cells were exposed to light activation. There was also a group that not activated by light. MTT analyses, AO/PI fluorescent staining, ROS level (Reactive oxygen species) were evaluated in each group.

Results: While there was a limited effect on HY without NP groups, significant loss of viability was observed in HY-CH-NPs at 24 hours. MTT assay revealed that the HY-CH-NP 600 nM group had a %56 decrease in cell viability within 48 hours. The same result was proved in all assays.

Conclusion: Since the nanoparticle allows to an increase in the uptake of HY, the expected anti-cancer effects have been observed at much lower doses.

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ORAL PRESANTATION 3

Therapeutic Effects of Kumquat (*Fortunella Japonica* Swingle)

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Introduction and Aim: Kumquat (*Fortunella japonica* S.) is the smallest fruit of the citrus family, natively distributed mainly in China and Japan. Rich in essential oils and high antioxidant content. Through the phytochemicals in the content, it exhibits many biochemical properties such as antioxidant, antimicrobial, and anticancer activity. In this study, we aimed to reveal the therapeutic effects of kumquat.

Materials and Methods: *Fortunella japonica* S. was extracted in 80% methanol. Total antioxidant, phenol, and flavonoid contents of different concentrations of the extract between 0.625 – 60 mg/mL were measured by photometric methods. The anticancer effects of the extract have been demonstrated *in vitro* on epidermoid carcinoma (A431), and human healthy skin fibroblast (CCD-1079Sk) cell lines. After cells were incubated with different concentrations of *Fortunella japonica* extract (0.625 – 60 mg/mL) for 24 hours; cell viability by the MTT test, and intracellular reactive oxygen species (iROS) levels by H_2DCF-DA fluorescent probe fluorometrically determined. Half maximal inhibitory concentration (IC_{50}) of the extract were calculated. Concentrations under IC_{50}, the apoptotic effect of cells with acridine orange/ ethidium bromide (AO/EB) double dye, the genotoxic effect by the micronucleus assay, and the sensitivity of the cell by clonogenic assay were demonstrated. The wound-healing effect of the extract was indicated in a wound model created with wound apparatus in cancer and healthy cells.

Results: The cytotoxicity and iROS increased, apoptosis and genotoxicity were induced with different doses of *Fortunella japonica* S. extract treatment to all cell lines dose-dependently (p<0.001). In the wound healing model, it has been shown that with increasing doses of the extract, the wound areas created in the health cells decrease.

Conclusion: Our study has revealed that *Fortunella japonica* S. extract has many biochemical effects. However, prospective detailed studies are needed to use this fruit in treating various diseases clinically and in drug production.

Keywords: *anticancer, antioxidant, cell culture, genotoxicity, wound healing*

ORAL PRESANTATION 4

L1Ta Retrotransposons as Rndogenous Mutagens in Papillary Thyroid Carcinoma

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Introduction and Aim: The incidence of papillary thyroid carcinoma (PTC) has increased in the last 30 years. New genetic variants have been identified in tall cell variant PTC (TV-PTC), the most common aggressive subtype with a higher incidence rate than classical PTC (C-PTC). This indicates that investigating novel intracellular mutagenic factors that affect classical and TV-PTC is crucial. L1Ta retrotransposons, an intracellular mutagenic factor in the human genome that can be activated in the early stage of carcinogenesis, have been observed to play a role in the pathogenesis of many different types of cancer. Therefore, we aimed to investigate the potential mutagenic roles of L1Ta retrotransposition in the pathogenesis of classical and TV-PTC.

Materials and Methods: L1Ta retrotransposition profiles of FFPE (formalin-fixed paraffin-embedded) DNA isolated from matched tumour / normal adjacent to tumour (NAT) tissue samples of histopathologically classified C-PTC and TV-PTC were compared using TE-NGS (Transposable Element Next Generation Sequencing) method.

Results: The insertions found in samples of tumour and NAT tissues of classical and TV-PTC patients were observed to be enriched primarily in intronic regions of genes in different signalling pathways. While L1Ta insertions in classical PTC samples accumulated in ERBB signalling pathway proto-oncogenes, the insertions detected in TV-PTC were more highly localised to tumour suppressor genes loci belonging to the WNT signalling pathway.

Conclusion: Our results suggest that novel L1Ta insertions detected among NAT tissue samples have evaded negative selection pressure and provided background genetic instability required for neoplastic transformation. The insertions localised in cancer-related genes loci that have been observed in tumour samples seem to have contributed to maintaining intra-tumoural heterogeneity and have played a role in determining both clinical outcomes and aggressiveness of PTC. Our findings reveal the importance of L1Ta retrotransposons as a potential therapeutic target in thyroid carcinogenesis.

Keywords: Retrotransposons, thyroid cancer, next-generation sequencing.

Acknowledgements: This work was supported by the Scientific and Technological Research Council of Turkey and the Ondokuz Mayis University Scientific Research Projects Unit.

ORAL PRESANTATION 5

Sequential Application of an Alternative Drug Repurposing Model Enhances Cytotoxicity in Hepatocellular Carcinoma

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Introduction and Aim: Hepatocellular carcinoma (HCC) is the seventh most common cancer type worldwide that ranks fourth in cancer-related deaths. Most HCC patients diagnose at an advanced stage and develop resistance to chemotherapy. Therefore, there is a need for new treatment models in HCC. Once the drugs that treat other diseases, drug repurposing, are used in combination, it can increase treatment efficacy, prevent drug resistance, and provide a time-saving and low-cost process with minimum risk of failure. This research aims to analyze the cytotoxic activity and drug/combination efficiency of two FDAapproved therapeutic agents, Valproic Acid (VPA, anti-epileptic) and Niclosamide (NIC, anti-helminthic), in the HepG2 liver cell line.

Materials and Methods: We treated HepG2 cells with VPA (1 mM-0.25 mM) and NIC (1 μM-0.25 μM) for 24-72 hours, either by concurrent or sequential application. For sequential administration (6-12h), we also evaluated viability by changing the order of drugs. We assessed cell viability by SRB assay and defined the anti-growth effect (GI50, TGI) and cytotoxicity (LC50) of drugs alone/combinations.

Results: The combinatorial therapy synergistically decreased cell viability compared to the drugs alone. The sequential application strategy was more cytotoxic than concurrent, considering LC50 values. Furthermore, pre-treatment by NIC exerted significant antigrowth activity at relatively lower doses than pre-treatment via VPA based on GI50 values.

Conclusion: The future success and clinical translation of this combination strategy may hold significant promise for the alternative therapy model for HCC patients.

Keywords: Hepatocellular carcinoma (HCC), Drug Repurposing, Cytotoxicity, Niclosamide, Valproic Acid

ORAL PRESANTATION 6

Lutein'in Tek Başına ve Sisplatinle Birlikte Sitotoksik ve Genotoksik Etkilerinin İncelenmesi

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Giriş/Amaç: Lutein, meyve ve sebzelerde en yaygın bulunan karotenoidlerden biridir. Karotenoidlerin antikanser etkileri, anti-oksidan ve pro-oksidan aktiviteleri arasındaki dengeye bağlı olarak değişebilir. Bu nedenle kanser hücrelerinde kemoterapötiklerle birlikte ayrıntılı olarak değerlendirilmelidir.

Metot: Bu çalışmada lutein tek başına ve sisplatinle kombine olarak hücre canlılığı üzerine etkileri MDA MB-231 ve HUVEC hücrelerinde MTT testi ile incelenmiştir. Uygulamaların MDA MB-231 meme kanseri hücrelerinde oksidatif DNA hasarı üzerine etkileri 8-OHdG Elisa kit kullanılarak, apopitotik etkileri ise caspase-3 kit kullanılarak değerlendirilmiştir.

Bulgular: Sonuçlarımıza göre 1,25-20 µM konsantrasyonlarında 24 saat lutein uygulaması HUVEC hücre canlığı üzerinde önemli bir etki göstermezken, 48 saat uygulamada hücre canlılığı %60'lara gerilemiştir. MDA MB-231 hücrelerinde ise hücre canlılığının 48 saatte daha fazla etkilendiği ve canlılık yüzdesinin %50'ye düştüğü gözlenmiştir. Sisplatinle eş zamanlı uygulamalarda hücre canlılığı üzerinde lutein konsantrasyonuna ve süreye bağlı sinerjistik bir etki saptanmıştır. Luteinin 10 µM konsantrasyonu MDA MB-231 hücrelerinde kontrole göre anlamlı düzeyde oksidatif DNA hasarı oluşturduğu belirlenmiş olup, bu etkinin sisplatinle eş zamanlı uygulamalarda daha fazla olduğu tespit edilmiştir. Yine bu hücrelerde kaspaz 3 aktivitesi değerlendirildiğinde sisplatinle eş zamanlı lutein uygulamasının kaspaz 3 düzeyini kontrole göre önemli düzeyde artırdığı gözlenmiştir.

Sonuç: Ön sonuçlarımız, yaygın kullanılan kemoterapötik bir ajan olan sisplatinle birlikte lutein kullanımının, meme kanseri hücre canlılığı ve DNA hasarı üzerinde etkili olduğunu

göstermektedir. Daha fazla ileri araştırmayla desteklenmeye ihtiyaç duyulmakla birlikte luteinin diyet olarak kullanımı kemoterapi etkinliğine olumlu katkısı olabilir.

ORAL PRESANTATION 7

Investigation of Cytotoxic and Genotoxic Effects of Lutein Alone and in Combination with Cisplatin

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Introduction / Aim: Lutein is one of the most common carotenoids in fruits and vegetables. The anticancer effects of carotenoids may vary depending on the balance between their anti-oxidant and pro-oxidant activities. Therefore, it should be evaluated in detail together with chemotherapeutics in cancer cells.

Materials and Methods: In this study, the effects of lutein alone or in combination with cisplatin on cell viability were investigated by MTT test in MDA MB-231 and HUVEC cells. The effects of the treatments on oxidative DNA damage in MDA MB 231 breast cancer cells were evaluated using the 8-OHdG elisa kit, and the apoptotic effects were evaluated using the caspase-3 elisa kit.

Results: According to our results, 1.25-20 µM concentrations of lutein did not have any significant effect on HUVEC cell viability at 24 h treatment, while cell viability decreased to 60% at 48 h treatment. On the other hand, it was observed that MDA MB 231 cell viability was more affected in 48 hours and the percentage of viability decreased to 50%. In simultaneous treatments with cisplatin, a synergistic effect was detected on cell viability, depending on lutein concentration and time.

It was determined that 10 µM concentration of lutein caused significant oxidative DNA damage in MDA MB 231 cells compared to the control, and this effect was found to be higher in simultaneous treatment with cisplatin. It was also observed that simultaneous treatment of lutein with cisplatin increased the level of caspase 3 significantly compared to the control.

Conclusion: Our preliminary results show that the use of lutein together with cisplatin, a widely used chemotherapeutic agent, has an effect on breast cancer cell viability and DNA damage. Although it needs to be supported by further analysis, the use of lutein as a diet may contribute positively to the efficacy of chemotherapy.

ORAL PRESANTATION 8

Prunus armeniaca L. (Acı Kayısı) Çekirdek Ekstresinin Genotoksik ve Sitotoksik Etkilerinin Değerlendirilmesi

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Özet: Rosaceae familyasının bir üyesi olan kayısı ağacı (*Prunus armeniaca* L.) üretimi ve insan beslenmesinde tüketimi dünya genelinde tercih edilen ticari ürünlerden biridir. Tatlarına göre tatlı kayısı (sweet apricot), yarı acı kayısı (semibitter apricot) ve acı kayısı (bitter apricot) olarak sınıflandırılan kayısı çekirdekleri; çeşitli polifenoller, flavonoidler ve siyanojenik glikozit amigdalin içermektedir. Amigdalin aynı zamanda vitamin B17 adıyla da anılmaktadır. Amigdalin alternatif tıpta ateş düşürücü, öksürük giderici ve bir antikanser ajanı olarak kullanılmakta; migren, kronik inflamasyon, astım ve diyabet gibi çeşitli hastalıkların tedavisinde de yer almaktadır. Bu çalışmada, acı kayısı çekirdeği ekstresinin (bitter apricot extract, BAE) genotoksik ve sitotoksik etkilerinin belirlenmesi hedeflenmiştir. BAE'nin genotoksik etkileri *in vitro* mikronükleus (MN) ve komet (tek hücre jel elektroforezi) testleri ile değerlendirilmiştir. BAE'nin yarattığı büyüme baskılayıcı etki, seçilen dozlarda (0,1, 1, 10, 100 ve 1000 µg/ml) tek başına ve doksorubisin, metotreksat ve 5-fluorourasil (5-FU) kemoterapötik ajanlarının seçilen dozları (0,01, 0,1, 1, 10, 100 µM) ile kombine edilerek meme kanseri hücre hatları (MCF-7, MDA-MB-231) üzerinde sulforhadamine B (SRB) hücre canlılık testi ile analiz edilmiştir. Elde edilen sonuçlara göre, her iki genotoksisite testinde BAE'nin yüksek dozlarda dahi anlamlı bir genotoksik etki yaratmadığı kaydedilmiştir. Ayrıca, tek başına BAE uygulamasının her iki hücre soyunda da büyüme baskılayıcı etkisinin zayıf olduğu belirlenmiştir (IC_{50} > 100 µg/ml). Ancak BAE ile 5-FU'nun etkili oldukları dozlardaki kombinasyonlarında sinerjistik etkileşim gözlenmiştir. Bulgularımız, BAE'nin büyüme baskılayıcı etkisinin tek başına zayıf olmasına rağmen, 5-FU ile kombinasyonunun sinerjistik etki göstermiş olması nedeniyle kanser tedavisinde bazı kemoterapi ajanlarının etkinliğini arttırabilme potansiyeline sahip olabileceğini düşündürmektedir. Anahtar kelimeler: Prunus armeniaca L., genotoksisite, sitotoksisite

ORAL PRESANTATION 9

Investigation of Triosephosphate Isomerase Targeting in Breast Cancer.

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Introduction/Aim: Warburg Effect (aerobic glycolysis) is one of the characteristic feature of cancer and contributes to the cancer progression. For this reason, glycolysis and energy metabolism are still a major area in anti-cancer research today. Triosephosphate Isomerase (TPI) is one of the key enzymes of glycolysis. TPI deficiency causes irreversible brain damage as well as muscle disorders and hemolytic anemia. It has been shown that TPI plays role in cancer progression. In our previous studies, we showed that TPI has higher expression in breast cancer cells, and also in patient tissue samples. However, there aren't enough studies on the TPI-cancer relation. TPI inhibition leads to the formation of a toxic intermediate, methylglyoxal (MG). So, inhibition of TPI may provide an advanced effect through MG production in tissues where glycolysis occurs in higher rate, like tumor tissues. Also, TPI has 4 tyrosine side chains and it's known to undergo nitro-tyrosination due to free radical formation. In this study, the effects of potential components (Resveratrol and Ornidazole) that may cause TPI inhibition in breast cancer and TPI-nitrotyrosination were investigated.

Materials and Methods: Resveratrol (10-300μM) and Ornidazole (1-200 μM) were applied at different concentrations for 24 and 48 hours in MCF-7 and MDA-MB-231 cells separately. Cell viability was determined by the SRB method. TPI levels were examined by ELISA and Western-Blot. Then, TPI-immunoprecipitation was performed to evaluate TPI-nitrotyrosination, and nitro-tyrosine and nitric oxide synthase (NOS) levels were determined by western-blot.

Results: Ornizdazole treatment didn’t cause a significant cytotoxic effect. Resveratrol has been shown to decrease cell viability and cause changes in TPI levels depending on the dose. Also, it was observed that Resveratrol could affect TPI nitro-tyrosination via NOS activity.

Conclusion: The effect of Resveratrol on TPI in breast cancer has shown for the first time. The findings of the study reveal a new mechanism that can be targeted in breast cancer.

ORAL PRESANTATION 10

Anticancer, Antibacterial, and Antiangiogenic Effects of Green Synthesized Hemocompatible Silver Nanoparticles

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Introduction / Aim: Silver nanoparticles (AgNPs) are metallic NPs having a wide range of uses, including biosensors, optoelectronics, clean water technologies, energy production as well as anticancer applications [1]. Since many chemical and physical NPs synthesis methods yield toxic by-products that are not eco-friendly, green synthesis procedures are increasingly being favored by researchers nowadays [1]. This study aimed to investigate the anti-cancer, anti-microbial, antioxidant, anti-angiogenic, and hemocompatibility properties of AgNPs green synthesized using apricot (*Prunus armeniaca)* seed shell extract.

Materials and Methods: Generated AgNPs were subjected to various characterization tests after the optimum synthesis technique was identified using the biogenic green synthesis method. The MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide) test was used to assess the effects of AgNPs at different concentrations on the human non-small cell lung carcinoma (H1299) and the human bronchial epithelial cell lines (Beas2B). The effects of the AgNPs on the angiogenesis process were evaluated with the *in ovo* chorioallantoic membrane (CAM)

assay. Aside from evaluating antibacterial activity in various strains (*Escherichia coli spp.*, *Staphylococcus aureus*, *Bacillus subtilis,* and *Shigella spp.*), antioxidant capabilities were studied using the DPPH (1,1diphenyl-2-picrylhydrazyl) free radical scavenging assay. Hemolysis and coagulation tests were used to determine the hemocompatibility of AgNPs.

Results: MTT test revealed that AgNPs were cytotoxic in a dose-dependent manner in the H1299 cell line. AgNPs also influenced *de novo* vessel synthesis and the total number of branching points, according to CAM assay results. NPs have been found antibacterial on different bacterial strains, had an antioxidant and blood clotting effect, and had no hemolytic effect.

Conclusion: AgNPs are a promising candidate with anticancer and antiangiogenic potential, according to *in vitro* cell culture studies and *in ovo* CAM assay results. Apart from that, they were found antibacterial and antioxidant. They can be investigated for use in different pathophysiological conditions including cancer.

Keywords: silver nanoparticle, biogenic green synthesis, angiogenesis, hemocompatibility, in ovo

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ORAL PRESANTATION 11

Cancer profile of Giresun City based on Giresun Training and Research Hospital datas

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Introduction / Aim: The most common cancer cases in the region were investigated by documenting the cancer cases diagnosed in the last 5 years in Giresun University Education and Research Hospital.

Materials and Methods: All cancer cases diagnosed in the last 5 years were determined by the electronic archive.The most common types of cancer and their distribution by years were investigated.

Results: Between 2017-2021, 3052 cancers were diagnosed. Skin cancer was reported most frequently (basal cell carcinoma 450cases, squamous cell carcinoma 250 cases, malignant melanoma14 cases). Except skin tumors, the most seen tumours were prostate (446cases), bladder (399cases), colon (320cases), breast (267cases), and lung cancers (243cases).The other tumors diagnosed were stomach (192cases), thyroid (135cases), endometrium (80cases), liver (61cases), kidney (47cases), hematological cancers (46 cases), testis (39 cases), esophagus (25cases) , soft tissue (16cases), pancreas (13cases), brain (11cases), cervix (8cases), larynx (7cases), nasopharynx (5cases) carcinomas.

Conclusion: The department of pathology at Giresun University is the only pathology laboratory in the whole province. 633 cancer cases were diagnosed in 2017, 693 were in 2018, 692 were in 2019, 465 were in 2020, and 569 were in 2021. According to years, it was noted that there was a decrease in the number of cancers in the last two years. According to Cancer Statistics 2017 data, the most common cancer types are lung, prostate, colon, bladder cancer in men, and breast, thyroid, colon, lung, cancers in women in our country.

Excluding skin tumors, prostate carcinoma was the most common tumor in men, and breast carcinoma in women. Apart from these, bladder, colon, and lung carcinomas were the most common types of cancer. The difference between the health minister dates and our results were

could be due to Hospital conditions and surgical operations possibilities, however, our results are considered to reflect the profile of the region.

ORAL PRESANTATION 12

Synergistic Anticancer Effect of Chalcone Derivatives and Wnt/B-Catenin Pathway Inhibitor Niclosamide Againts Lung Cancer Cells

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Introduction and Aim: Lung cancer is the leading cause of cancer death in both sexes all over the world. Although development in treatment options in non-small cell lung cancer (NSCLC), the overall survival ratios of lung cancer is still poor because most of the patients are diagnosed at an advanced or metastatic stage. Therefore, there is an urgent need for developing strategies to enhance the efficacy of treatment in the NSCLC. Niclosamide has been shown to inhibit the Wnt/ β-Catenin pathway effectively in cancer cells by various mechanisms. Chalcone derivatives have the potential therapeutic agent in cancer treatment. In this study, the anticancer activities of niclosamide-chalcone derivatives combination were investigated in human lung cancer cells (A549 and H1299).

Materials and Methods: The cytotoxic effect of niclosamide-chalcone derivatives combination was determined by SRB viability test. In addition, the cytotoxicity of the combination in healthy human bronchial epithelial cells (BEAS-2B) was evaluated. In order to determine apoptosis, we make triple fluorescent staining of cancer cells and we evaluate gene expression levels of apoptotic proteins by PCR.

Results: It was found that niclosamide-chalcone derivatives combination synergistically inhibited cell growth in both A549 and H1299 cells dose-dependently and was not toxic in healthy cells at the same doses. It was observed that niclosamide-chalcone derivatives combination killed cells via apoptosis in fluorescent staining.

Conclusion: The results show that niclosamide-chalcone derivatives combination therapy has high cytotoxic and apoptotic potential in lung cancer cells. It was determined that this combination could be a potential drug in the treatment of lung cancer.

Keywords: Niclosamide, chalcones, cytotoxicity, lung cancer, apoptosis

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ORAL PRESANTATION 13

Goldenberry (*Physalis Peruviana* L.) extract exacerbates apoptotic and autophagic effects in epidermoid carcinoma

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Introduction and Aim: A goldenberry (*Physalis peruviana* L.) is one of the most promising exotic fruits in terms of its biocapacity. Some studies have been shown that this fruit has antimicrobial, antioxidant, and anticancer properties. This study investigates the anticancer and skin wound healing effects of *Physalis peruviana* L. on epidermoid carcinoma (A431) and fibroblast (CCD1079Sk) cells.

Materials and Methods: The antioxidant content of *Physalis peruviana* L. of 80% methanol extracts (PPEE) for 24 hours with different concentrations (0.15-20 mg/mL) was determined by the photometric methods. The cytotoxicity was determined on A431, and CCD1079Sk cells colorimetric by using *in vitro* MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay and intracellular reactive oxygen species (iROS) by 2',7'-dichlorofluorescein-diacetate (H_2DCF-DA) the fluorometric method, then half maximal inhibitory concentration (IC_{50}) was calculated. After 24-hour exposure of cell lines to the extract concentrations below the IC_{50} on cell lines; apoptosis by the Acridine Orange/Ethidium Bromide double dye method, cell sensitivity is by the clonogenic assay, and genotoxicity was determined using the micronucleus method. The wound model was created using CytoSelect™ 24-Well Wound Healing Assay plate and apparatus on the CCD1079Sk cell line. Expressions of apoptotic and autophagic proteins were measured by western blot.

Results: Antioxidant activities of PPEE were found to increase dose-dependent. In epidermoid carcinoma cells, different concentrations of PPEE increased cytotoxicity, iROS, apoptosis, and DNA damage in a dose-dependent manner. In addition, wound areas shrunk with increasing

doses of PPEE in the fibroblast cell line. Expressions of apoptotic and autophagic proteins increased in a dose-dependent manner.

Conclusion: PPEE has higher antioxidant and proliferative effects on skin fibroblast cells at low doses, while epidermoid carcinoma cells have cytotoxic, genotoxic effects. This indicates the potential of the agent as an anticancer drug in the future.

Keywords*:* anticancer, antioxidant, *Physalis peruviana* L.*,* wound healing

ORAL PRESANTATION 14

Cichorium intybus L. (Beyaz hindiba) Ekstresi ile Bazı Antikanser İlaç Etkileşimlerinin Belirlenmesi

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Cichorium intybus, asteraceae familyasına ait bir bitki olup gerek toprak üstü gerekse kök kısımları dâhil olmak üzere dünyanın çeşitli bölgelerinde gıda, çay ve gıda katkısı olarak tüketilen bir bitkidir. Bu çalışmanın amacı, *C. intybus* bitkisinden elde edilen ekstre ile bazı kemoterapötik ajanların kombinasyonları arasındaki etkileşimleri büyüme baskılayıcı etki yönünden değerlendirmektir.

Bitkinin yapraklarından asidik ortamda metanol: H_2O (17:3) ekstresi hazırlanmıştır. Hazırlanan ekstre liyofilize edildikten sonra DMSO ile çözülmüş ve meme kanser hücre soyları MCF-7 ve MDA-MB-231 hücreleri üzerine son konsantrasyon 0,1-1000 µg/ml olacak şekilde pipetlenmiştir. İkili kombinasyon çalışmaları için doksorubisin, metotreksat ve 5-fluorourasil 0,01-100 µM doz aralığında kullanılmıştır. Etkileşimlerin analizinde CalcuSyn v2.1 kullanılmıştır. Ayrıca, floresans mikroskopta Hoechst 33342 ve propidyum iyodür ikili boyaması ile apoptotik hücre ölüm analizi gerçekleştirilmiştir.

C. intybus ekstresinin büyüme baskılayıcı etkisi MCF-7 ve MDA-MB-231 hücrelerinde sırasıyla 98,3 ve 429 µg/ml IC_{50} değerleri ile orta veya zayıf şeklinde değerlendirilmiştir. İkili kombinasyon uygulamalarında ise çoğunlukla additif ve bazı uygulamalarda ise kısmi antagonistik etkileşimler tespit edilmiştir. İkili boyama sonuçları, her iki hücre soyunda da apoptotik bir hücre ölümünün gerçekleşmediğini düşündürmektedir. Sonuç olarak, beyaz hindibanın bazı kemoterapi ajanları ile antagonistik etkileşimde bulunma olasılığı nedeniyle kemoterapi alan hastalar tarafından bu bitkinin tüketiminde dikkatli olunması yarar sağlayabilir.

ORAL PRESANTATION 15

Echium vulgare Bitkisinden Elde Edilen Ekstrelerin Büyüme Baskılayıcı Etkilerinin Değerlendirilmesi

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Echium vulgare (engerek otu), Akdeniz havzasında yetişen ve geleneksel tıpta yılan ısırıklarına karşı kullanılan bir bitkidir. Özellikle köklerinden hazırlanan merhemler topikal olarak yaraların iyileştirilmesinde ve kas ve ligament gerilmelerinde kullanılmaktadır. Fitokimyasal içerik bakımında öne çıkan bileşikler pirolizidin alkaloitleridir. Çalışmamızın amacı, *E. vulgare* bitkisinden elde edilen farklı ekstreler ile bazı kemoterapötik ajanların kombinasyonları arasındaki etkileşimleri büyüme baskılayıcı etki yönünden değerlendirmektir. Bitkinin yapraklarından ve köklerinden asidik ortamda ve metanol:H_2O (7:3) karışımında üç farklı ekstre hazırlanmıştır. Hazırlanan ekstreler liyofilize edildikten sonra DMSO ile çözülmüş ve meme kanser hücre soyları MCF-7 ve MDA-MB-231 hücreleri üzerine son konsantrasyon 0,1-1000 µg/ml olacak şekilde pipetlenmiştir. İkili kombinasyon çalışmaları için doksorubisin, metotreksat ve 5-fluorourasil 0,01-100 µM doz aralığında kullanılmıştır. Etkileşimlerin analizinde CalcuSyn v2.1 yazılımından yararlanılmıştır. Hücre ölüm modu analizi, ekstrelerin farklı dozları kullanılarak floresans mikroskopta Hoechst 33342 ve propidyum iyodür ikili boyaması ile gerçekleştirilmiştir. *E. vulgare* ekstrelerinde büyüme baskılayıcı etkinin, kullanılan ekstreye ve hücre soyuna bağlı olarak zayıf (IC_{50} > 100 µg/ml) veya orta (30 µg/ml < IC_{50} < 100 µg/ml) şiddette olduğu belirlenmiştir. İkili kombinasyon uygulamalarında çoğunlukla sinerjistik veya antagonistik etki gözlenmezken elde edilen ekstrelerden birinin doksorubisin ve 5-fluorourasil ikili kombinasyonlarında sinerjistik etkileşimler tespit edilmiştir.

İkili boyama sonuçları, her iki hücre soyunda da apoptotik hücre ölümünün gerçekleşmediğini düşündürmektedir. Sonuç olarak, *E. vulgare* ekstresinin bazı kemoterapi ajanlarıyla sinerjistik

etkileşimde bulunabileceği verisinden hareketle farklı tip kanser hücreleri ve kemoterapi ajanları ile dizayn edilebilecek kapsamlı denemelerden benzer veya daha etkin kombinasyonların elde edilebileceği düşünülmektedir.

ORAL PRESANTATION 16

Validated piRNAs in Ovarian Cancer Stem Cells

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Introduction/Aim: Ovarian cancer (OC) is leading cause of gynaecologic cancer deaths in women causes women death. While treatment is commonly successful, some cases (10–20%) show resistance to chemotherapy which is followed by recurrence. The main reason of chemoresistance is remaining therapy resistant cells. Cancer stem cells are one of the chemoresistant cell types in cancer cells population. Piwi-related small RNAs (piRNAs) are non-coding and important RNAs for stem cell regeneration and survival. Based on their epigenetic regulation roles, they are intented to control CSCs. We aimed to detect significantly dysregulated piRNAs in ovarian CSCs.

Materials and Methods: First, piRNAs that are differentially expressed in various stem cell populations were listed from literatures. PiRNA expression analysis was performed in CSCs in cell lines with ovarian cancer stem-like cells and in peritoneal fluids samples taken from patients. The expression of these piRNAs were analyzed in 2D and 3D, quiescent and non-quiescent, and CD133/ALDH (+/+) and (-/-) ovarian cancer cell lines.

Results: The results showed that ovarian cancer stem cell have differentially expressed piRNAs compared to non-stem ovarian cancer cells. PiR-823, piR-36712 and piR-020326 are significantly expressed in the most of comparisons including patient samples. However, the quiescent and non-quiescent cells showed different pattern in piRNA expressions than the other comparisons.

Conclusion: Our results supported that ovarian CSC have significant pattern of piRNA expression compared to ovarian cancer cells. This is an important finding to prove the role of piRNAs in ovarian cancer stemness features. With furhter studies,the role of piRNAs in the formation of ovarian CSCs and in the biology of ovarian cancer recurrence can be demonstrated.

ORAL PRESANTATION 17

Assessment of Single Nucleotide Variants in *hGPRC5A* gene using *in silico* Tools

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Introduction and Aim: G-protein-couple receptor, family C, group 5 member A (*GPRC5A*) encodes a transmembrane protein and induced by retinoic acid. Dysfunctional GPRC5A was reported to activate numerous signal transduction cascades and its tumor suppressor role was emphasized especially in lung cancer in recent studies. In this study, we aimed to analyze the functional consequences of SNVs in human *GPRC5A* gene using *in silico* tools.

Materials and Methods: Missense, nonsense, frameshift, splice acceptor/donor, 5'UTR and 3'UTR SNVs were filtered using the Variation viewer database. The functional consequences were obtained using PolyPhen2 and Mutation Taster databases, while the allele frequencies of these variants were determined using GnomAD database. The regulatory effects were interpreted using the RegulomeDB database and the post-translational modifications were evaluated using PhosphoSite Plus.

Results: Total 2565 variants (3 splice acceptor, 3 splice donor, 13 nonsense, 20 frameshift, 42 five prime UTR, 338 missense, 2146 three prime UTR) were obtained in *GPRC5A* gene. From the 372 coding variants 338 were missense and 57% of them were analyzed as possibly/probably damaging and 51% as disease causing according to PolyPhen2 & Mutation Taster web sites respectively. Only 170 variants were found to have allele frequency in GnomAD database and among them a single variant has MAF>0.01. Regulatory important variants are interpreted with a score of ≤ 2 and comprise only %10 of total variants. A total of 22 posttranslational modifications, 16 phosphorylation and 6 ubiquitination were detected in GPRC5A protein and 17 of these corresponded to a SNV.

Conclusion: The role of GPRC5A increases in cancer biology, since its dysregulation is associated many cancer types. The results of this study could give a brief view of how the functional consequences in *GPRC5A* gene affects its functionality in molecular perspective.

ORAL PRESANTATION 18

Detection of Acute Leukemia from Blood Plasma with Surface-enhanced Raman Spectroscopy and Machine Learning

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Introduction and Aim: Acute leukemia (AL) classified as acute myeloid leukemia (AML) and acute lymphocytic leukemia (ALL) are hematologic malignancy that arise from either lymphoid or myeloid cell line, especially among children and adults. Early detection of AL is important for clinical treatment and reducing mortality. AL is currently detected using blood, bone marrow test, imaging, and spinal fluid tests. However, these tests are expensive and time consuming. To overcome these disadvantages, Surface-enhanced Raman Spectroscopy (SERS) which enhanced Raman signals by interaction of plasmonic nanostructures with analyte, is proposed as an alternative method. In this study, it was aimed to detect AL from blood plasma with SERS and machine learning.

Materials and Methods: Silver nanoparticles (AgNPs) were synthesized using $AgNO_3$ and sodium sitrate. Synthesized AgNPs were centrifuged to form 16x concentrated AgNPs. SERS substrate was formed by dropping 16x AgNPs onto CaF_2. To obtain SERS spectra of plasma obtained from blood samples, plasma samples were dropped onto the SERS substrate. The collected spectra were analyzed in range of 400-1800 cm^{-1}. The spectra were discriminated with machine learning to highlight difference between AL and healthy plasma.

Results: AL and healthy plasma samples were dropped onto the SERS substrate and SERS spectra were collected by excitiation with 785 nm laser. Peaks around 636, 725, 816, 960, 1049, 1132, 1202, and 1329 cm^{-1} were observed on spectra. SERS spectra demonstrate many similar peaks except for some differences in relative band intensities. Discrimination of SERS spectra due to high spectral similarity was performed using machine learning. With results obtained, it has been shown that SERS and machine learning is method that can be applied for detection of AL.

Conclusions: In conclusion, SERS and machine learning provide a rapid, low-cost, and promising tool for detection of AL from blood plasma.

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ORAL PRESANTATION 19

Integrated analysis of copy number variation and genome-wide expression profiling in colorectal cancer

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Introduction/Aim: The goal of this study was to detect the association between copy number variations (CNVs) and gene expression changes to identify novel prognostic and therapeutic targets.

Materials and methods: 50 paired CRC formalin-fixed, paraffin-embedded (FFPE) samples (100 samples) were subjected to global copy number variations and gene expression analysis using Affymetrix SNP 6.0 and HGU133-X3P arrays, respectively. Partek Genomic Suite 6.6. were used for paired CNV analyses, gene expression data analysis, hierarchical clustering, and pathway enrichment. CNVs and gene expression profiling analysis were integrated to provide further insight into CRC development and to identify CNV-driven genes for diagnosis, prognosis, and drug target.

Results: Whole-genome CNV analysis comparing the paired tumor-control samples revealed gains in 704 genes and losses in 190 genes with a frequency 20% in colorectal cancer samples. DNA losses in chromosome 18q21.1 with a frequency of 40% and amplifications in 8q24.3 (36%) were found the most frequent alterations in tumors. Some of the genes such as TRAPPC9 and NIBP were novel and reported for the first time with our study. Genome-wide expression profiling showed 320 genes to be up-regulated and 525 genes to be down-regulated in CRC compared with matched controls (FDR $\leq$0.001, |log2FC|$\geq$ 1). We developed a prognostic risk score to predict the *risk* of *CRC patients* by combining the expression values of the selected genes and stage. Furthermore, integration of CNV and gene expression data identified 19 overlapping genes with changes in copy number and gene expression.

Conclusions: In conclusion, by integrating genomic and transcriptomic profiling studies, we successfully identified 19 overlapping genes associated with CRC pathogenesis and clinically useful candidate genes for diagnosis, and drug targets. Herein, we also report for the first time the CNV-driven alteration of these nineteen genes. Validation of the selected candidate genes is currently ongoing in the independent cohort.

This study is supported by TUBITAK with grant number: 109S477

Keywords: sporadic colorectal cancer, copy number variations, gene expression profiling, integration, biomarker

ORAL PRESANTATION 20

In ovo: dinosaur's offspring as an alternative in vivo model

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The chick chorioallantoic membrane (CAM) is an extraembryonic membrane that developed in fertilized chicken eggs, containing a rich network of blood vessels. Due to its highly vascularized nature and susceptibility to tumor formation CAM allows for studying angiogenesis, invasion, and metastasis of tumors. According to Turkish legislation, the CAM model system does not pose any ethical or legal problems until the 14th day of egg development day, making it an appealing option to other animal research. We used the in ovo CAM assay, which is well-known for measuring the anti-neovascularization potential of diverse compounds regardless of synthesis technique as well as assessing anti-tumor agent efficacy by testing the drug on the generated tumor. Following our improved methodology, we generated specificsized tumors from various cancer cell lines that express distinct mutations in different tissues. To optimize medication administration, we specifically chose HCT116 colorectal cancer cell lines regarding their mutations and tumorigenic capability. We utilized a variety of approaches to improve and analyze the drug's impact, and we tested until the EDD13, which has no ethical or legal concerns. Different drug administration methods resulted in a variety of outcomes. Filter paper and intravenous drug administration have both proven to be extremely effective. We also manage to quantify the results of both angiogenesis and tumor-forming assays using an AI-based analyzing service. Which improved the quality of our work and provided us with a better perspective than what the rest of the world has been using to analyze data from CAM assays. Following our research on in vivo studies, our up-to-date improved methodology offers significantly similar results in far less time and much less cost.

ORAL PRESANTATION 21

Investigation of effects of acetylsalicylic acid on pancreatic stellate cells-mediated pancreatic cancer aggressiveness

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Introduction and Aim: Pancreatic cancer (PaCa) is one of the deadliest and incurable cancer types. It has been known that PaCa has a unique tumor microenvironment (TME) which contributes to tumorigenesis. Pancreatic stellate cells are the most abundant cells in pancreatic TME. They contribute to the aggressiveness of cancer and they are active even in intraepithelial neoplastic lesions. This indicates that these cells could have tumor-initiating abilities. One of the approaches to targeting PSCs is acetylsalicylic acid (ASA), the active ingredient of aspirin. Previous studies showed that ASA inhibited the proliferation and induced apoptosis in various cancer types including PaCa. Some studies have shown that regular use of aspirin reduces the incidence of cancer. Although there are studies indicating the role of ASA on cancer cells in the literature, there is no study showing its effect on PSC-mediated cancer aggressiveness. In this study we aimed to examine the effects of ASA on aggressive cancer behaviours by changing PSC secretome.

Materials and Methods: First of all, the active and passive states of PSC cells were evaluated via α-smooth muscle and Oil Red O stainings, respectively. Next, PSC cells were treated with various doses of aspirin, and doses of 2.5 and 1.25 mM that were not toxic to cells were selected for further experiments. Conditioned media were collected from untreated-PSC cells and 24 h ASA pre-treated PSC cells and then were applied to PANC-1 and BxPC-3 PaCa cell lines. The viability of cancer cells was evaluated with the sulforhodamine B (SRB) test, and their migration abilities were analyzed with a wound healing assay. Then the two groups were compared with each other. In this way, it was examined how the differences in the medium between ASA-treated and un-treated PSC cells affected the aggressive character of cancer cells.

Results: As expected, media collected from untreated PSC cells increased the viability and migration of cancer cells, while media collected from ASA-treated PSC cells decreased these abilities. One of the possible reasons for this is thought to be the ASA reduction of various cytokines and chemokines in the secretome of PSC cells. In future analyzes, it is considered to examine the changes in these contents and illuminate the possible mechanisms.

Conclusion: According to the information obtained from the studies so far, targeting PSCpancreatic tumor cells interaction using the prevalent anti-inflammatory drug ASA might be a promising strategy for PaCa treatment.

ORAL PRESANTATION 22

Anticancer Potential of Novel Benzofuran-Chalcone Hybrids and Their Water Soluble Sodium Salts on Human Lung and Breast Cancer

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Introduction and Aim: Cancer is one of the most important health problems, one of the leading causes of death all around the world. There is still a need for new compounds to be discovered for cancer treatment. Therefore, the main aim of this research was to develop new benzofuran-chalcone hybrids and their salts and investigate their enhanced anticancer activity.

Materials and Methods: Primarily, 1-(7-ethoxy-1-benzofuran-2-yl) ethanone (1) and 1,1'-(7-ethoxy-1-benzofuran-2,4-diyl)diethanone (2) were synthesized as the starting reagent. The new 1,1'-(7-ethoxy-1-benzofuran-2,4-diyl)diethanone was used as precursor of two new series of chalcones 3a-c and 4a-c, which were obtained through Claisen-Schmidt condensation using different substituted aromatic aldehydes. The synthesized benzofuran-chalcone salts 4a-c were soluble in water at room temperature. Structural analysis of the synthesized compounds was characterizated by elemental analysis, FT-IR, ^{1}H-NMR and ^{13}C-NMR spectroscopy techniques. The anticancer activities of the compounds were determined by SRB viability assay in human lung cancer (A549, H1299) and breast cancer (MCF-7, MDA-MB-231) cell lines. Findings for apoptosis were determined by flow cytometry analysis and PARP-ELISA method.

Results: Results of *In vitro* SRB analysis of the compounds showed that chalcone hybrids 3b, 3c and 4c were very effective on both cancer types in a dose and time dependent manner. Especially chlacone hybrid 3b were found to be the most powerful among three effective hybrids in breast cancer cells compared to 4c being more toxic in lung cells.

The treatment of all cancer cell types with benzofuran-chalcone hybrids 3b, 3c and 4c caused a significant increase of percentages of early and mainly late apoptotic cells indicating their apoptosis inducing effect via Caspase 3/7 Activity Assay. In addition to that measurement of

PARP cleavage; an excellent tool to confirm presence of apoptosis after chemotherapeutic agent treatment was investigated. Results showed that 4-6 fold change in PARP cleavage relative to untreated control in all cell types.

Conclusion: As a result, newly synthesized chalcone hybrids have the potential to be the potent chemotherapeutic agent for both lung and breast cancer treatment.

Key words: Benzofuran, Chalcone, Lung Cancer, Breast Cancer, Anti Cancer Agents

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ORAL PRESANTATION 23

Investigation of the KMT2C Mutation-Induced Multidrug Resistance Mechanism in CRISPR Stable Lung Cancer Cells

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Introduction and Aim: Lung cancer is the leading cause of cancer death all over the world. Non-small cell lung cancer (NSCLC) is the most common lung cancer type which accounting for about 85% of all cases. The KMT2C gene also known as MLL3, encodes a histone methyltransferase that modifies the chromatin structure and control gene transcription. KMT2 mutations occur frequently in NSCLC and are associated with high mutation loads and poor survival. However, the effects of the KMT2C mutation in the NSCLC have not been fully determined. In this study, multi-drug resistance genes affected by KMT2C mutation in NSCLC patients were analyzed with multi-omic data. Additionally, we aim to investigate multidrug resistance effect depending on KMT2C expression in both wild-type NSCLC cell lines (A549, H1299) and their KMT2C mutant forms which generated by the CRISPR/Cas-9 method.

Materials and Methods: Genes and pathways associated with multidrug resistance were searched in the online databases. Pathways and junction genes were created using the ClusterProfilier package in the R software among the genes determined after screening. Genes identified before in-vitro analysis were screened in KMT2C mutant NSCLC patient data. RNA sequence, miRNA and methylation data of NSCLC patient cohort found in the TCGA database were used (TCGA-LUAD, n=529). Differential gene/miRNA expression was analyzed using the Deseq2 package in R software, and methylation analyzes were analyzed using the ELMER package. CRISPR/Cas-9-mediated KMT2C mutant stable cells were generated in non-small cell lung cancer cell lines A549 and H1299 cells for in-vitro analysis. Genes with statistically significant changes as a result of omic analyzes were validated in KMT2C mutant cell lines by RT-PCR and western blot analysis.

Results: In omic analyzes, it was observed that the expressions of 106 genes and 5 miRNAs which found in the pathways of multidrug resistance changed depending on KMT2C expression and mutation. In addition, these genes were confirmed by RT-PCR method and the proteins belonging to genes were confirmed in both wild-type and KMT2C mutant NSCLC cell lines by Western Blot analysis.

Conclusion: Our study showed that the KMT2C mutation has an important place in the formation of treatment resistance by inducing multidrug resistance mechanisms. New therapeutic agents to target KMT2C may play a significant role in achieve drug resistance in NSCLC.

ORAL PRESANTATION 24

Anticancer Effects of Sodium Butyrate Combined With Cisplatin in Human Neuroblastoma Sh-Sy5y Cells

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Introduction and Aim: Cisplatin as a frontline treatment strategy in neuroblastoma can lead to various adverse effects and poor prognosis in children. New effective and less-toxic approaches in neuroblastoma are required to prevent the complications of high dose cisplatin alone. This study aimed to determine whether a histone deacetylase (HDAC) inhibitor, sodium butyrate (NaBu) combined with cisplatin has an anti-cancer effect on human neuroblastoma SH-SY5Y cells and to explore its underlying mechanism.

Materials and Methods: The effect of NaBu and cisplatin on the proliferation and apoptosis of SH-SY5Y cells was detected by MTT assay, colony formation assay, flow cytometry and DAPI staining. The expressions of apoptosis and nuclear factor kappa B (NF-κB) signaling pathway-related proteins were determined by Western blot.

Results: NaBu or cisplatin alone inhibited proliferation of SH-SY5Y cells, while the combination of the two generated significantly higher responses. NaBu did not enhanced the effect of cisplatin on apoptosis and inhibition of colony formation in SH-SY5Y cells. However, the combination of NaBu and cisplatin caused a significant increase in Bax/Bcl-2 ratio. Exposure of SH-SY5Y cells to NaBu increased NF-κB protein levels and decreased the protein expression of IκBα, whereas cisplatin treatment caused a statistically significant decrease in the protein expression levels of NF-κB. NaBu in combination with cisplatin enhanced the expression of NF-κB protein compared to control. p53 and phosphorylated IκBα protein expression did not differ among groups.

Conclusion: Combined therapy of NaBu and cisplatin inhibits cell proliferation, but fails to induce significant levels of apoptosis and suppress colony-forming ability of SH-SY5Y neuroblastoma cells compared with cisplatin alone. The ineffectiveness of NaBu could be

associated with upregulation of antiapoptotic transcription factor NF-κB. Further research is needed to understand the molecular mechanisms that underlie the anticancer effect of NaBu in conjuction with cisplatin and develop treatment strategies for neuroblastoma.

Keywords: Sodium Butyrate, Cisplatin, Neuroblastoma, SH-SY5Y, Histone Deacetylase

ORAL PRESANTATION 25

ZAP70 Activation Compensates for Loss of Class IA PI3K Isoforms Through Activation of the JAK–STAT3 Pathway

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Introduction and Aim: Tyrosine kinases have crucial functions in cell signaling and proliferation (1). The phosphatidylinositol 3-kinase (PI3K) pathway is frequently deregulated in human cancer and is an essential regulator of cellular growth (2). We aimed to determine which tyrosine kinases contribute to resistance elicited by PI3K silencing and inhibition.

Materials and Methods: To mimic catalytic inactivation of the PI3K isoforms p110α and p110β; specific p110α (BYL719) and p110β (KIN193) inhibitors were used in addition to genetic knock-out in *in vitro* assays.

We used an activated tyrosine kinase library (3) to determine the signaling modalities contributing to the PI3K inhibitor resistance. Cell viability was assessed using crystal violet staining, whereas cellular transformation ability was analyzed by soft-agar growth assays. Untransformed mouse embryonic fibroblasts (MEFs), hTERT immortalized RPE1 cells, MCF10A and human mammary epithelial cells (HMECs) as well as carcinogenic MCF7 and T47D cell lines have been employed in our studies.

Results: In our molecular genetic screen, activated *zeta chain of T-cell receptor-associated protein kinase 70* (ZAP70) generated resistance to PI3K inhibition. This resistance was via activation of the *Janus kinase*/*signal transducer and activator of transcription 3* (JAK/STAT3) axis. We demonstrated that activated ZAP70 has a high transforming capability associated with the formation of malignant phenotype in untransformed cells and has the potential to be a tumor-initiating factor in cancer cells.

Conclusion: ZAP70 may be a potent driver of proliferation and transformation in untransformed cells and is implicated in resistance to PI3K inhibitors in several cellular models of human cancers.

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ORAL PRESANTATION 26

Kinase module of the mediator complex confers tamoxifen resistance in ER-positive breast cancer

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Introduction/aim: Tamoxifen resistance is a major hurdle for the effective treatment of estrogen receptor-positive (ER+) breast cancer. The Mediator kinase module is a dissociable component of the Mediator complex and regulates Mediator function in several ways. Although the kinase module is involved in the pathogenesis of different cancers, its role in tamoxifen resistance is unknown.

Materials and methods: Here, we correlated the expression of kinase module components with the survival of tamoxifen-treated ER+ patients to investigate the clinical relevance of the Mediator complex. We performed *in vitro* proliferation assays in acquired tamoxifen-resistant (TamR) cell line models using siRNA/shRNA-mediated knockdown of Mediator-subunit 13 (MED13) and the recently developed highly selective inhibitor of Mediator kinase, CDK8 (cyclin-dependent-kinase 8). We combined downstream pathway analysis, Western blotting, mRNA stability assays, xenograft and transgenic mouse models to identify novel modulators of tamoxifen resistance.

Results: We found that MED13 and CDK8 levels were significantly higher in tamoxifen-treated patients, and that higher expression of both CDK8 and MED13 strongly correlated with worsened patient survival and tamoxifen response. Importantly, MED13 and CDK8 were markedly overexpressed in TamR cells compared to their sensitive counterparts. *In vitro* inhibition of either MED13 *via* siRNAs/shRNAs or CDK8 by the selective inhibitor SNX631,

dramatically increased tamoxifen sensitivity in the cells. Of note, targeting MED13 or CDK8 resulted in inhibition of HER2/mTOR signaling and induced apoptosis. Remarkably, combining MED13 inhibition by shRNA knockdown with tamoxifen improved the inhibition of tumor growth *in vivo* compared to standalone treatment groups. Similarly, combining SNX631 and tamoxifen suppressed xenograft tumor growth better than single agents and extended survival in an aggressive transgenic mouse model.

Conclusion: Our results reveal the clinical relevance of kinase module of the Mediator complex in tamoxifen resistance of ER+ breast cancer and provide pre-clinical evidence to target CDK8 or MED13 to overcome tamoxifen resistance.

ORAL PRESANTATION 27

Probing for potential genes as novel biomarkers in head-and-neck cancer: prognostic and diagnostic approach

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Introduction / Aim: Head and neck cancers (HNCs) are a diverse illness that accounts for 9 percent of all malignancies of the body. HNCs comprise of a diverse collection of larynx, hypopharynx, oropharynx, oral cavity, and nasopharyngeal cancers. Even CT and PET are used to identify and stage HNC; innovative diagnostic techniques are necessary for the early identification of HNC with the maximum sensitivity and specificity, especially for the clarification of HNC subtypes. In the realm of genomics and proteomics, the discovery and subsequent development of biomarkers is regarded by many as the method with the highest degree of specificity that is most often used. The primary objective of our study is to perform functional gene enrichment and clustering to identify the significantly expressed and/or suppressed genes as a potential biomarker for the development and progression of head and neck cancer (HNC) in terms of function, mechanism, and metabolic processes.

Materials and Methods: Numerous geodatasets were analyzed to identify genes associated with head-and-neck cancer. A clustering analysis was conducted to establish the links between the genes. In this work, three distinct geodata sets were examined to improve precision and dependability. Initially, genes were extracted from the NCBI Geodataset (GSE6631,GSE55549 and GSE138206) area using the R programming language. To make the study statistically significant, genes having a p value larger than 0.05 were eliminated from the list. Following these steps, genes are categorized as up-regulated or down-regulated based on their logFC values. R's openxlsx and dplyr packages were used to create a hierarchical cluster of two distinct gene lists.

Genes are interpreted according to their distance from one another because of this investigation. PathfindR was utilized to identify our genes and their linked pathways. For this goal, the experimental results of our genes were utilized to improve the study's credibility.

Results and Conclusion : As a result of our bioinformatics studies, we identified 12 important genes in 3 geodata sets. These are MAL TGM3, KRT4, SPINK5, CRISP3, SCEL, COL1A2, FN1, MMP1, PTHLH, SPP1 and POSTN genes. As a further study, we will prove our study by analyzing these genes experimentally.

ORAL PRESANTATION 28

Evaluation of AKR1B1 expression in the CRC tumor microenvironment

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Introduction and aim: AKR1B1 is a member of the aldo-keto reductase family of enzymes that participate in the polyol pathway of aldehyde metabolism and is aberrantly expressed in colon cancer. We previously showed that high expression of AKR1B1 was associated with enhanced motility, inflammation and poor clinical outcome in colon cancer patients (1,2). As the expression of this gene is also strongly and positively correlated with mesenchymal marker expression and a high AKR1B1 expression is associated with a CMS4 (consensus molecular subtypes) subtype which is rich in stroma (2), in this study, we aimed to explore the specific cell types that express AKR1B1 in the tumor microenvironment, and evaluate whether the expression of AKR1B1 in the tumor microenvironment contributes towards the prognostic predictions observed.

Materials and Methods: Publically available microarray data of colon tumors were downloaded from GEO database and RMA normalized. Based on microarray data, stromal and immune cell presence were predicted using ESTIMATE method and fractions of 22 distinct immune cell types were estimated using CIBERSORT algorithm (3,4).

Results: Bioinformatic analyses of publically available transcriptomic data of colon tumors showed that the expression of AKR1B1 was significantly higher in the stromal compartment compared to the epithelial compartment of CRC tumor tissues. Using ESTIMATE method, we showed that AKR1B1 was positively correlated with both immune and stromal fractions ($r>0.50$, $p<0.001$). Next, CIBERSORT data was utilized to specify immune cell types that are more likely to express AKR1B1, and our results showed that the tumors with higher macrophage fractions had higher AKR1B1 expression.

Discussion: As the prognostic relationship of AKR1B1 was dramatically different when tumors were stratified based on stromal and immune cell fractions *in silico*, we overall conclude that AKR1B1 is expressed by cells in the tumor microenvironment and this may have a major contribution towards its prognostic role.

Keywords: Colorectal Cancer (CRC), Aldo-keto reductases, AKR1B1, stroma, tumor microenvironment

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ORAL PRESANTATION 29

THE ROLE OF EXOSOMAL INHIBITORS IN EPIGENETIC REGULATION

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Introduction / Aim: DNA methylation is one of the main mechanisms of gene regulation and is catalyzed by DNA methyltransferases (DNMTs). These enzymes are divided into two groups based on their functions; maintenance DNMT (DNMT1) and *de novo* DNMTs (DNMT 3A and DNMT3B). Aberration of DNA methylation occurs frequently in prostate cancer and has been associated with increased DNMT enzyme expression. Exosomes are one of the key mechanisms in cell-cell communication and play an important role in not only tumor progression but also epigenetic reprogramming in recipient cells. We aimed to determine, firstly whether DNA methyltransferase enzymes are among the exosomal cargo molecules derived from prostate cancer cells, secondly how exosomal DNMTs affect the expression of DNMTs in recipient cells, and finally the effect of spesific exosome inhibitors on the expression of DNMTs. Materials and Methods: The expression of DNMTs was analyzed by qPCR in exosome, recipient cells with/without treatment with an exosome inhibitor (GW4869). Protein expression was determined by immunoblotting. Exosome was isolated using exosome isolation reagent. Results: We demostrated that *DNMT* mRNAs (*DNMT1, DNMT3A, DNMT3B*) were involved among exosomal cargo molecules in prostate cancer-derive exosomes. Thereafter, we observed an increase in *DNMT* mRNA levels, especially *DNMT3A,* in cells treated with exosomes depending on concentration and time. Finally, we determined that in a dose-independent manner, GW4869 decreased the expression of *DNMT*s in cells containing exosomes at the transcriptional level. However, we observed that GW4869 significantly diminished the expression of *DNMT* mRNAs in both cells containing exosomes and non exosome.

Conclusion: We are the first to show that prostate cancer derive exosome containing *DNMT* mRNAs may contribute to the reprogramming of DNA methylation in the recipient cells and we also suggest that exosome inhibitors can be used as new DNMT inhibitors. Further studies are needed to support our results.

ORAL PRESANTATION 30

FOXM1 inhibitörü FDI-6'nın, metastatik meme adenokarsinom hücre hattında VEGFR protein etikileşimi ve ekspresyonu üzerinde etkilerinin in-vitro ve in-siliko belirlenmesi

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Yapılan çalışmalar yeni bir FoxM1 inhibitörü olan FDI-6'nın FoxM1 inhibisyonu ile tümör oluşumunu azaltmada rol aldığını göstermesine karşın bu bileşiğin anjiyogenik bir protein olan VEGFR ile nasıl bir etkileşime girdiği ve anjiyogenezi baskılamada rolü olup olmadığı bilinmemektedir. Yaptığımız çalışmada FDI-6 ve VEGFR proteininin atomik düzeyde moleküler etkileşimini belirlemek amacıyla *in-siliko* olarak sırayla Moleküler Docking, Moleküler dinamik simülasyon hesaplamaları gerçekleştirilmiştir. *In-vitro* olarak FDI-6 bileşiğinin MDA-MB-231 ve HUVEC hücre hatlarında sitotoksisitesi belirlendikten sonra hücre migrasyonu üzerindeki etkilerini göstermek amacıyla yara iyileşmesi deneyi gerçekleştirildi. Western blot yöntemi ile de VEGFR protein ekspresyonu değişimi gösterilmiştir. Elde ettiğimiz moleküler docking bulgularına göre FDI-6 ve VEGFR etikileşimi sonucunda -8,7 kcal/mol skoru elde edildi. Moleküler dinamik simülasyon çalışması FDI-6 bileşiğinin VEGFR ile 100 ns boyunca stabil etkileşim kurduğunu göstermiştir. MTT Sitotoksisite sonuçlarına göre FDI-6'nın HUVEC hücre hattında 8µM'dan itibaren hücre canlılığının etkilediği MDA-MB-231 hücre hattında ise 64 µM'dan itibaren hücre canlılığını etkilediği belirlenmiştir. 8 µM FDI-6 muamelesinin hücre migrasyonunu anlamlı düzeyde azalttığı ve VEGFR protein ifadesini azalttığı gözlenmiştir.

Sonuç olarak FDI-6, anjiyogenik bir protein olan VEGFR'yi baskılarak metastazı baskılayabilir. Buna karşın bu çalışmanın FDI-6 bileşiğinin diğer anjiyogenik ve metastatik proteinler ile etkileşiminin araştırılması ve *in-vivo* deneyler ile doğrulanması önerilmektedir.

ORAL PRESANTATION 31

In-vitro and in-silico investigation of effects of the FOXM1 inhibitor FDI-6 on VEGFR interaction and expression in the metastatic breast adenocarcinoma cell line

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Although studies have shown that FDI-6, a new FoxM1 inhibitor, plays a role in reducing tumor formation by inhibiting FoxM1, it is not known how this compound interacts with VEGFR, an angiogenic protein, and whether it has a role in suppressing angiogenesis. In our study, to determine the molecular interaction of FDI-6 and VEGFR protein at the atomic level, in-silico Molecular Docking and Molecular dynamic simulations were carried out. After determining the cytotoxicity of FDI-6 compound in MDA-MB-231 and HUVEC cell lines in-vitro, a wound healing experiment was performed to show its effects on cell migration. The change in VEGFR protein expression was also shown by western blot method.

According to the molecular docking findings we obtained, a score of -8.7 kcal/mol was obtained as a result of the interaction of FDI-6 and VEGFR. Molecular dynamics simulation study showed that FDI-6 compound stably interacts with VEGFR for 100 ns. According to MTT cytotoxicity results, it was determined that FDI-6 affected cell viability from 8µM in HUVEC cell line and from 64 µM in MDA-MB-231 cell line. It was observed that 8 µM FDI-6 treatment significantly reduced cell migration and decreased VEGFR protein expression.

As a result, FDI-6 can suppress metastasis by suppressing VEGFR, an angiogenic protein. However, this study is recommended to investigate the interaction of FDI-6 compound with other angiogenic and metastatic proteins and to be confirmed by in-vivo experiments.

ORAL PRESANTATION 32

Investigation of the role of extracellular vesicles in prostate cancer to taxane resistance

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Introduction and Aim: Prostate cancer (PCa) is the most common type of cancer and the second leading cause of cancer-related deaths in men. In the advanced stages of the disease, traditional treatments usually fail (1) and intrinsic or acquired drug resistance complicates the treatment. In recent years, extracellular vesicles (EVS) have also been proposed to play a role not only in tumor progression, angiogenesis or migration of tumor cells but also in drug resistance (2, 3). While miRNA content of EVs is vastly studied and is shown to have an effect on resistance, mRNAs have been largely neglected. Therefore, in our study we examined the exosomal mRNAs obtained from Docetaxel (DOX) and Cabazitaxel (CBZ) resistant Du145/22RV1 cells and investigated their role in the context of acquired taxane resistance.

Materials and Methods: EVs were isolated from the supernatants of drug-resistant cells and characterized by western blot, NTA and ELISA. Total RNA from these EVs was isolated and the mRNA amount of selected targets, namely ABCB1 and NNMT genes, which were found to be upregulated in resistant cells as determined by RNAseq analysis, were analyzed via RTqPCR. EV cytotoxicity was measured with MTT. Parental (sensitive) cells were exposed to a sub lethal dose of EVs excreted from the resistant cells and evaluated for morphological changes by light microscopy and taxane response through measurement of cell viability.

Results: The nontoxic EV number was determined and a slight toxic effect was observed at 72 h for high numbers of EVS (CBZ EV and PAR EV), but no toxic effect was observed for low numbers of EVS (DTX EV, CBZ EV and PAR EV). There was no change in cell morphology on parental Du145 and 22RVI cells upon addition of EVs regardless of where they were isolated

from. EVS isolated form CBZ-resistant 22RV1 or Du145 cells conferred varying degrees of protection against CBZ in parental cells. No protective effect of EVs isolated from DTX-resistant cells was observed following DOX treatment in any of the cells. Whilst increased amounts of ABCB1 (multidrug resistance pump, also known as MDR1) mRNA were also observed in EVS from DTX and CBZ resistant cells, there was no increase in NNMT expression (associated with chemotherapy resistance).

Conclusion: Although the gene expression of ABCB1 and NNMT was both elevated in cells against two different drugs in two different cell lines, and only ABCB1 increase was reflected in the EV content. These results hint at possible different contribution of mRNAs in the EVS in drug resistance mechanism.

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2) Namee et al. NM, 2018 Dec;1870(2):123-136.

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ORAL PRESANTATION 33

Soloxolone Methyl İnduces Apoptotic Markers in Mammospheres

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Introduction and Aim: Breast cancer (BC) is the most common type of cancer among women in the world and is the main cause of cancer related death in women. Unfortunately, 30-40% of BC patients develop resistance to these treatments and metastatic disease may occur. Cancer stem cells (CSC), which are the main cause of resistance in breast cancer treatment, are defined as cells that renew themselves and can transform into many different cell types. For this reason, studies proving that CHDs increase the risk of recurrence and metastasis in breast cancer, and new treatment approaches and drugs for breast cancer are needed. Glycyretinic acid, derived from the plant Glycyrrhiza glabra (licorice root), shows anticancer effect such as suppression of tumorigenesis and induction of apoptosis. In this study, the cytotoxic and apoptotic effects of Soloxolone methyl compound, which is a semi-synthetic derivative of glycyrrhetinic acid, were investigated in human breast cancer cell line (T-47D) and cell population rich in cancer stem cell population (Cancer cells with CD44+/CD24- antigen; mammosphere) obtained from breast cancer cells.

Material and Methods: The growth inhibitory effects of Soloxolon methyl were determined using ATP assay. Fluorescent staining (Propidium iodide), caspase-cleaved cytokeratin 18 (M30 antigen), and flow cytometry analysis were used to determine the mode of the cell death (apoptosis/necrosis). In addition, apoptosis at protein levels was investigated by Western Blotting technique. The cytotoxic effect of Soloxolone Methyl in mammosphere cells derived from T-47D cells was determined using the ATP cell viability assay. Fluorescent staining

(Hoechst 33342 and Propidium iodide) method was used to determine the cell death mode (apoptosis/necrosis) caused by Soloxolone methyl in mammosphere cells.

Results: Soloxolone methyl has been proven to decrease cell viability and induce apoptosis markers in both T-74D cells and mammosphere cells in a dose- and time-dependent manner. An increase in apoptotic proteins related to IRE1-a, Bip, Chop, Pro-Caspase-3, Cleaved Caspase-3 and Cleaved Parp was also detected in T-47D cells.

Conclusion: Soloxolone methyl was found to be cytotoxic in both T-47D cells and cell population rich in cancer stem cell population obtained by inducing apoptosis from breast cancer cells. This in vitro study, in which we obtained promising findings, has the potential to guide us to understand whether it can offer new opportunities for therapeutic targets in further in vivo assays.

This study was supported by Bursa Uludag University Research Fund with the project no TGA-2021-513

Keywords: Soloxolone methyl, breast cancer, cancer stem cell, apoptosis

ORAL PRESANTATION 34

Cu(II) Quercetin Complex Inhibits Migration and Induces ROS-Mediated Apoptosis in Human Lung Cancer Cells

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Introduction and Aim: Lung cancer ranks first in cancer-related deaths. Despite the technological and medical developments in treatment in recent years, there is a need for new targets and new drugs in lung cancer. Studies on metal complexes are increasing due to the promising effects of metal compounds used in the treatment of many types of cancer, including lung cancer. In this study, the anticancer activities and mechanisms of action of Cu(II) complexes of flavonoid-derived quercetin and phenanthroline ligands were investigated in human lung cancer cells (H1299).

Materials and Methods: The cytotoxic effect of Cu(II) quercetin was determined by ATP and SRB viability tests. In addition, the cytotoxicity of the complex in healthy human bronchial epithelial cells (BEAS-2B) was evaluated. The toxicity of the cisplatin drug used in the treatment of lung cancer and its complex quercetin and 1,10-phenanthroline ligands were determined and analyzed in comparison with the Cu(II) complex. In order to determine apoptosis, triple fluorescent staining, M30-antigen test by ELISA method, Annexin-V and Caspase 3/7 Activity measurements by flow cytometry were performed. In addition, the production of reactive oxygen species (ROS), which is an indicator of apoptosis due to oxidative stress, was examined. Pan-caspase and ROS inhibitor were used to confirm that cellular death occurs via caspase and ROS-induced apoptosis. The effect of the complex on the cell cycle was evaluated by flow cytometry. Finally, the effect of the complex on cell migration was investigated.

Results: It was found that Cu(II) quercetin complex inhibited cell growth in H1299 cells dose-dependently and time-dependently, and was not toxic in healthy cells at the same doses. It was determined that the complex had higher cytotoxic activity than Cisplatin. In apoptosis analyses, it was observed that Cu(II) quercetin complex killed cells via apoptosis pathway. Increased

ROS levels in the cell showed that death may occur by apoptosis. In addition, it was observed by cell cycle analysis that the complex has the potential to induce apoptosis and inhibit migration by migration assay.

Conclusion: The results show that Cu(II) quercetin has high cytotoxic and apoptotic potential in lung cancer cells. With further analysis, it was concluded that it can be used as a promising agent in the treatment of lung cancer.

This study was supported by Bursa Uludag University Research Fund with the project no FGA-2021-374.

Keywords: Cu(II) complex, quercetin, cytotoxicity, lung cancer, apoptosis

ORAL PRESANTATION 35

Investigation of the Molecular Mechanism of TET2 Mutation-Induced Metastasis in CRISPR Stable NSCLC Cell Line Models

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Introduction and Aim

Lung cancer has become a global health problem. About 80% of cases are non-small cell lung cancer (NSCLC) and adenocarcinomas are the most common in this group. Majority of cases already develop advanced disease and approximately 50% are metastatic at diagnosis. Genetic and epigenetic processes follow each other in the metastasis mechanisms of cancer cells 1. At this point, the genetic spectra of Ten-Eleven Translocation 2 (TET2) enzymes, which are epigenetic regulators, are still unclear 2. In this study, metastasis mechanisms depending on TET2 expression in NSCLC adenocarcinomas were investigated with multi-omic data. In addition, the results were evaluated using TET2 mutant cell lines (A549, H1299) generated by the CRISPR method.

Materials and Methods

Mutation, methylation, RNA and miRNA sequence data of NSCLC adenocarcinoma patient group were downloaded from TCGA (TCGA-LUAD, n=529) database for omic analysis. TNM staging was performed according to patient data, metastatic and non-metastatic groups were formed. In addition, subgroups related to TET2 mutation and expression were formed. Differential gene/miRNA expression was performed in R with the "DESeq2" package, and differential methylation analysis was performed with the "ELMER" package. Functional gene enrichment analysis according to the methylation levels of genes/miRNAs was created in the "clusterProfilier" package.
TET2 mutant NSCLC adenocarcinoma cell lines (non-metastatic A549, metastatic H1299) were generated in-vitro using the Crispr-Cas9 method. Migration capacity of cells was measured with the scratch assay. In addition, statistically significant genes as a result of omic data were analyzed by RT-PCR method, and proteins belonging to genes were analyzed by western blot analysis.

Results

Statistically significant changes were observed in migration capacities in scratch assay performed in metastatic and non-metastatic NSCLC cell lines. In omic analyzes, it was observed that the expressions of 142 genes and 7 miRNAs changed depending on TET2 expression and mutation. In gene enrichment analyzes, changes were observed especially in the pathways of multidrug resistance. In addition, these genes were confirmed by RT-PCR method and the proteins belonging to genes were confirmed in TET2 mutant NSCLC cell lines by western blot analysis.

Conclusion

The study includes findings that may suggest new therapeutic targets by inducing the metastasis mechanism of loss of TET2 expression between metastatic and non-metastatic groups. It also

has the potential to guide us to understand whether TET2 expression can offer new opportunities in metastatic NSCLC.

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ORAL PRESANTATION 36

Nanoparçacıklar ile Akıllı Gen Terapi Sistemlerin Geliştirilmesi

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Giriş: Kanser tedavilerinde son yıllarda iyileşimler gözlemse de halihazırda tercih edilen kemoterapi, hormonal ve ameliyat tedavi başarı oranlarına ulaşmayı kısıtlamaktadır. Bundan dolayı yeni kanser tedavi sistemlerinin geliştirilmesi üzerine yoğun çalışmalar yürütülmektedir. Gen terapi yaklaşımları ile gönderim sistemlerinin geliştirilmesi başlıca yenilikçi tedavi sistemleridir. Gen terapi ajanları viral ve viral olmayan taşıyıcılar ile taşınmaktadır. Viral olmayan taşıyıcılar içerisinde nanoparçacıklar özellikle COVID-19 salgınına yönelik geliştirilen nanotabanlı aşılar ile ön plana çıkmaktadır. Nanotabanlı gen taşıma sistemleri; viral ajanlara göre daha az immünojenisiteye neden olması, biyouyumlu yapıda olması ve yüksek hacim/yüzey alanına sahip olmaları nedenleriyle tercih sebebidir. Fakat bu nanotaşıyıcılar; i)serumda stabil olarak kalma, ii)kansere hedeflenebilme, iii)hücre membranından geçebilme, iv)endozom/lizozomdan kaçış gibi biyolojik bariyerleri aşacak kabiliyette olmalıdır. Bu konuşmada; AB-COST, TÜBİTAK1001 ve ERU-BAP-DOSAP projelerimiz kapsamında geliştirdiğimiz nanotabanlı akıllı gen taşıyıcılar ile gerçekleştirdiğimiz otofaji ve apoptoz yolaklarını siRNA'lar ile baskılayarak kansere karşı elde ettiğimiz etkin tedavi sistemleri hakkında bilgiler vereceğim.

Metot: i) Polimer tabanlı akıllı gen taşıma sistemimizi ATRP yöntemi ile sentezleyip polimer yapıyı "click" reaksiyon ile β-CD yapısının üzerine aşıladık. **ii)**Diğer nanotaşıyıcı olarak siRNA altın nanoparçacığa (AuNP) konjüge edilerek üzerine DOX anti-kanser ajanı yüklenmiştir. Her iki nanoformulasyonun DLS, UV/Vis spektroskopi, NTA, STEM ile karakterize edilmiştir. Geliştirilen gen taşıyıcı nanoformulasyonların meme kanseri üzerinde in-vitro olarak toksisiteleri, flow sitometri ile hücresel döngüleri ve apoptoz etkinlikleri, WB ile apoptoz/otofaji yolaklarındaki protein değişimleri ve terapötik etkinlikleri incelenmiştir.

Sonuç: Polimer ve AuNP tabanlı gen taşıma sistemleri sırası ile 200 ve 80 nm civarındadır. Her iki formulasyon RNAse varlığında siRNA'ları korumuş ve stabil kalmışlardır. Otofaji inhibe edilip DOX tedavisi uygulandığında ve apoptozu engelleyen protein (BCL-2) inhibe edilerek DOX uygulandığında daha etkin tedavi sonuçları elde edilmiştir. siRNA'ların nanoformulasyonlar ile hücre içe alımları artmıştır. WB'a göre otofaji ve apoptoz ile ilgili proteinlerin seviyelerinde azalma gözlemlenmiştir.

Yorum: Geliştirilen bu akıllı nanoformulasyonlarıyla otofaji/apoptoz yolaklarına yönelik daha etkili gen terapi tedavileri gerçekleştirilebilinir.

Teşekkür
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ORAL PRESANTATION 37

Investigation of the KMT2C Mutation-Induced Multidrug Resistance Mechanism in CRISPR Stable Lung Cancer Cells

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Introduction and Aim

Lung cancer is the leading cause of cancer death all over the world. Non-small cell lung cancer (NSCLC) is the most common lung cancer type which accounting for about 85% of all cases. The KMT2C gene also known as MLL3, encodes a histone methyltransferase that modifies the chromatin structure and control gene transcription. KMT2 mutations occur frequently in NSCLC and are associated with high mutation loads and poor survival. However, the effects of the KMT2C mutation in the NSCLC have not been fully determined. In this study, multi-drug resistance genes affected by KMT2C mutation in NSCLC patients were analyzed with multi-omic data. Additionally, we aim to investigate multidrug resistance effect depending on KMT2C expression in both wild-type NSCLC cell lines (A549, H1299) and their KMT2C mutant forms which generated by the CRISPR/Cas-9 method.

Materials and Methods

Genes and pathways associated with multidrug resistance were searched in the online databases. Pathways and junction genes were created using the ClusterProfilier package in the R software among the genes determined after screening. Genes identified before in-vitro analysis were screened in KMT2C mutant NSCLC patient data. RNA sequence, miRNA and methylation data of NSCLC patient cohort found in the TCGA database were used (TCGA-LUAD, n=529). Differential gene/miRNA expression was analyzed using the Deseq2 package in R software, and methylation analyzes were analyzed using the ELMER package. CRISPR/Cas-9-mediated KMT2C mutant stable cells were generated in non-small cell lung cancer cell lines A549 and H1299 cells for in-vitro analysis. Genes with statistically significant changes as a result of omic analyzes were validated in KMT2C mutant cell lines by RT-PCR and western blot analysis.

Results

In omic analyzes, it was observed that the expressions of 106 genes and 5 miRNAs which found in the pathways of multidrug resistance changed depending on KMT2C expression and mutation. In addition, these genes were confirmed by RT-PCR method and the proteins belonging to genes were confirmed in both wild-type and KMT2C mutant NSCLC cell lines by Western Blot analysis.

Conclusion

Our study showed that the KMT2C mutation has an important place in the formation of treatment resistance by inducing multidrug resistance mechanisms. New therapeutic agents to target KMT2C may play a significant role in achieve drug resistance in NSCLC.

ORAL PRESANTATION 38

Inhibition of 6-phosphoructo-2-Kinase and Ornithine Decarboxylase Oncogenic Properties of Pancreatic Adenocarcinoma Cells

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Introduction &Aim

Pancreatic adenocarcinoma is one of the deadliest cancers, and incidence is on the rise. Novel therapeutic approaches are needed to combat this deadly disease. Activating mutations in the *KRAS* gene confers an aggressive metabolic phenotype in pancreatic adenocarcinoma, which may present therapeutic vulnerabilities. Hyperactive KRAS stimulates glycolysis and polyamine synthesis pathways that are associated with malignant properties, including proliferation and chemoresistance. In this study, we set out to study the effect of dual targeting of 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase-3 (PFKFB3), an activator of glycolysis, and ornithine decarboxylase 1 (ODC1), the rate-limiting enzyme of polyamine synthesis pathway, on the oncogenic properties of pancreatic adenocarcinoma cells.

Material & Methods

PANC-1 and MIA PaCa-2 cell lines were used as pancreatic adenocarcinoma models to test the hypothesis. PFKFB3 and ODC1 mRNA expressions were silenced using specific siRNA molecules. Enzymatic activities of PFKFB3 and ODC1 were inhibited using clinical grade inhibitors, AZ PFKFB3 26 and difluoromethylornithine (DFMO), respectively. Forty-eight hours after silencing or drug treatment, cell viability was assessed by crystal violet assay. Clonogenic assays were also performed to determine the capacity of cells treated with combination of AZ PFKFB3 26 and DFMO to grow as single colonies.

Results

Combined silencing of PFKFB3 and ODC1 potently suppressed the proliferation of the cells, compared with PFKFB3 or ODC1 silencing alone. Combined pharmacological inhibitions of PFKFB3 and ODC1 exhibited a greater cell suppressive effect relative to individual inhibitons. Dual targeting of PFKFB3 and ODC1 markedly decreased the number of colonies, suggesting that PFKFB3 and ODC1 may cooperate to increase the clonogenic and proliferative potential of pancreatic adenocarcinoma cells.

Conclusion

Combined inhibition of glycolysis and polyamine synthesis pathways via PFKFB3 and ODC1 may be a rational therapeutic strategy in the management of pancreatic adenocarcinoma.

ORAL PRESANTATION 39

Determination of Anti-cancer Activity of 3-Nitrophenyl Chalcone Derivative on Colon Cancer Cells

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Introduction and Aim: The incidence of cancer's, which is the second leading cause of death after cardiovascular diseases, is increasing daily. According to recently statistical data, one out of every ten people is diagnosed with colon cancer. Depending on the increase observed, there is a need for new targeted treatments. Chalcones, which are naturally found in plants or can be synthesized artificially, are compounds belonging to the flavonoid family and have a wide biological activity, including anti-cancer. In this study, the anti-cancer effects and mechanisms of benzofuran ring-linked (3-nitrophenyl chalcone derivative in human colon cancer cells (HCT-116, HT-29) was investigated.

Materials and Methods: The potential cytotoxic effect of the 3-nitrophenyl chalcone derivative on colon cancer cells viability was determined by the SRB method. Furthermore, the cytotoxicity of the 3-nitrophenyl chalcone derivative in healthy human colon cells (CCD18-Co) was evaluated. On the other hand, a combination study was also conducted with 5-fluorouracil (5-FU), a chemotherapeutic drug. The mechanism by which cell death occurs (apoptosis/necrosis) was analyzed under a fluorescent microscope with the Annexin-V/Hoechst/Propidium iodide triple staining method. The Caspase 3/7 activity involved in the apoptotic pathway was examined by flow cytometry. The cell cycle analyses were also done using flow cytometry. The effect of the 3-nitrophenyl chalcone derivative on the migration and colony formation abilities in cancer cells were investigated. Finally, changes in apoptosis-related proteins, one of the cell death mechanisms, were evaluated using the Western Blot method.

Results: Treatment with the 3-nitrophenyl chalcone derivative showed to be a dose-dependent increase in cytotoxic activity in human colon cancer cells and did not toxic in healthy human colon cells at the same doses. Fluorescent staining, Caspase 3/7 activity and Western Blot Studies showed that death through apoptosis in both cancer cells. In addition, flow cytometry results showed that cell division was suppressed in the G0/G1 stage in both cancer cells. Lastly, migration and colony formation abilities were observed to decrease in both cancer cells.

Conclusion: The results show that the 3-nitrophenyl chalcone derivative has high cytotoxic and apoptotic potential in HCT-116 and HT-29 human colon cancer cells. It was concluded that prospective in vivo experiments are required for its use as a promising agent in the treatment of colon cancer.

Keywords: Chalcone derivatives, cytotoxicity, colon cancer, apoptosis

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POSTER PRESENTATION 1

Effect of Butylhydroxytoluene on Lactate Dehydrogenase and Glucose 6 Phosphate Dehydrogenase Activities in Rat Tissues

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Introduction and Aim: Butylated hydroxytoluene (BHT) is primarily used as a food additive for its antioxidant properties. BHT is an antioxidant additive used to prevent the deterioration of oils and fats. It is used to preserve the freshness of packaged foodstuffs, potato chips, chewing gums and many foods and beverages preferred by young people and children. Recently, it has been reported that BHT metabolites cause cancer in mice. Therefore, the use of this substance, which was previously used in baby foods, is no longer allowed.

LDH is a stable cytoplasmic enzyme found in all cells. LDH is rapidly released into the cell culture supernatant when the plasma membrane is damaged. The glucose-6-phosphate dehydrogenase (G6PDH) enzyme is one of the most important enzymes of the pentose phosphate metabolic pathway. In this study, the effect of BHT exposure on LDH and G6PDH activities in liver, kidney, brain and lung tissues of rats was investigated. LDH and G6PDH activity were monitored, cytotoxicity caused by BHT was evaluated and damage in the studied tissues was interpreted.

Materials and Methods: Wistar-Albino rats weighing 200-250gr were used in the study. The animals were divided into control and experimental groups, and 3 rats were handled each time for the experimental group and the control group. 125, 250 and 500mg/kg doses of BHT were administered intraperitoneally. 12 hours and 24 hours following injection, the rats were killed by cervical dislocation and liver, kidney, brain and lung tissues were removed quickly. The activities of LDH and G6PDH were determined.

Results: The experiment results showed that BHT administration increases LDH activities significantly in the brain compared to the control groups. However, a significant decrease in LDH activities was observed in the liver and kidney. Although G6PDH activity showed decreases and increases compared to control values, these differences are statistically insignificant.

Conclusion: The results obtained indicate that BHT at the doses used leads to a change in the activity of LDH and thus damage to the cells of the body.

POSTER PRESENTATION 2

Anti-Inflammatory Effect of Polymeric Nanoparticles Melittin Complex on LPS-Stimulated Raw 264.7 Cell

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Introduction and Aim: Inflammation is a common phenomenon that comes naturally to maintain tissue homeostasis and is triggered by adaptive immune systems. This phenomenon normally leads to infection release and recovery, but inflammation can cause immune disorders when not properly progressed. Aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) have ulcerogenic side effects as well as anti-inflammatory effects. Melittin is a naturally occurring cationic peptide derived from the toxic component in the venom of the European honeybee *Apis mellifera*. As a non-steroidal anti-inflammatory drug, bee venom has been used traditionally in eastern traditional medicine, more recently for the relief of pain, rheumatoid arthritis, and the treatment of chronic inflammatory diseases. However, melittin induces the pore formation in the cell membrane and causes cell lysis. To overcome this disadvantage, polymeric nanoparticles will be used as a carrier system.

Materials and Methods: Novel negatively charged SPMA/PMMA was synthesized by RAFT polymerization and nanoparticles were formed by nanoprecipitation method. The nanoparticle-melittin complex was realized by electrostatic bonding. To prove melittin binding to nanoparticles we used DLS and ζ-potential measurements.

Results: After positively charged melittin was complexed with the particles, the size of particles was slightly increased from 269.3nm to 314.9 nm, whereas the charge of the particles were increased from -43.9 mV to -35.0 mV.

Conclusion: DLS and ζ-potential results show that melittin bound successfully to the polymer. In further, the anti-inflammatory effect of the complex we synthesized will be examined on LPS-stimulated RAW 264.7 murine macrophage cell line.

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POSTER PRESENTATION 3

CARTHAMUS TINCTORIUS L. EXTRACTS INHIBIT METASTASIS OF MDA-MB-231 BREAST CANCER CELLS

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Introduction and Aim: Breast cancer is the most common type of cancer in women and the most common cause of cancer-related death after lung cancer. While approximately 70-80% of non-metastatic cancers can be treated, breast cancer with distant metastases is considered incurable with current treatments. Although the common treatment methods in the treatment of breast cancer are chemotherapy, radiotherapy and surgery, the search for alternative treatments continues. The leading alternative treatments are medicinal plants which actually inspire the production of many cancer drugs. In this study, the proliferative and metastatic effects of Carthamus tinctorius L.(safflower), known for its many therapeutic properties, on metastatic breast cancer were investigated.

Materials and Methods: Safflower leaves were extracted in water, alcohol and oil and the extracts were applied to 0.04 g/ml metastatic breast cancer cells. To evaluate the mechanisms of different extracts of the safflower plant on metastatic breast cancer cells; MTT assay, wound healing assay and gene expression analysis were performed.

Results: It is found that, there is no difference in proliferation between the cells to which the safflower extracts were applied and the control cells. However, all safflower extracts, especially the oil extract, significantly reduced the metastatic potential (migration and MMP9/TIMP1 gene expression ratio) of breast cancer cells.

Conclusion: It is concluded that safflower contents are potent chemicals which inhibit the cellular mechanisms underlying the spreading of cancer cells and further analysis may lead to new initiatives in drug design research.

Keywords: Carthamus Tinctorius L., Plant Extraction, Breast cancer, Proliferation, Metastasis

POSTER PRESENTATION 4

Identification of Differentially Expressed Genes in Papilary Thyroid Carcinoma Patients with Hashimoto's Thyroiditis Compared To Patients Without Hashimoto's Thyroiditis Using An in Silico Approach and Investigation Of These Genes' Roles in The Progress of Papillary Thyroid Carcinoma

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Introduction and Aim: The most prevalent type of differentiated thyroid cancer is papillary thyroid carcinoma (PTC). PTC is linked to a number of risk factors, including iodine deficiency and autoimmune lymphocytic thyroiditis (also known as Hashimoto's thyroiditis) (HT). Hashimoto's illness is the most common type of thyroiditis, and it's similar to PTC in that it's more common in areas where there's a lot of iodine. Papillary cancer is more common and less severe in HT patients. However, whether HT has a decisive causal role in the PTC is unknown. The goal of this study was to use *in silico* analysis to find differentially expressed genes in PTC patients with HT. Future research on the subject will benefit by determining the association between distinct gene expressions and cancer development.

Materials and Methods: Data from gse138198 published in 2020 were used to identify differentially expressed genes in the presence of HT in PTC patients. After the data was normalized with the RMA method, using various statistical analyzes (heaierical clustering, t-test, fold change, variance, etc.), genes that were expressed differently between two groups, PTC without Hashimoto (G1) and PTC with Hashimoto (G2) were determined. Additional analyses were used to discover the functions of these genes and the pathways to which they belong (pathway analysis, network analysis, genset enrichment analysis).

Results: A total of 42 genes (fc>2, p-value<0.05) were found to be expressed differently in the two groups. Other genes, with the exception of two, were shown to be elevated in the G1 group. Many genes in the G1 group belong to immunological pathways, according to pathway and network analyses, and 1508 gensets were considerably (FDR <25%) enriched.

Conclusion: It has been demonstrated that the existence of HT in PTC patients has a role in cancer progression.

Keywords: Papillary thyroid carcinoma, Hashimoto's thyroiditis, gene biomarker, cancer progress

POSTER PRESENTATION 5

Thymoquinone-oxime; a New Agent in the Treatment of Lung Cancer

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Introduction and aim: Lung cancer is the most common cause of cancer-related death globally. Most lung cancers are identified in advanced stages due to a lack of early-stage detection, limiting the therapy choices available[1]. Thymoquinone (TQ) is known to have anticancer effects, including induction of apoptosis, anti-proliferation, generation of intracellular reactive oxygen species (iROS), cell cycle arrest, and anti-metastasis/anti-angiogenesis. Combining TQ with traditional anticancer drugs may have better therapeutic potential[2,3]. It is believed that adding new functional groups to the structure of TQ can increase its activity. As a result, the purpose of our study was to look at the therapeutic effects and benefits of TQ-oxime in the treatment of lung cancer.

Materials and Methods: After NMR was used to identify the structure of the novel synthesized substance, cytotoxicity by ATP technique, genotoxicity by comet assay, and apoptosis by annexin V-FITC were utilized to examine the anticancer mechanism of TQ-oxime in the lung cancer cell (A549) and healthy lung epithelial cell (BEAS-2B). iROS were measured using H_2DCF-DA dye, intracellular calcium with Fura-2AM dye, and MMP levels with DiOC6(3) dye.

Results: TQ-oxime induced cytotoxicity, genotoxicity and apoptosis in cancer cells with increasing dose-dependent (2.5-200 μM) iROS production. MMP levels decreased as intracellular calcium levels increased. MMP levels decreased significantly whereas cytotoxicity, apoptosis, DNA damage, intracellular calcium, and iROS levels increased in cancer cells compared to healthy cells (p<0.001).

Conclusion: As a consequence, novel approaches based on bioactive molecule derivatives have been found to be beneficial in an *in vitro* model of lung cancer. Thanks to these findings, as well as future *in vivo* research, TQ-oxime is being evaluated as a therapeutic option for lung cancer.

Keywords: anticancer, apoptosis, lung cancer, reactive oxygen species, thymoquinone-oxime

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POSTER PRESENTATION 6

Etoposide counteracts against VEGF-enhanced CAM surfaces to regulate neovascularization

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Introduction and Aim: The chick chorioallantoic membrane (CAM) is an extraembryonic membrane with a dense network of blood and lymphatic vessels. CAM assay, the in-ovo method, has higher viability of the embryo but offers limited access to the CAM. According to Turkish law, the CAM model system does not raise any ethical or legal concerns until the 14th day of incubation, thus being an attractive alternative to other animal experiments. Thereby we introduced a well-known drug called Etoposide to the CAM angiogenesis experiment in various doses w/wo VEGF enhanced areas to improve the vessel networking and proliferation of vascular endothelial cells and evaluate the anti-angiogenic properties of this well-known anti-cancer drug.

Materials and Methods: We performed in ovo CAM assay, which is renowned throughout the world assessing the anti-neovascularization capacity of various chemicals regardless of the synthesis method. We used a specific filter paper protocol to administer the drug on the CAM. Following this optimized protocol by us. We experimented until the EDD13 which doesn't raise ethical or legal concerns.

Results: We used etoposide in TDC based dosage method. Following 50/100 TDC etoposide administration to the specific site of the CAM, etoposide significantly countered the neovascularization in a time-dependent manner without decreasing chick survivability. We enhanced the CAM surface with the VEGF administration in the same way as the drug and performed the same drug administration strategy to counter-stimulate vascular endothelial cell proliferation and migration. Which has proven effective against the stimulated surface as well.

Conclusion: Our results suggest that Etoposide is not only a well-known anti-cancer drug but it is a potent anti-angiogenic drug even against VEFG-enhanced surfaces of the CAM.

POSTER PRESENTATION 7

The Effect of Nrf2 Inhibition on Chemosensitivity in Colorectal Cancer Cells

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Introduction/Aim: Colorectal cancer (CRC) is an important disease that ranks second in cancer-related deaths. Irinotecan is one of the chemotherapeutics widely used in the treatment of this disease. Nrf2 (Nuclear factor erythroid-derived 2-like 2) inhibition causes increased oxidative stress in cancer cells. Nrf2 inhibition increases the effect of cancer drugs cancer cells. The effect of ML385, an Nrf2 inhibitor, on CRC cancer cells and its combination with irinotecan has not been studied previously.

Materials and Methods: The human CRC cancer cell lines HCT-116 and HT-29 were used during the study. The time and dose dependent effects of ML385 and irinotecan on cell viability were determined using the Sulforhodamine B (SRB) test. The change in reactive oxygen species at the doses where the combination was effective was determined by 2′-7′-dichlorodihydrofluorescein diacetate (DCFH-DA) dye.

Results: IC_{50} values of 24h-treatment of irinotecan were 78.31 μM and 176.6 μM for HCT116 and HT29, respectively. When we evaluated cell viability for 48h, IC_{50} values were 25.39 μM and 15.23 μM for HCT116 and HT29, respectively. In HCT116 and HT29 cell lines, ML385 decreased the IC_{50} of irinotecan. Irinotecan caused oxidative damage for both cell lines. ML385 + irinotecan combination increased ROS levels in both cell lines.

Conclusion: Using the ML385 is highly effective in reducing the dose and possible side effects of irinotecan by interfering the antioxidant defense system of cancer cells. Studies are ongoing to determine the apoptotic/necrotic populations in drug combination treatment. Further studies are needed to investigate the changes in downstream targets of Nrf2 in irinotecan therapy.

POSTER PRESENTATION 8

The Expression Level Comparison of Cancer Related Genes On Healthy And Cancerous Ovarian Tissue Samples

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Introduction and Aim: Ovarian cancer (OC) is the most lethal gynecological cancer. The disease is generally diagnosed in the advanced stages (Stage III or IV). It was observed that the prognosis and survival were worse than the cases of endometrial and cervical cancer (1). Our study, it was aimed to analyze different gene groups related to other gynecological diseases than OC and to investigate their roles in OC as candidate biomarkers.

Materials and Methods: The study was conducted with 10 high-grade serous ovarian cancer (HGSOC) patients' tumor tissue and 10 healthy individuals' ovarian tissue. Total RNAs were isolated and translated to cDNA. Real-Time qPCR was used to measure the expression of mRNA with SYBR Green. CT values were analyzed by the 2^(-ΔΔCt) method to get fold change values of the test (JUN, FRA2, VEGFA, FOS, KRAS, MMP-9, MMP-2, and TIMP-2) and control (GAPDH) genes. Two-tailed Mann-Whitney U test and p-values were used to compare OC patients and healthy controls.

Results: Most of the genes were differentially expressed in OC compared to the controls. P-values were significant ($P<0.05$) for JUN, FRA2, MMP-9, FOS, and KRAS but not for VEGFA, MMP-2, and TIMP-2. Although TIMP-2 generally showed lower expression, 3 patients have shown significant overexpression in OC. Similarly, the expression level of JUN was different (overexpressed) in the two patients compared to whole samples.

Conclusion: The genes we found to be significant were also important for some of the cancer pathways. MMP-9 was found as correlated with better overall survival in patients with grade III OC which support our findings. Decreased FOS level is also associated with apoptosis in other cancers like oral squamous cancer. Decreased expression of JUN and FRA2, same as our findings, decreases endogenous BRCA1 expression which is significant in HGSOC. KRAS mutations are common in ovarian cancer which is the same direction as our findings.

POSTER PRESENTATION 9

How to use big data in health informatics for discovery of diagnostic and prognostic biomarkers in cancer?

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Introduction and aim: Cancer is a complex and heterogeneous disease. One of the most important information obtained from translational (laboratory to clinic) and reverse translational medicine (clinic to laboratory) approaches with the combination of current technological approaches that have emerged in the field of health with the development of technology in recent years is that personalized diagnosis and treatment methods can be the right and valid approach. Many histological and radiological diagnostic methods are routinely used in the diagnosis of cancer. However, these diagnostic methods allow the diagnosis of the disease in advanced stages. For this reason, there is a need to constantly discover biomarkers that are sensitive and have high specificity for cancer types whose primary is known. Routinely, many histological, biological and radiological diagnostic methods are used in the diagnosis of cancer. However, these diagnostic methods allow the diagnosis of the disease in advanced stages. In recent years, bioinformatics is very important in obtaining transcriptomics, proteomics and genomic data revealed by experimental studies as well as in the regulation of information collected from the fields of biology and medicine. [1].At the same time, with the increasing studies with the development of technology, the accumulation of knowledge about various diseases and especially cancer is increasing. Thanks to research based on genome studies of various organisms, it enables the production of data for databases at a greater rate. At the same time, providing access to other platforms with a single user identity is also a great convenience for users [2].

Results: The NCBI Gene Expression Omnibus (GEO) database, an international public repository that stores highly efficient gene expression levels and other genomic data for various

diseases, can be used in cancer biomarker discovery[3]. Data sets can be obtained with the R programming language. It allows us to reach the difference in gene expression levels between tumor tissue and normal tissue. It can first parse the data according to p values and classify the meaningful data according to the logFC value. After this process, existing variables can be analyzed with various clustering and statistical studies. After these analysis procedures, various biomarkers can be detected.

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POSTER PRESENTATION 10

Cytotoxic Potential of *Salvia candidissima Subsp. candidissima* on Breast Cancer Cells

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Introduction and Aim

Breast cancer is the leading cause of cancer-related deaths in women worldwide. The studies of plant-based natural anti-cancer treatments has gained interest. Salvia species and their derivatives are rare in Turkiye and have been proposed for their potential anti-cancer properties. The goal of this study is to investigate the potential cytotoxic/apoptotic activities of methanol extract of *Salvia candidissima Vahl. subsp. candidissima* (SCE) on MCF-7 and MDA-MB-231 breast cancer cells.

Materials and Methods

A GCXGC-TOF/MS system and a dual stage commercial thermal desorption injector were used to determine the chemical components of SCE. MTT and ATP viability tests were used to investigate the anti-growth activity. The apoptosis-inducing effect was assessed using a fluorescence staining method. Caspase-cleaved keratin 18 (ccK18, M30-antigen) levels measured by M30-CytoDeath ELISA Kit.

Results

The results showed that SCE suppressed the viability of the MCF-7 and MDA-MB-231 breast cancer cells in a dose-dependent manner ($p<0.05$), based on the findings of both MTT and ATP cell viability tests and pyknotic cell nuclei were observed via fluorescent staining in both cell lines after 48 hours of treatment. The treatment group had greater levels of caspase-cleaved keratin 18 in the MCF-7 cell line than the untreated group. These results showed that SCE induces apoptosis, cause cell death in MCF-7 and MDA-MB-231 cell lines.

Conclusion

Salvia candidissima Vahl. subsp. candidissima might be a therapeutic strategy in the treatment of breast cancer with further in vitro and in vivo studies.

POSTER PRESENTATION 11

Inhibition of Autophagy Sensitizes Breast Cancer Cells to Doxorubicin

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Introduction and Aim: Although apoptosis is the most frequently utilized cell death pathway in cancer therapy, current research reveals that other mechanisms, particularly autophagy, may provide a novel cancer treatment approach. While the impact of autophagy on tumor development is controversial, evidence suggests that autophagy enhances tumor growth and spread in established malignancies. Nonetheless, autophagy has recently been proposed as a plausible cause for the evolution and progression of anticancer drug resistance. In this study, combined DOX and autophagy-related siRNA treatment was utilized employing a "smart" nanoparticle system, based on the hypothesis that this combination would elevate DOX sensitivity in metastatic breast cancer cells.

Materials and Methods: MDA-MB-231 cells were cultured in vitro and cell viability was detected by resazurin viability assay. Colony formation assay was used to measure cell growth.

Wound-healing assay was conducted to assess cell invasion. Western blot was carried out to determine autophagy. Apoptosis and cell cycle arrest were assessed using flow cytometry. Staining with AO was used to detect acidic vesicular organelles.

Results: We demonstrated that using a "smart" nanoparticle approach to deliver the siRNA can efficiently suppress the autophagy-related gene, inhibit cellular autophagy and exhibit improved anticancer effects. Furthermore, co-utilizing of the autophagy-related gene and the chemotherapeutic drug was more effective than either agent alone. The inhibition of cell proliferation, colony formation, and migration in the cells demonstrated this. Nevertheless, this combination increased apoptosis, as the proportion of cells in the sub-G1 phase showed 4.8-fold greater apoptosis in the case of the co-treatment than DOX treatment alone. The combined treatment also inhibited PARP, Cyclin D1, and P-Src signaling in tumor cells. Finally, AO staining confirmed that autophagy suppression is evident.

Conclusion: Taken together, our findings showed that combining autophagy suppression with chemotherapy delivered by "smart" nanoparticles for breast cancer therapy has a synergistic effect.

Keywords: Breast cancer, Autophagy, Gene Silencing, Doxorubicin, Synergistic efficacy

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POSTER PRESENTATION 12

Comparison of Extracellular Vesicles' mRNAs Obtained from Tumor Lobe-Specific Pulmonary Vein and Peripheral Blood in Non-Small Cell Lung Cancer and Its Effect on Prognosis

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Introduction and Aim: Studies have shown that circulating tumor cells passing through pulmonary venous blood shed significantly elevated levels than peripheral. Regarding that the extracellular vesicles (EVS) are secreted from tumor cells at a higher rate than normal cells, the concentration of EVs passing through pulmonary veins is also expected to be relatively higher than in peripheral veins of the lung of non-small cell lung cancer (NSCLC) patients [1,2]. EVs derived from tumors mediate cancer metastasis, tumor growth, and invasion by modulating the tumor microenvironment in recipient cells via their nucleic acid, protein, miRNA, and mRNA contents [3]. Thus, this study aims to determine, and compare the relative concentration of EVs obtained from pulmonary and peripheral veins of NSCLC patients and then, analyze mRNA content transported via EVs to screen candidate biomarkers for NSCLC progression and aggressiveness regarding tumor stages.

Materials and Methods: Serum samples were collected from the pulmonary and peripheral veins of 5 NSCLC patients to isolate EVs. EVs were characterized by western blot and NTA. Total RNA from these EVs was isolated to analyze mRNA level expression of promising candidate genes by RT-PCR.

Results: According to the NTA analysis of EVs, a 1.5-fold increase was observed in the quantity of EVs obtained from the pulmonary vein compared to the peripheral. Moreover, although Bag-1 expression slightly changed, NFKB and Bcl-2 expression were considerably higher in EVs obtained from pulmonary veins.

Conclusion: Quantitatively, more EVs were transferred through the pulmonary veins compared to the peripheral. Increased sample size may provide a better comparison in tumor progression markers such as NFkB, Bcl2, and Bag-1 expression at the mRNA level. Candidate biomarkers and exosome size and concentration will be the indicator of tumor progression according to the stages of tumors.

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POSTER PRESENTATION 13

Anti-metastatic effect of melittin on metastatic breast cancer cells

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Introduction: Bee venom (BV) is a natural compound with the capacity to be used in the treatments of many diseases such as cancer. BV consists of a lot of compounds, and melittin is the most abundant peptide within BV. Its cytotoxic effect has been widely studied but its anti-metastatic effect remains elusive. This study aimed to determine the anti-metastatic potential of melittin compared to the widely used chemotherapy drug cisplatin.

Materials and methods: MDA-MB-231 metastatic breast cancer cells were cultured as recommended by the manufacturer. After they reach at confluency, the anti-metastatic functions of the agents were investigated by performing a 'wound healing assay'. The used concentrations of cisplatin and melittin were as follows 8, 4, 2, 1 ug/uL and 2, 1.5, 1, 0.5 µg/µL, respectively. Control cells were untreated. Wound areas were captured at 0, 6, 24, 30, 48, 54, 72 hours using the camera of AxioVert inverted microscope, and wound areas were calculated using ImageJ program. The data were statistically analysed with SPSS software to determine the most appropriate dose and incubation time for the anti-metastatic properties of the agents used in the MDA-MB-231 cell line.

Results: The most significant anti-metastatic conditions for melittin and cisplatin were found as 1 µg/µL for 30 hours, and 4 µg/µL for 24 hours, respectively, compared to the untreated counterparts.

Conclusions: Melittin is concluded to be more advantageous anti-metastatic agent for breast cancer as it is effective at four-fold low dose compared to cisplatin, but Melittin needs to have more time to function than cisplatin.

POSTER PRESENTATION 14

CRISPR/Cas9-Mediated Genomic Deletion of 6-Phosphofructo-2-Kinase-2 Alters Aminoacid Metabolism of Pancreatic Cancer Cells

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Introduction & Aim: Pancreatic cancer is characterized by extensive metabolic changes that are associated with maintenance of oncogenic properties. 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatases (PFKFB1-4) are key regulators of enhanced aerobic glycolysis that is frequently observed in tumor cells. Although the third isozyme of PFKFB family of enzymes, PFKFB3, is invoked as the primary activator of glycolysis in tumor cells due to its ubiquitous expression and relatively high kinase acvitity compared with other isozymes, our recent study suggests a role for PFKFB2 in proliferation and glycolytic phenotype of pancreatic adenocarcinoma cells. In the current study, we aimed to determine the effect of genomic PFKFB2 deletion on amino acid metabolism of pancreatic adenocarcinoma cells.

Material & Methods: A CRISPR/Cas9 method was used to create *PFKFB2*-null PANC-1 and MIA PaCa-2 cells. Liquid chromatography coupled with triple quadrupole mass spectrometry (LC-MS/MS) was used to analyze amino acids in the media of exponentially growing cells.

Results: Compared with control cells, PFKFB2 deletion led to significant changes in the levels of several amino acids and amino acid derivatives, particularly in PANC-1 cells. Asparagine consumption was lower in PFKFB2-null cells, compared with control cells. PFKFB2 deletion reduced cysteine export from the cells. Importantly, gamma amino butyrate (GABA) levels are significantly reduced in PFKFB2-null cells compared with control cells, suggesting an increased consumption of GABA upon PFKFB2 inactivation.

Conclusion: PFKFB2 inactivation leads to changes in amino acid metabolism of pancreatic adenocarcinoma cells.

POSTER PRESENTATION 15

Comparison of Two and Three-Dimensional Models of Placenta Using Choriocarcinoma Cells and Umbilical Cord Vein Endothelial Cells

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Introduction and Aim: The placenta is a rather complex tissue. The use of a single cell in its modeling is insufficient to fully reflect the tissue *in vivo*. In this study, mono and co-cultures of HUVEC cells were cultured together with BeWo cells, and placenta tissue was modeled in 2D and 3D (spheroid formation with Petri Dish ® molds) systems.

Materials and Methods: MTS Viability analyzes (3-(4,5-dimethylthiazol2-yl)-5-(3 carboxymethoxyphenyl)-2-(4sulphophenyl)-2H-tetrazolium) with different cell ratios to determine the ideal co-culture group in spheroids created using the 2D system and Petri dish® molds, according to the doubling times of the cell lines were performed. Cell localizations in the system were determined by fluorescent staining (CellTracker live dyes). Changes in the amount of human chorionic gonadotropin (β-hCG) hormone production in spheroids and 2D groups were determined by measuring by ELISA. The localization of epithelial (E)-cadherin, one of the connecting proteins involved in the structure of the placental barrier, and filamentous (F)actin, one of the cytoskeletal elements of the zonula occludens (ZO-1) were demonstrated by immunofluorescence staining.

Results: 3:1 (BeWo:HUVEC) cell group in the 2D and 3D systems has showed the ideal rate at the percent viability and CellTracker staining. The amount of hormone production (3:1) in mono and co-culture groups was higher in spheroids compared to 2D. It has been observed that the junctional proteins in BeWo cells are located in the cell membrane and the skeleton element F-actin is densely and regularly located in the cytoplasm and under the cell membrane.

Conclusion: Spheroids co-cultured in 3D systems were suitable for investigating xenobiotics for further toxicological studies. The spheroid-forming abilities of choriocarcinoma cells and endothelial cells were demonstrated in Petri Dish® molds used.

POSTER PRESENTATION 16

The Search of The Antı-Cancer Actıvıty of Chalcone Complexes in Human Prostate Cells

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Introduction and Aim: Cancer, which is one of the most important diseases of our age, is a deadly multi-stage disease caused by genetic and environmental conditions and uncontrolled division and proliferation of cells. Prostate cancer, which is the fourth most common disease in the world, is the second most common cancer in men in Turkey. The fact that there is no definitive solution for this disease yet makes it necessary to conduct promising new studies. Derived chalcones for cancer treatments are pharmacologically active compounds found in plants. The anticancer effects of two benzofuran-substituted chalcone derivatives (Complex 1 and Complex 2) synthesized and characterized in this study were investigated in human prostate cancer cell lines (LNCaP and PC-3).

Material and Methods: The cytotoxic effect of the complexes on cell viability was determined by SRB viability tests for 72 hours. The fluorescent staining (Hoechst 33342+Annexin-V+Propidium Iodide) method was used to determine the cell death responsible for the cytotoxic effects of chalcone derivatives.

Results: As a result, it was observed that the chalcone derivatives Complex 1 and Complex 2 had a cytotoxic effect on LNCaP and PC-3 human prostate cancer cells. As a result of Hoechst/Annexin-V/Propidium iodide triple fluorescent staining, Complex 1 and Complex 2 applied to human prostate cancer cells appear to induce apoptosis.

Conclusion: In the light of these results, it is promising to investigate advanced anticancer mechanisms of Complex 1 and Complex 2 in human prostate cancer cells.

This study was supported by Bursa Uludag University Research Fund with the project no FLO-2022-821

KeyWords: Prostate cancer, Anticancer, Chalcones, Apoptosis

POSTER PRESENTATION 17

Impact of GST-T1, GST-M1 and p53 Gene Polymorphisms on Brain Cancer Risk in Turkish Population

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Introduction and Aim: Functional variants of glutathione-S-transferase (GST)-M1, GST-T1, p53 might modulate brain cancer risk by altering the rate of metabolism and clearance of carcinogens from the brain tissue. In this study, the role of GST-M1, GST-T1, p53 polymorphisms on brain tumor was investigated.

Materials and Methods: Brain tumor tissues of 143 patients were obtained from the Gülhane Training and Research Hospital, Department of Neurosurgery between 2019 and 2020. In the xenobiotic mechanism, the null allele frequency in the GST-T1, GST-M1 gene regions of Phase II enzymes by qPCR method were investigated. Single nucleotide polymorphism encoding Arg/Pro conversion in the p53 gene region was analyzed in 120 cases by sequence analysis method. The data were analyzed statistically with patient's demographic and clinical data.

Results: GST-M1, GST-T1, p53 genotypes of the patient group were determined. The most frequent genotype was null genotype (0/0) for GST-M1 ($\chi 2=39.756$, $p<0.001$). GST-M1 null allele frequencies were 30.8%, 23.1%, 44.3% for 1/1, 1/0, 0/0, respectively. The most frequent genotype was GST-T1 1/1 following by GST-T1 1/0 ($\chi 2=0.335$, $p=0.846$). GST-T1 null allele frequencies were 64.3%, 30.8%, 4.9% for 1/1, 1/0, 0/0, respectively. GST-M1 null genotype might be associated with the development of brain tumors. Genotype distribution obtained in p53 exon4 codon72; Arg/Arg was determined as 31(25.8%), Arg/Pro 70(58.3%) and Pro/Pro

19(15.8%) in the case group. The frequency of Arg and Pro alleles in the case group was determined as 0.55 (*OR 95% CI 1,393*) and 0.45(*OR 95% CI 1*), respectively.

Conclusion: The null allele frequency encountered in the GST-M1, GST-T1 gene regions is consistent with the rates in the gene pool called Caucasian in the literature. GST-M1 gene polymorphism may play a crucial role in brain carcinogenesis in Turkish patients. This study based on clinical data is thought to help to understand the important epidemiological features of brain tumors.

Keywords: Brain Tumors, GST-T1, GST-M1, p53, Polymorphism

POSTER PRESENTATION 18

Analysis of the effects of Single Nucleotide Variants in human PRF1 gene using *in silico* tools

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Introduction and Aim: Granule mediated cytotoxicity, including perforin and granzyme B is a way of lysing mechanisms of infected or cancer cells through Cytotoxic T lymphocytes and natural killer cells. The first step of this type of cytotoxicity starts with the formation of perforin pores in the target cell membrane and ends with cell lysis & apoptosis. Familial hemophagocytic lymphohistiocytosis type 2 (FHL2) (MIM# 603553), a rare lethal disorder is observed during infancy in an autosomal recessive pattern. Our aim in this study is to investigate the effects of single nucleotide variants in human PRF1 gene using *in silico* tools and evaluate their effects on the pathophysiology of malignancy and infection.

Materials and Methods: Variation viewer database was used to acquire missense, nonsense, frameshift, splice acceptor/donor, 5'UTR and 3'UTR SNVs. The functional consequences were investigated using PolyPhen2 and Mutation Taster databases, while the allele frequencies of these variants were obtained using GnomAD database. The regulatory effects were interpreted using the RegulomeDB database and the post-translational modifications were evaluated using PhosphoSite Plus.

Results: Total 850 SNVs of which 550 missense, 20 nonsense, 231 three prime UTR, 55 five prime UTR, and 3 splice acceptor/donor variants were obtained in PRF1 gene. Among coding variants 60.5% was interpreted as possibly/probably damaging in PolyPhen2 and 40.2% as disease causing in Mutation Taster web site. RegulomeDB tool analyzes 651 variants and 11 of them has a score very close to 1.0. In GnomAD database 420 SNVs have allele frequency and only 6 of them have a MAF>0.01. There are only 3 phosphorylation on perforin protein and all of these PTMs target a SNV site.

Conclusion: The molecular consequences of SNVs in perforin gene could give a brief information about how to affect its expression and function in infections and malignancies.

POSTER PRESENTATION 19

The Role of The Mir-200 Family in Epithelial-Mesenchymal Transition in Ovarian Cancer

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Introduction and Aim: Ovarian cancer (OC) has the highest mortality among gynecological cancers (1). The main cause of deaths from OC is distant metastasis in advanced stages. Metastasis is the transition of cells from epithelial phenotype to mesenchymal phenotype (EMT) (2). We aimed to examine the target genes of one specific miRNA and the proteins translated by target genes. The aim is to show the relationship of miRNAs and the EMT process in patients with epithelial OC and to elucidate the metastasis mechanism for early diagnosis.

Materials and Methods: The gene expression analysis of hsa-miR-200c-3p considering to play a role in the EMT, was performed using the ovarian tissues obtained from healthy individuals and advanced EOC patients. Target genes were determined by in-silico methods and one of the target genes, ZEB1, is analyzed in same samples with immunohistochemistry (IHC). Also, vimentin and e-cadherin cell surface antigens important in EMT has been investigated.

Results: Hsa-miR-200c-3p was found significantly ($p < 0.05$) increased in EOC however, the expression of ZEB1 decreased significantly ($p < 0.05$) in EOC. The correlation analysis showed a strong negative correlation between hsa-miR-200c-3p and the ZEB1 gene ($r=-0,75$; $p<0,00$). IHC staining the staining found the intensity and prevalence of ZEB1 and e-cadherin proteins were higher in EOC ($p < 0.05$). However, it has been showed that the intensity and extent of staining of vimentin protein decrease in cancerous tissues ($p < 0.05$). There was no positive correlation between ZEB1 mRNA and protein.

Conclusion: Because of the decreased level, ZEB1 cannot sufficiently bind to the mRNA of e-cadherin and CDH1 genes. Thus, the expression of e-cadherin increased. The decreasing level

of vimentin protein, a mesenchymal biomarker in OC tissues, relates to the transition from mesenchymal to epithelial. Therefore, we suggest that hsa-miR-200c-3p is a novel candidate biomarker in the diagnosis of OC.

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POSTER PRESENTATION 20

6-Phosphofructo-2-Kinase-2 Inactivation Rewires Glucose Metabolism in Pancreatic Cancer Cells

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Introduction and Aim: Pancreatic cancer is a lethal malignancy with an aberrant glucose metabolism. Elucidation of key players in regulation of the glucose metabolism in pancreatic cancer may uncover novel therapeutic vulnerabilities. 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatases (PFKFB1-4) synthesize fructose-2,6-bisphosphate (F2,6BP), a potent activator of glycolysis. The contribution of the second PFKFB isozyme, PFKFB2, to the metabolic and oncogenic phenotype of tumor cells is currently unknown.

Material and Methods: A CRISPR/Cas9 method was used to create *PFKFB2*-null PANC-1 and MIA PaCa-2 cells. Proliferation of control (PFKFB2-WT) and *PFKFB2* knockout (PFKFB2-KO) cells was determined using sulforhodamine B assay. Colony formation assays were performed to study the effect of PFKFB2 loss on the capacity of cells to grow as single colonies. ^{1}H nuclear magnetic resonance (^{1}H NMR) spectroscopy and ion chromatography-Fourier transform mass spectrometry (IC-FTMS) were used to determine the effect of PFKFB2 loss on glucose-derived carbon metabolism. For tracing, the cells were cultured in media containing $^{13}C_6$-glucose. The requirement of PFKFB2 for tumorigenicity was assessed by a xenograft study.

Results: Compared with *PFKFB2-WT* cells, colony formation capacities of *PFKFB2-KO* cells were markedly reduced; however, *PFKFB2-KO* cells exhibited a higher proliferative potential when seeded in regular confluency. Total ^{13}C-labeled lactate and alanine levels were significantly reduced in PANC1$^{PFKFB2\text{-}KO}$ cells, suggesting that PFKFB2 is required for the

glycolytic flux in PANC-1 cells. Although the *PFKFB2* deletion did not affect the glycolytic flux in MIA PaCa-2 cells, it significantly decreased labeled acetate levels, suggesting that PFKFB2 may control the fate of pyruvate derived from glucose. Consistent with increased proliferative capacity, aspartate synthesis from glucose was enhanced in PANC1$^{PFKFB2\text{-}KO}$ cells.

Conclusion: PFKFB2 may serve heretofore an undetermined function in rewiring glucose metabolism that may be associated with oncogenic potential of pancreatic adenocarcinoma cells.

POSTER PRESENTATION 21

Anticancer, Antibiofilm, Antimicrobial Effects and Anti-Quorum Sensing Inhibition Potentials of Endemic Plant Alchemilla Oriturcica

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Plants have been used for thousands of years as alternative therapy remedies and represent a potential for new therapeutic compounds. This study investigated the anticancer, antimicrobial, and anti-quorum sensing (anti-QS) potentials of methanol of endermic Alchemilla oriturcica flowers. Antimicrobial activity was analyzed by the agar diffusion method using nine gram-negative and five-gram positive bacteria, and two yeasts. Anticancer activity was assessed by MTT assay using normal ARPE-19 cells, and A549, CRL-2923, HT-29, and HeLa cancer cell lines. Anti-QS features of the extracts were determined by violacein production inhibition of Chromobacterium violaceum strains, and by inhibition of biofilm formation of Pseudomonas aeruginosa PAO1 strain. The methanol extracts of A. oriturcica, whose antimicrobial activity was first screened in this study, showed strong antifungal activity against Candida albicans and C. parapsilosis with MIC values of 7.81 and 15.62 µg/mL, respectively. The anticancer results of the study showed that A. oriturcica methanol extract dose-dependent cytotoxic effects on normal and cancer cells, the most affected cell lines at ≤300 µg/mL concentrations were A549 and HeLa cells. The differences between these with the ARPE-19 cell line were statistically significant at $p<0.05$.

INVITED TALK 1

Molecular and cellular changes induced by Metformin resistance in TNBC cells

Irem DOGAN TURACLI

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Metformin is one of the most prescribed drugs for the treatment of type II diabetes (T2D). Its anti-proliferative effect also provides advantage for the treatment of cancer. Especially, decreased risk of breast cancer was observed in women with T2D using Metformin on a long-term basis compared with other antidiabetic drugs. Despite many of the studies mentioning the positive effects of Metformin in inhibiting the proliferation of cancer cells, there are also studies which question this idea as well. It has been shown that long term Metformin usage increased the risk of developing Estrogen Receptor (ER) negative and Triple Negative Breast Cancer (TNBC). The heterogeneous genomic profile of TNBC and the complex interplay with its environment can influence tumor progression and alter resistance mechanisms. The genetic and epigenetic differences even within the similar histological type of cell lines and tumors can lead to opposite behaviors to therapies. Our study provides the first piece of evidence that TNBC cells can develop resistance to Metformin with demonstrating metastatic characteristics. The molecular changes in RNA and protein expression levels arise with morphological and migratory changes in Metformin resistant TNBC cells. Following on from this work, we focused on how miR-26a-5p is implicated in this response to Metformin by examining the differences in miRNA expression levels in increasing doses of acquired-resistance cells. The downregulated miR-26a-5p expression in resistant cells was replaced with miRNA mimics. Then, we screened the migratory changes and expression of the genes which may be targets of miR-26a-5p and could also be involved in PI3K inhibitor response. It is clear that TNBC cells can respond differently to Metformin resistance and change their molecular and cellular functions during carcinogenic evolution process. Also, miRNAs may be used as a potential biomarker of acquired Metformin resistance in TNBC that should be taken into consideration for future targeted therapies.

INVITED TALK 2

Intratumor Heterogeneity and Drug Resistance in Colorectal Cancer

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Advancements in personalized medicine, and intratumoral heterogeneity observed in cancer have gained importance in recent years, especially with increased therapy resistance and disease recurrence in patients. Since the access to vital resources is not equal for all cells, tumor cells compete for resources (glucose, oxygen, growth factors etc.) in their microenvironment. In addition to access to resources, microenvironmental alterations, which can be physiological changes as well as therapy-dependent changes, don't affect the tumor cell population homogeneously. All these factors cause selection of specific tumor cells that can adapt to altered conditions. Continuously fluctuating environment cause more aggressive subpopulations with different mutations and/or epigenetic alterations to arise and proliferate in the tumor population, and result in intratumoral heterogeneity. This cellular heterogeneity enables the survival and growth of different subclones under specific conditions, thereby causing tumor relapse, metastasis, or radiochemotherapy resistance. Studies have shown that therapy-resistant subclones selected in this heterogeneous population share certain mutations and epigenetic patterns. These mutual genetic alterations being preserved in various cancer types, added on to our knowledge about cancer biology and aroused the interest about how non-mutual genetic alterations provide advantage to different subclones. As being one of the most prominent examples, intratumor genetic heterogeneity contributes significantly to the development of resistance to treatment in colorectal cancers (CRC). Many studies have been conducted to date to predict the response to treatment in colorectal cancers showed that the observed genomic heterogeneity in CRC may be due to specific copy number and specific mutation spectrum, or both. As resistance to therapy not being a biological characteristic of the whole tumor cell population and developing by the death of the sensitive cells and a group of resistant cells taking over the entire population, if these resistant cells can be distinguished and their genomic differences from the non-resistant neighboring cells can be determined, new therapy targets and approaches could be developed and our knowledge about tumor biology could expand substantially.

Keywords: Intratumor Heterogeneity, Anticancer Therapy Resistance, Colorectal Cancer

INVITED TALK 3

ROTTLERİNİN KESKİN KILICI TÜMÖR MİKROÇEVRESİNDEKİ MDSC'LERİ HARAKİRİYE ZORLAR

Prof. Dr. Gamze TANRIÖVER

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Meme kanseri, kadınlarda ölüme sebebiyet veren en yaygın kanser tiplerinden biri olup; bunlar arasında da tedavisi en zor olanı üçlü negatif meme kanseri (ÜNMK)'dir. Rottlerin, doğal polifenolik bir birleşikdir ve PKCδ, MAPKAP-2, Akt/PKB ve eEF2 kinazı inhibe ettiği bilinmektedir. Bu inhibisyon, hücre proliferasyonunu azaltmaktadır. Doksorubisin (Doxo), meme kanseri tedavisinde sıkça kullanılan bir kemoterapötiktir. Ancak, kemoterapötiklerin olumsuz etkileri nedeniyle bu tedaviye ilave ajanların eklenerek daha etkin sonuçların alınması son yıllarda yapılan çalışmaların hedefi haline gelmiştir.

Myeloid kökenli süpressor hücreler (MDSC); mikroçevreye salınan çeşitli sitokinlerin etkisiyle immatür myeloid hücrelerden farklanan ve immünsüpresif fonksiyona sahip hücrelerdir. Bu hücreler tümör gelişimi süresince tümör dokusunda ve lenf nodlarında yerleşmektedirler. Bu hücreler tümör büyümesini desteklemekte ve anti-tümoral immün yanıtı baskılamaktadırlar.

Projemiz Rottlerinin, eEF2 kinazı inhibe ederek anti-tümöral immün yanıtı tetikleyebileceği ve MDSC'leri baskılayarak tümöre destek hücreler üzerinde etkili olabileceği hipotezinden yola çıkarak kurgulanmıştır. Bu doğrultuda çalışmamızın ana hedefi; Rottlerinin, eEF2 kinaz üzerindeki inhibe edici etkisini göz önüne alarak bu inhibisyonun in vivo primer tümör gelişimi ve organ metastazlarındaki etkisinin, MDSC'ler üzerinden değerlendirilmesidir.

Çalışma planında in vitro deneylerimizden elde edilen veriler, 4T1 fare meme kanseri hücre hattı kullanılarak in vivo deney modeline aktarılmıştır. Ortotopik olarak oluşturulan metastatik meme kanseri modelimizde, Rottlerin ve Doxo'nun bireysel ve kombine etkileri; hem primer tümör hem de metastatik organlardan akciğer ve karaciğerdeki MDSC yanıtları açısından yorumlanmıştır. Sonuçlarımız, Rottlerin ve Doxo'nun kombine tedavisinin MDSC'leri oldukça sınırladığını, ortamda işlev gösteremeyecek şekilde ekspresyonlarının düştüğünü göstermektedir.

Rottlerinin, eEF2 kinaz üzerindeki inhibisyonunun ÜNMK'de primer tümör büyümesi, metastaz, immün yanıt ve MDSC'ler üzerindeki etkisini gösteren bir çalışma literatürde yer almadığından; çalışmamızın sonuçları Rottlerin ve Doxo'nun kombine tedavisinin klinikte kullanılabilecek yeni kombine tedaviler üzerinde aydınlatıcı etkisi olabileceğini göstermektedir.

Bu proje Tübitak (#119S564) tarafından desteklenmiştir.

Anahtar Kelimeler: Meme kanseri, Rottlerin, eEF2 Kinaz, miyeloid kökenli supressor hücre.

INVITED TALK 4

Multifaceted Roles of Nrf2 in Cancer

Caner GEYİK, PhD

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Nuclear factor-erythroid 2-related factor 2 (Nrf2) is a transcription factor that regulates several important metabolic pathways including redox homeostasis, xenobiotic metabolism, and biosynthesis. Under basal conditions, Nrf2 is attached to Keap1, a protein responsible for Nrf2 ubiquitination and subsequent proteasomal degradation. Oxidative stress releases the Nrf2 from Nrf2/Keap1 complex. Nrf2 translocate to nucleus and binds antioxidant response element (ARE) to regulate the gene expression. The roles of Nrf2 in cancer is variable. Before carcinogenesis, it has protective roles mostly due to activation antioxidant systems, counteracting oxidative stress and DNA damage. Also, it exhibits protective role for inflammation induced cancer. Given that several phase II enzymes are downstream targets of Nrf2, detoxification of xenobiotics add another protective characteristic to Nrf2 pathway.

On the other hand, Nrf2 have important properties that helps cancer cell survival. Several studies show increased Nrf2 expression in cancer tissues such as lung, colorectal, or pancreas. Considering cancer cell metabolism, activation of biosynthetic pathways is important for perpetual proliferation. For instance, pentose phosphate pathway and purine biosynthesis enzymes are upregulated in constitutive Nrf2 activity. Increased antioxidant defence enzymes in cancer cells work for the scavenging excess reactive oxygen species, preventing apoptotic cell death. In addition to these advantages provided, Nrf2 induced drug transporter proteins increase the rate of drug efflux from cancer cells, contributing to the drug resistance.

Role of Nrf2 pathway in cancer is gaining importance as evidenced by PubMed search string (“Nrf2” AND “cancer”). Over 4000 studies have been published in the last decade, more than 2000 being in the last 4 years. Nrf2 inhibition strategy is promising in cancer therapy. Designing Nrf2 inhibitors and using them in combination with a conventional chemotherapeutic might overcome drug resistance. Our preliminary data shows, a novel Nrf2 inhibitor, ML385, increased irinotecan chemosensitivity in colorectal cancer cell lines. Further studies needed to elucidate the effects Nrf2 inhibition on drug metabolism to overcome drug resistance.

INVITED TALK 5

The Use of Comprehensive Genomic Profiling for Patients with Metastatic Cancers

Özlem Er, MD

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Maslak Acıbadem Hospital
Professor of Medical Oncology

Comprehensive genomic profiling (CGP) has a growing importance in treatment of cancer. The search for effective and specific treatment has led to considerable interest in this topic. Comprehensive genomic profiling takes part in characterizing the tumor to find vulnerabilities and then targeting these vulnerabilities. Actionable tumor mutations are increasing. There are tumor agnostic molecular markers such as MSI, HRD, TMB, NTRK important in treatment selection. Molecular tumor boards (MTB) have a role in analysis and interpretation of genetic data.

CGP gives therapeutic guidance at initial diagnosis and relapse at first line of treatment as well as second and further lines of treatment require new biomarkers. ASCO provisional clinical opinion published in 2022 states that

- Patients with metastatic or advanced cancer should undergo genomic sequencing in a certified laboratory if the presence of one or more specific genomic alterations has regulatory approval as biomarkers to guide the use of or exclusion from certain treatments for their disease.
- Multigene panel–based assays should be used if more than one biomarker-linked therapy is approved for the patient's disease.
- Multigene testing may also assist in treatment selection by identifying additional targets when there are few or no genotype-based therapy approvals for the patient's disease.

In summary, molecular profiling helps physicians in therapeutic decision making by analysing the molecular profiles of cancer patient samples.

INVITED TALK 6

Glutamate Metabolism Modulation in Intracranial Tumors and Glioblastoma Cell Line

Gizem Dönmez Yalçın

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Introduction and Aim: Glioblastoma multiform is a primary brain tumor derived from glial cells. Glutamate accumulation in brain leads to excitotoxicity which leads to the death of neurons to create space for the growing glial tumor in brain. Glutamate Transporter 1 (GLT-1), Glutamine Synthatase (GS) and Glutamate Dehydrogenase (GDH) are major glutamate metabolism modulators that help the glutamate cycle function in brain. We aim to investigate the modulation of glutamate metabolism in glioblastoma.

Materials and Methods: Molecular biology techniques such as western blotting, qPCR and glutamate assay were used in the study.

Results: In our previous study, we showed that the mRNA expression of GLT-1 was significantly lower in primary brain tumors when compared to control brain tissues. GLT-1 expression was inversely correlated with the tumor grade, implicating its potential role in tumor progression (Donmez Yalcin et al. 2020). In a following study, we showed that all types of intracranial tumors displayed lower GS mRNA expressions compared to controls. GDH mRNA expression was found to be similar in all groups (Akkulak et al. 2022).

We then carried out mechanistic studies and investigated how glutamate metabolism is regulated by glutamate transporter 1 (GLT-1) degradation pathway in glioblastoma and glial cell lines (Dagdelen et al. 2021). We found that GLT-1 protein expression was increased significantly in glioblastoma cells whereas PKC protein and total ubiquitin were found to be decreased in glioblastoma cells although not significantly. The glutamate accumulated in the medium and lysates of glioblastoma cells is reduced compared to glial cells.

Conclusion: GLT-1 which absorbs excess glutamate and GS which metabolizes excess glutamate are reduced in intracranial tumors, expectedly, leading to excitotoxicity. Inversely, we observed an increase in GLT-1 levels in glioblastoma cells, unexpectedly. We keep on

investigating the underlying molecular mechanisms which may help therapies against glioblastoma targeting excitotoxicity.

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INVITED TALK 7

Molecular Oncology from A Surgeon Perspective

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Cancer is the out-of-control of cellular proliferation and cellular death as a result of changes in cellular processes. Cancer cells disrupt the function of normal tissues where they are or spread. It impairs the individual's quality of life and causes premature death.

Despite being in the same pathological stage, there are some differences between the prognosis of the patients. This situation reveals the need for new prognostic and predictive factors other than TNM stage. Besides conventional classification, molecular diagnosis cancer classification with molecular phenotypes and we can predict nature and personality of each cancer.Personalized medicine and tailored treatment for each unique cancer type and for each individual.

When considering a breast cancer, the diagnosis of invasive breast cancer will not be enough. Besides the patient's age, morphological features and spread of the tumor, Molecular examination such as ER, PR, c ERP B2 receptor determination and also Ki67 activity should be made investigated in the patient to categories genetic subtypes of breast cancer to decide hormonal, targeted, chemotherapy, or surgery in management of breast tumor.

In colorectal cancer, APC gene, KRAS mutations, p53 tumor-suppressor mutations, MSI, and HER-2/neu overexpression are important in prognosis of the disease and also determining the treatment protocols.

For thyroid cancer, we use molecular markers for diagnosis, prognosis, surveillance and treatment. BRAFV600E. RAS mutated serum thyroglobulin (Tg) level, TgAb are molecular testing is considered as an adjunct to define the cancer risk and to reduce the rate of diagnostic surgery in thyroid cancers.

In summary; molecular oncology is important to diagnose and monitor disease, detect risks, and decide which treatments will work best for each individual patient. Molecular oncologist should be a part of oncology council besides surgeon, medical oncologist, pathologist, radiologist, radiation oncologist, psychologist and extra.


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